IPIC2025

INTERNATIONAL PRIMARY IMMUNODEFICIENCIES CONGRESS

DIAGNOSIS AND CLINICAL CARE

PRAGUE, CZECH REPUBLIC
5-7 NOVEMBER, 2025

CONGRESS **REPORT**

CONGRESS ORGANISERS

INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

ABOUT IPOPI

The International Primary Immunodeficiencies Congress (IPIC) is organised every two years by IPOPI (the International Patient Organisation for Primary Immunodeficiencies).

IPOPI is a non-profit global patient organisation and the leading advocate for primary immunodeficiency (PID) patients and associated conditions worldwide, working in collaboration with patient advocates, healthcare professionals, health authorities, experts, industry, policymakers, and global institutions.

IPOPI is dedicated to improving the quality of life for people with PID and associated conditions by raising awareness, promoting equitable access to early diagnosis and personalised treatment through global collaborations, partnerships and innovative solutions.

IPOPI has a growing membership and currently represents 79 National Member Organisations (NMOs) worldwide.

STRATEGIC PLAN 2026- 2030

Our activities are carried out with a strategy-driven approach and geared towards the following four strategic objectives:

1. Expand global access to early diagnosis and patient-centred care for PIDs and associated conditions.
2. Strengthen NMO capacity-building programmes
3. Drive global education and data-sharing initiatives
4. Expand collaborative initiatives and partnerships

FIND US ONLINE

IPOPI is active on Facebook, Linkedin and Instagram and we look forward to meeting you there as well!

www ipopi.org	@ IPOPI_PID	@ IPOPIPID
@ IPOPI	@ ipopi.bsky.social	@ IPOPIPID

SUPPORTING ORGANISATIONS

IPIC2025 ORGANISING COMMITTEE

- **Ms Martine Pergent,** Organising Committee President, IPOPI President.
- **Prof Adli Ali,** Head of Department of Paediatrics, Faculty of Medicine, Universiti Kebangsaan Malaysia
- **Prof Tadej Avcin,** Head of Department of Allergology, Rheumatology and Clinical Immunology at the Children's Hospital, University Medical Centre Ljubljana, and Professor of Paediatrics at the University of Ljubljana, Faculty of Medicine, Slovenia.
- **Dr Anne Barasa,** Head of the Unit of Immunology, Department of Human Pathology, and Consultant Pathologist and Lecturer at the University of Nairobi Faculty of Health Sciences, Kenya.
- **Prof Fabio Candotti,** Professor of Medicine at the University of Lausanne and Head Physician in the Division of Immunology and Allergy of the Lausanne University Hospital, in Lausanne, Switzerland.
- **Nurse Rosalind Fisher,** INGID president and Nurse at the Department of Clinical Immunology, Oxford University Hospitals NHSFT, UK.
- **Prof Elie Haddad,** Clinical Scientist in Paediatric Immunology, Professor of Paediatrics at the University of Montreal, Canada.
- **Prof Martin van Hagen,** Internist-immunologist at the Department of Internal Medicine, head of section Clinical Immunology at the Erasmus MC in Rotterdam, Netherlands.
- **Mr Bruce Lim,** IPOPI Vice-chair, Malaysia.
- **Dr Nizar Mahlaoui,** Scientific Committee President, Manager of the French National Reference Centre for Primary Immune Deficiencies (CEREDIH), France.
- **Mr Johan Prévot,** IPOPI Executive Director.
- **Dr Lorena Regairaz,** Vice President of LASID, Professor in Immunology, Medicine University, La Plata, and Chief of Immunology Unit at Hospital Sor Maria Ludovica, Argentina.
- **Dr Lizzy Rivers,** Paediatric Immunologist at Great Ormond Street Hospital, UK
- **Prof Silvia Sánchez-Ramón,** Head of Immunology Dept., Consultant Clinical Immunologist and Associate Professor at the Hospital Clínico San Carlos, School of Medicine, Complutense University of Madrid, Spain.
- **Prof Anna Sediva,** Vice-head of the Department of Immunology, 2nd Medical Faculty, Charles University and Motol University Hospital, Prague, Czech Republic.
- **Prof Surjit Singh,** Head of the Paediatrics Department and Paediatric Allergy/Immunology Unit at PGIMER, Chandigarh, India.

IPIC2025 SCIENTIFIC COMMITTEE

- **Dr Nizar Mahlaoui,** Scientific Committee President, Manager of the French National Reference Centre for Primary Immune Deficiencies (CEREDIH), France.
- **Prof Siobhan Burns,** Professor of Translational Immunology and Clinical Director for Immunity at the UCL Institute for Immunity and Transplantation, Royal Free London NHS Foundation Trust, United Kingdom.
- **Dr Virgil Dalm,** Internist-clinical immunologist in the Primary Immunodeficiency Centre at Erasmus MC University Medical Center, Netherlands.
- **Prof Alain Fischer,** Necker Enfants Malades Hospital. Inserm. Paris-Descartes University. Imagine Institute. Collège de France. Paris, France.
- **Prof Steven Holland,** Director of the Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, USA.
- **Prof Pamela Lee,** Clinical Associate Professor Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong.
- **Prof Klaus Warnatz,** Senior Physician, Head of Division of Immunodeficiency, Department of Rheumatology and Clinical Immunology and Center for Chronic Immunodeficiency (CCI), University Medical Centre Freiburg, Germany.

IPIC2025 EXECUTIVE COMMITTEE

- **Ms Martine Pergent** - President, France – IRIS
- **Mr Bruce Lim** - Vice-President, Malaysia – MyPOPI
- **Ms Otilia Stanga** - Treasurer, Romania – ARPID
- **Ms Roberta Anido Pena** - Argentina – AAPIDP
- **Ms Whitney Ayoub Goulstone** - Canada - ImmUnity Canada
- **Ms Cynthia Olotch** – Kenya – PIDs Kenya
- **Ms Tracy Shaw** – USA – Immune Deficiency Foundation (IDF)
- **Mr Dimas Adhi Sugiharto** – Indonesia – Perhimpunan Pasien Imunodefisiensi Primer Indonesia (PPIPI)
- **Dr Nizar Mahlaoui** (Ex Officio) - France - Chair of Medical Advisory Panel
- **Prof Martin Van Hagen** (Ex Officio) - Netherlands - Vice-Chair of Medical Advisory Panel
- **Prof Silvia Sanchez-Ramon** - Spain - Vice-Chair of Medical Advisory Panel
- **Mr Johan Prévot** (Ex Officio) - Belgium/Portugal - Executive Director

IPIC2025 | IPOPI CONGRESS REPORT

The International Primary Immunodeficiency Congress 2025, IPIC2025, took place in the charming city of Prague, Czech Republic, from November 5 to 7, 2025. The congress, a global meeting focusing on the diagnosis and clinical care of primary immunodeficiencies (PIDs) and associated conditions, welcomed over 900 attendees from 70 countries. Supported by a unique patient-centred scientific programme, the meeting brought together leading scientific and medical experts, patient organisation representatives, nurses, industry representatives, and other key stakeholders. The CME-accredited event focused on innovations in the field, global updates, complex case studies, transplantation and organ-specific challenges, secondary immunodeficiencies, ethical considerations, and patient-centred care. With 10 plenary sessions and 258 poster presentations, IPIC2025 once again established itself as a central event for PID professionals – including world-leading experts, clinicians, junior doctors, nurses, patient representatives, and industry partners – to expand their knowledge, foster collaboration, and improve patient outcomes worldwide.

- **Global Commitment to Patients:** The strong attendance and engagement at the conference reflected a shared international commitment to enhancing patient outreach, diagnosis, and care. Through formal and informal exchanges, participants demonstrated a collective dedication to advancing the field of PIDs for the benefit of patients worldwide.
- **Integration of Science, Ethics, and Clinical Practice:** A central theme across the conference was the need to integrate cutting-edge scientific advances with clinical expertise and ethical reflection. As diagnostic technologies and therapeutic options rapidly expand, meaningful progress in the field of PIDs depends on thoughtful interpretation, multidisciplinary collaboration, and patient-centred decision-making across diverse clinical and cultural contexts.
- **Progress Driven by Collaboration:** The conference underscored the critical role of collaborative efforts and multidisciplinary approaches in advancing the field of PIDs and associated conditions and optimising patient care. Developments in computational techniques, innovative targeted treatments, genetics, and collaborative efforts across the world are driving meaningful progress and improving patient outcomes.

WEDNESDAY 5 NOVEMBER 2025

TIME	SESSION	SPEAKERS
15.00 - 19.00	Registration Opens	
17.00 - 17.45	**Opening Session Including Keynote Address**	**Chairs: Dr Nizar Mahlaoui** and **Martine Pergent**
	Opening Remarks	**Johan Prévot** and **Martine Pergent**
	Keynote Speech: Boundaries of Immunity and Where to Find Them	**Dr Martin Zach**
17.45 - 19.00	**SESSION 1: Use of AI Tools to Improve the Clinical Management of Immunodeficiencies**	**Chairs: Prof Siobhan Burns** and **Prof Adli Ali**
	Lecture 1: An Artificial Intelligence Framework for Personalised Early and Timely Diagnosis and Prognosis of PIDs	**Dr Nicholas Rider**
	Lecture 2: AI Tools for Early Detection of Bronchiectasis	**Dr Daan Caudri**
	Lecture 3: Use of Human Phenotype Ontology and AI in Clinical Practice to Improve Diagnosis and Treatment for Primary Immunodeficiency Disorders	**Dr Maaike Kusters**
19:15	Welcome Reception	

THURSDAY 6 NOVEMBER 2025		
TIME	**SESSION**	**SPEAKERS**
07.30 - 08.30	***Industry-Sponsored Symposium***	
08.00 - 08.30	***Guided Poster Walk 1*:**	
	Leveraging AI and Disruptive Technologies for Data-Driven Advances in PID Clinical Care	**Prof Adli Ali**
	Diagnosis and Newborn Screening Advances	**Prof Pamela Lee**
08.30 - 10.00	**SESSION 2: Precision Pathways: Innovating Targeted Therapies**	**Chairs: Prof Stuart Tangye** and **Prof Tadej Avcin**
	Video: "Living with STAT-3 Deficiency"	**Patient Representative** (mother of a patient)
	Lecture 1: JAK Inhibitors Treatment in IEI	**Dr Carsten Speckmann**
	Lecture 2: The Role of Interferon Gamma in HLH	**Dr Fabrizio De Benedetti**
	Lecture 3: Targeted Therapies for Monogenic Inborn Errors of Immunity	**Prof Paolo Palma**
10.00 - 10.30	***Coffee Break and Guided Poster Walk 2:***	
	PID Treatment Advances (personalised treatments, targeted therapies, gene therapies, novelties in Ig replacement therapy,…)	**Prof Fabio Candotti**
	Life with PID – Insights and Quality of Life	**Nurse Patricia Luck**

TIME	SESSION	SPEAKERS
10.30 - 12.00	**SESSION 3: Secondary Immunodeficiencies**	**Chairs: Dr Virgil Dalm** and **Whitney Ayoub Goulstone**
	Lecture 1: "Overlapping Primary and Secondary Immunodeficiencies in Hematological Cancer"	**Prof Silvia Sanchez-Ramon**
	Lecture 2: B-Cell and Non-B-Cell Targeted Immunomodulation Causing Immunodeficiencies	**Dr Sara Barmettler**
	Lecture 3: Optimal Ig Therapy Regimen for SID (when to start, dosage, when to stop)	**Prof Stephen Jolles**
	Lecture 4: Nursing Perspective on Holistic Treatment of SID Patients	**Nurse Emily Carne**
12:00 - 13:00	***Industry-Sponsored Symposium***	
13:00 - 14:00	***Industry-Sponsored Symposium***	
13.00 - 14.15	***Lunch and Poster Walk***	

TIME	SESSION	SPEAKERS
16.15 - 17.30	**SESSION 5: Breaking Topics from Around the World**	**Chairs: Dr Anne Barasa** and **Bruce Lim**
	Lecture 1: Asia Pacific Society for Immunodeficiencies (APSID) – XLA HSCT vs IgRT	**Prof Pamela Lee**
	Lecture 2: African Society for Immunodeficiencies (ASID) - Haploidentical HSCT in Tunisia	**Prof Monia Ouederni**
	Lecture 3: Clinical Immunology Society (CIS) - The Impact of Newborn Screening on Racial and Ethnic Disparities in SCID HSCT Outcomes	**Prof Elie Haddad**
	Lecture 4: European Society for Immunodeficiencies (ESID) – Challenges of Access to Gene Therapy for Primary Immunodeficiencies	**Prof Fabio Candotti**
	Lecture 5: Latin American Society for Immunodeficiencies (LASID) – Newborn Screening	**Dr Lorena Regairaz**
17:30 - 18:30	***Industry-Sponsored Symposium***	
20.00	Congress Dinner – Venue: Francouzská Municipal House	

FRIDAY 7 NOVEMBER 2025

TIME	SESSION	SPEAKERS
08:00 - 09:00	***Industry-Sponsored Symposium***	
09.00 - 10.30	**SESSION 6: The Current Status of Gene Therapy in PID**	**Chairs: Prof Fabio Candotti** and **Otilia Stanga**
	Lecture 1: Harnessing the Power of Gene Addition: A Vintage Tool for Contemporary IEI Cure	**Prof Marina Cavazzana**
	Lecture 2: Can We Cure Genetic Diseases by Rewriting DNA?	**Prof Ayal Hendel**
	Lecture 3: CAR T and CAR NK Approaches in Immune Diseases	**Dr Thanyavi Chinsuwan**
	Lecture 4: New Avenues for Gene Editing / Genomic Medicine in PIDs	**Prof Claire Booth**
10.30 - 11.00	***Coffee Break and Guided Poster Walk 4:***	
	PID Management of Comorbidities and Organ Complications, Including the Liver	**Prof Martin Van Hagen**
	Autoinflammation, autoimmunity and primary immune regulatory disorders (PIRDs)	**Dr Tadej Avcin**

TIME	SESSION	SPEAKERS
11.00 - 12.30	**SESSION 7: Ethics Session – Philosophical and Ethical Considerations of Clinical Boundaries in Genomics**	**Chairs: Dr Lizzy Rivers** and **Roberta Anido** **Invited panel:** **Prof Martin Zach** **Prof James Taylor** **Prof Stuart Tangye** **Prof Claire Booth** **Nurse Rosalind Fisher** **Dr Vera Frankova** **Prof Adli Ali**
12:30 - 13.45	***Lunch and Poster Walk***	
12:30 - 13:30	***Industry-Sponsored Symposium***	
13:45 - 14:45	***Industry-Sponsored Symposium***	
14.45 - 15.15	**Young PID Investigators: Poster Winners' Session**	**Chairs: Dr Lorena Regairaz** and **Martine Pergent**
	"Analysis of Genetic Overlap Between Inborn Errors of Immunity and Neurodevelopmental Disorders"	**Dr Ines Serra**
	"Machine Learning-Driven Analysis of Epigenetic Signatures in Primary Immunodeficiency Disorders: Investigating Histone Modification Dynamics"	**Dr Rohit Rajput**
	"Clinical Trial Design and Safety Profile of HDR-Edited CD4 T Cells for the Treatment of Hyper IgM1"	**Dr Daniele Canarutto**

TIME	SESSION	SPEAKERS
15.15 - 15.45	***Coffee Break and Guided Poster Walk 5:***	
	Management of Infections in PID	**Dr Ibtihal Benhsaien**
	Other Topics	**Dr Lizzy Rivers**
15.45 - 17.00	**SESSION 8: "Mystic Liver": Management of Hepatic Manifestations**	**Chairs: Prof Martin Van Hagen** and **Cynthia Olotch**
	Introduction	**Prof Martin Van Hagen**
	Lecture 1: Liver Manifestations in CVID - Clinical Cases	**Dr Leif Hanitsch**
	Lecture 2: Assessment and Management of Liver Abnormalities in PID	**Dr Neil Halliday**
	Lecture 3: New Developments in Liver Regeneration Therapies, Stem Cells, and Organoids	**Prof Luc van der Laan**
	Testimony	**Patient representative**
17.00 - 17.45	**Closure talk** ***Seeing the Whole Picture:*** A Comprehensive Approach to Genetic Evaluation	**Chair: Dr Nizar Mahlaoui**
	Invited Speaker	**Prof Stuart Tangye**
	Closing Remarks	**Martine Pergent**

The IPIC 2025 International Primary Immunodeficiencies Congress, PRAGUE, Czech Republic 05/11/2025 - 07/11/2025, has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with **13.5 European CME credits** (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

Through an agreement between the Union Européenne des Médecins Spécialistes and the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 CreditsTM. Information on the process to convert EACCME® credit to AMA credit can be found at **https://edhub.ama-assn.org/pages/applications**.

Live educational activities, occurring outside of Canada, recognised by the UEMS-EACCME® for ECMEC®s are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.

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AI	Artificial intelligence
APSID	Asia Pacific Society of Immunodeficiencies
ASID	African Society of Immunodeficiencies
AT	Ataxia Telangiectasia
BTK	Bruton's Tyrosine Kinase
CAR	Chimeric antigen receptor
CAAR-T	Chimeric Autoantibody Receptor T
CGD	Chronic granulomatous disease
CIS	Clinical Immunology Society
CTLA-4	Cytotoxic T-lymphocyte-associated protein 4
CVID	Common variable immune deficiency
EMA	European Medicines Agency
ESID	European Society for Immunodeficiencies
FDA	Food and Drug Administration
GMP	Good Manufacturing Practice
GoF	Gain-of-Function
HDR	Homology-Directed Repair
HLH	Haemophagocytic lymphohistiocytosis
HSCT	Haematopoietic stem cell transplantation
IEI	Inborn Errors of Immunity
IgRT	Immunoglobulin Replacement Therapy
IPIC	International Primary Immunodeficiencies Congress
IPOPI	International Patient Organisation for Primary Immunodeficiencies
KRECs	Kappa-deleting Excision Circles
LAD1	Leukocyte Adhesion Deficiency Type 1

LASID	Latin American Society for Immunodeficiencies
NDDS	Neurodevelopmental Disorders
NMO	National Member Organisation
PID	Primary immunodeficiency
PIRDs	Primary Immune Regulatory Disorders
PTCy	Post-Transplant Cyclophosphamide
SAD	Secondary Antibody Deficiency
SCID	Severe combined immunodeficiency
SID	Secondary Immunodeficiency
TRECs	T-cell Receptor Excision Circles
WAS	Wiskott Aldrich syndrome
XLA	X-linked agammaglobulinaemia

OPENING SESSION: INCLUDING KEYNOTE ADDRESS

Chaired by **Dr Nizar Mahlaoui** and **Ms Martine Pergent**

Opening Remarks by **Ms Martine Pergent** and **Mr Johan Prévot**

KEYNOTE SPEECH: Boundaries of Immunity and Where to Find Them – Dr Martin Zach

- The PID field is growing, diversifying, and becoming more complex
- Scientific advances demand new conceptual frameworks, not only new technologies
- Collaboration across disciplines and openness toward new ways of thinking are essential for future progress

Ms Martine Pergent, the president of IPOPI, and **Mr Johan Prévot**, IPOPI's executive Director, opened the congress by welcoming attendees to Prague. They announced a record-breaking audience, highlighting strong engagement and growth of the conference, reflecting the increasing relevance and momentum of the PID field and community. Importantly, IPOPI announced its new national member organisations, bringing the total to 79 patient organisations worldwide advocating for patient needs. A tribute was paid to Jose Drabwell, Past-President and Board Member of IPOPI, recognising her legacy through the IPOPI Jose Drabwell Research Grant Programme, an initiative that promotes scientific and clinical research in PID and associated conditions. A new Vice Chair of IPOPI's Medical Advisory Panel was also announced – Professor Silvia Sánchez-Ramón – strengthening the leadership of the panel with a leading expert. Ms Pergent made a statement regarding the emerging nomenclature of Inborn Errors of Immunity (IEI) in research and clinical settings to replace PID, underscoring not just the psychological impact of associating the word 'errors' with people, but mainly the advocacy difficulties that may stem from this change due to legislation, policies, and frameworks that specifically mention primary immunodeficiencies. While the field of PID and associated conditions is rapidly evolving and increasingly complex, Ms Pergent made a strong call for patient-centred research, policymaking, and representation to drive advances and improve the patient journey worldwide.

Dr Martin Zach delivered a keynote speech that challenged the field's traditional framework by posing questions to the audience. Notably, as PIDs are considered genetic conditions, attendees were invited to consider the role of genes beyond immunity and how the traditional framework shapes research priorities and clinical approaches. Recognition that immune-related genes can have non-immune functions, and vice versa, is the first step towards a holistic approach to clinical care of PIDs. Adaptability to pathology demonstrates how genetic variation can influence infection development and outcomes. Therefore, the concept of a single, unidirectional interpretation of immune genes and activity is too narrow to accurately reflect the biological complexity of the immunodeficient patient. Approaches to PIDs need to be broad and interdisciplinary, starting with the community's openness to new perspectives, to improve how research, clinical care, and patient care are conducted.

SESSION 1: USE OF AI TOOLS TO IMPROVE THE CLINICAL MANAGEMENT OF IMMUNODEFICIENCIES

Chaired by **Prof Siobhan Burns** and **Prof Adli Ali**

An Artificial Intelligence Framework for Personalised Early and Timely Diagnosis and Prognosis of PIDs – **Dr Nicholas Rider**

AI Tools for Early Detection of Bronchiectasis – **Dr Daan Caudri**

Use of Human Phenotype Ontology and AI in Clinical Practice to Improve Diagnosis and Treatment for Primary Immunodeficiency Disorders – **Dr Maaike Kusters**

- AI can contribute significantly to reducing diagnostic delay in PID and improving early detection of complications like bronchiectasis while allowing for the relationship between physicians and patients to be strengthened.
- Validation of AI models needs to be local and across multiple patient populations to retain accuracy and predictive capabilities.
- While AI tools can integrate complex variables, for example, multi-omics" plus clinical data, and support healthcare professionals in their practice, they cannot replace clinicians' inference, contextual judgment, and decision-making.

Dr Nicholas Rider opened the session with an introduction to the potential role of artificial intelligence (AI) in the healthcare system, which strives to provide high-quality care at the lowest possible cost. While AI can significantly increase value by improving quality, it also carries risks that must be actively mitigated, including issues related to safety, privacy, resilience, and environmental sustainability. Current approaches to AI implementation in healthcare systems start with diagnosis. Diagnostic lag is a significant issue worldwide – the time between the onset of disease-related symptoms and a correct diagnosis spans 5 to 20 years, leading to poorer outcomes and increased burden. AI-driven strategies are currently being developed and tested to reduce diagnostic lag and improve clinical care and patient experiences in the field of PIDs. These methods have demonstrated the ability to reduce diagnostic delay by at least 3 years, achieve an average diagnostic accuracy above 70%, and provide physicians with useful,

concise recommendations for further investigation. Implementation and scalability of these AI models worldwide to support primary care physicians in identifying and initiating appropriate workups for patients with PID are essential to patient benefit. This integration in the healthcare system relies on training healthcare professionals, refining clinical procedures, implementing supportive policies, and developing infrastructure.

Dr Daan Caudri focused on bronchiectasis, a serious and often under-recognised complication in PID. Using a clinical case of a 12-year-old boy with X-linked agammaglobulinemia (XLA), he illustrated that lung structure changes are not always visible on lung function tests and substantial lung damage can occur with only 'mild' symptoms, particularly in PID. Recognising the signs of the vicious vortex that drives the pathology of bronchiectasis, which destroys airways, in a timely manner is crucial for preventing disease progression. CT scanning is the gold standard for diagnosing bronchiectasis early, and modern ultra-low-dose protocols make it possible to reduce radiation exposure. However, qualitative methodologies are insufficient to significantly optimise early detection or enable longitudinal monitoring, while quantitative methodologies are time-consuming and dependent on expert interpretation. AI tools help physicians standardize the analysis of clinical imaging data by segmenting airways and adjacent arteries, calculating airway-to-artery ratios, quantifying bronchial wall thickness and airway dilation, and detecting and measuring mucus plugging. These quantitative models show strong agreement with expert manual measurements, and reliable detection of findings and treatment responses, and, if implemented, would facilitate early detection of reversible lung changes and prevention of severe bronchiectasis in both paediatric and adult patients with PID.

Dr Maaike Kusters described the implementation of ambient voice technology during clinic visits as an example of an AI tool to improve clinical documentation and physician-patient interactions. The basis for this tool was the awareness that patient and family perspectives are critical to understanding lived experience and unmet needs yet are often not collected or integrated into clinical care. This technology aims to listen to and annotate exclusively medical information that the physician later reviews and edits, allowing them to look into patients' eyes and have a human conversation during the visit. This proved to increase the clarity of the documentation and enhance patient communication and trust in the physician, strengthening their bond. This accurate data collection is also important to aid the immunologist in making the correct diagnosis, as all symptoms can be relevant, and even the same mutation within the same family may present differently. Dr Kusters also emphasised the need to validate AI tools for paediatric populations because variability is greater across ages and not "textbook", and children are not small adults. Validating AI tools on children's data and for rare diseases can make them more useful for diagnosis and disease monitoring, thereby ensuring personalised care for paediatric patients.

SESSION 2: PRECISION PATHWAYS: INNOVATING TARGETED THERAPIES

Chaired by **Prof Stuart Tangye** and **Prof Tadej Avcin**

Video: Living with Stat-3 Deficiency – Patient testimony: **Ms Suzie Martin**

JAK Inhibitors Treatment in IEI – **Dr Carsten Speckmann**

The Role of Interferon Gamma in Hemophagocytic Lymphohistiocytosis (HLH) – **Dr Fabrizio de Benedetti**

Targeted Therapies for Monogenic Inborn Errors of Immunity – **Prof Paolo Palma**

- Due to the heterogeneity of PIDs, clinical trial design and approval of biologics as targeted therapies remain challenging, leading to off-label use.
- More data is needed on long-term safety, dosing, monitoring biomarkers, and how to stratify and select patients for targeted therapies to allow for the development of harmonised guidelines and consensus recommendations, and safe use of these medicines.
- Validation of biomarkers and integration of complex data into actionable clinical decisions will allow for precision immunology that delivers true personalised care.

Suzie Martin, a 42-year-old patient from France with a PID linked to a STAT3 gain-of-function (GoF) mutation, shared her testimony on being treated with a JAK inhibitor. Despite years of symptoms beginning in childhood with recurrent ENT infections and evolving into immune thrombocytopenia, inflammatory and lymphoproliferative manifestations, the diagnosis of the PID was only made at 38 years old of age. Once the diagnosis was made, ruxolitinib was initiated and significantly reduced the onset of primary symptoms and improved her overall health. More importantly, Suzie reports that her immunologist helped her understand her condition following the genetic diagnosis and that the therapy was repurposed (off label), and that she felt safe in the shared decision-making process for adjusting doses based on her symptoms. Her outlook on the future was positive, noting that the targeted therapy has allowed her to resume previously on-hold life projects and that the stabilisation of her condition and the increase in quality of life are a direct by-product of clear communication and partnership with her immunologist.

Dr Carsten Speckmann followed the patient testimony by reviewing the current use of JAK inhibitors in STAT1 and STAT3 GoF. STAT1 and STAT3 GoF are characterised by severe multisystem immune dysregulation, and treatment options are scarce, with hematopoietic stem cell transplantation (HSCT) associated with poor survivability. Although not currently approved for PID indications everywhere, JAK inhibitors have potential to treat PIDs by targeting the STAT signalling pathway, and are considered targeted therapies for STAT1 and STAT3-GoF. Studies show, similarly to the testimony, increased stability and marked improvement in patient-reported well-being. Currently, dosing is variable, and there's no consensus on when to stop treatment due to a lack of clinical evidence. Consensus initiatives on indications, contraindications, dosing, monitoring, pharmacokinetics, and pre-HSCT use can guide the community in assessing which patients need this therapy and the long-term safety of this treatment.

Prof Fabrizio De Benedetti reviewed the current understanding of HLH and the associated macrophage activation syndrome. Recent data consistently demonstrate that interferon-γ and other cytokines play a pivotal role in macrophage activation syndrome, a vicious hyperinflammatory cycle characterised by excessive activation of innate and adaptive immunity, leading to multiorgan failure and, if untreated, death. These cytokines may have diagnostic, treatment, and monitoring potential as biomarkers to guide patient management. Targeted therapy with emapalumab (an anti–interferon-γ monoclonal antibody) has been approved by the FDA for the treatment of primary HLH, however, monitoring for secondary effects remains necessary. Future management of these patients could be based on these cytokines to stratify patients by risk, enable precision-targeted therapy, and develop early diagnostic tools.

Prof Paolo Palma closed the session by addressing the difficulties of using targeted therapies for PIDs, notably due to their high variability and sometimes unknown molecular diagnosis. In this context, therapy selection is difficult as many lack formal indication due to PID phenotypic heterogeneity, limited evidence from clinical trials and absence of validated biomarkers. Prof Palma proposed a multi-layered diagnostic and therapeutic framework, integrating flow cytometry, omics, epigenetics, genetic sequencing, imaging and clinical metadata to develop case-based, personalised, precision medicine. This strategy enabled not only the rational selection of biologics as targeted therapies but also the measurement of immunological markers and clinical outcomes. Precise vaccinology was mentioned as an emerging targeted therapy in PID with demonstrated benefits, though data are still limited.

SESSION 3: SECONDARY IMMUNODEFICIENCIES

Chaired by **Dr Virgil Dalm** and **Ms Whitney Ayoub Goulstone**

Overlapping Primary and Secondary Immunodeficiencies in Haematological Cancer – **Prof Silvia Sanchez-Ramon**

B-cell and non-B-cell Targeted Immunomodulation Causing Immunodeficiencies – **Dr Sara Barmettler**

Optimal Ig Therapy Regimen for SID (when to start, dosage, when to stop) – **Prof Stephen Jolles**

Nursing Perspective on Holistic Treatment of the SID Patients – **Nurse Emily Carne**

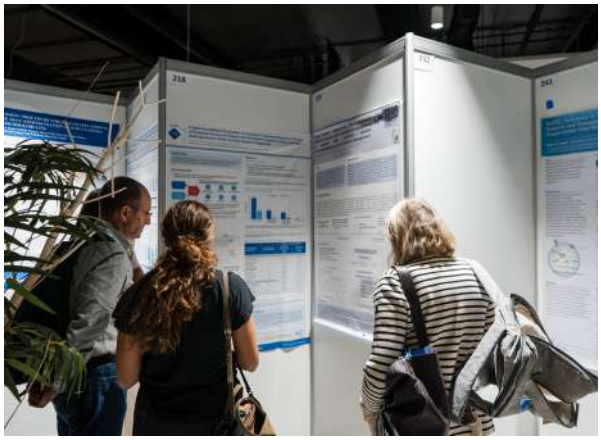
- Proactive and multidisciplinary approaches to help distinguish PIDs underlying secondary immunodeficiencies (SIDs)
- Current evidence demonstrates that B-cell and non-B-cell targeted immunomodulation strategies worsen patient outcomes and warrant baseline immunologic evaluation and ongoing monitoring of immunoglobulin levels before, during, and after treatment.
- Development of guidelines based on clinical judgment and context rather than strict cut-offs is imperative to improve the outcomes of patients with SIDs.
- Patients with SIDs have different experiences and needs, warranting adaptation of immunodeficiency management models based on patients with PID to ensure equitable access to care.

Prof Silvia Sanchez-Ramon opened the session by addressing the complex overlap between PIDs and SIDs in patients with haematological malignancies. Despite diagnostic and therapeutic challenges in distinguishing the two immunodeficiencies, early identification is crucial to tailor therapeutic choices, develop surveillance strategies and preventive care during and after haematological treatment, and provide genetic counselling for patients and family members. Achieving this would prevent SID-associated morbidity and mortality and increase the diagnosis of patients with PID, thus personalising their treatment to the real cause. To achieve this, clinical approaches should be proactive and multidisciplinary, with referrals for immunological evaluation. Prof Sanchez-Ramon presented data demonstrating that this change in methodology improves patient quality of life and optimises the use of hospital resources.

Dr Sara Barmettler provided a comprehensive overview of how modern biologic immunomodulatory therapies contribute to the development of SIDs. B-cell-targeted therapies such as anti-CD20 (e.g. rituximab), anti-CD19 and CAR (Chimeric Antigen Receptor) T-cell therapies, plasma cell–directed therapies (e.g. CD38, BCMA) were correlated with worsening hypogammaglobulinemia, a significant increase in severe infections, and increased mortality, with the use of immunoglobulin replacement therapy (IgRT) associated with reduced serious infections and reduced mortality. A similar trend was observed for non-B-cell-targeted therapies such as T-cell modulators (e.g., abatacept), TNF-α inhibitors, IL-6, IL-17, and IL-12/23 inhibitors, displaying worse outcomes when therapies are combined. Such poor outcomes and morbidity can be significantly reduced with baseline immunologic evaluation, ongoing monitoring of immunoglobulin levels, and infection risk assessment before, during, and after immunomodulatory treatment. Dr Barmettler stressed the need for individualised management strategies to balance therapeutic efficacy with immune safety.

Building on the previous lectures, **Prof Stephen Jolles** explored the rapidly evolving landscape of secondary antibody deficiency (SAD) in the context of modern haematological therapies. SAD is no longer a late or rare complication, but a frequent, predictable, and sometimes profound consequence of these treatments. Rapid and deep onset of SAD in patients, sometimes faster than traditional diagnostic tools can detect, requires a shift from static cutoffs and the adoption of reactive and even preventive interventions. IgRT and clinical decisions should be guided by baseline immunologic assessment, IgG monitoring, history and presence of infections during treatment, and multidisciplinary discussion between haematologists and immunologists. Prof Jolles concluded by stressing that, with rapid therapeutic innovation, primary and secondary antibody deficiencies should not be managed separately, and that continuous reassessment of practice is essential to ensure safe, effective, and patient-centred care.

Nurse Emily Carne concluded the session by providing a nursing and patient-centred perspective on the management of SIDs. While treatment principles may overlap with PIDs, the experience, expectations, and care pathways faced by patients with SIDs often differ substantially. Haematological patients sometimes perceive needing IgRT as a 'step backwards' in their treatment journey. Dependency on a new treatment or the concept of chronicity is also oftentimes not understood, leading to treatment acceptance challenges, while PID patients are aware that their condition is chronic. Additionally, if patients with SIDs have experienced severe infections, anxiety increases regarding losing access to IgRT. While PID patients often see many specialists, haematological patients frequently only meet with and trust one specialist, which can be an initial challenge. Specialist nurses play a critical role in bridging gaps between immunology, oncology, and patient lived experience. Increased awareness of how patient autonomy in treatment (e.g., the use of subcutaneous IgRT) can improve quality of life exemplifies the benefits of interdisciplinary education and collaboration. Early nursing involvement, shared-care models between specialities and early access to patient-centred care are essential for the appropriate support of patients with SIDs.



SESSION 4: PATHOGEN PARADOX – TACKLING COMPLEX INFECTIONS IN THE IMMUNODEFICIENT PATIENT (CASE STUDIES)

Chaired by **Prof Anna Sediva** and **Prof Charlotte Cunningham-Rundles**

Opening Video: Facing Recurrent Severe Infection – Patient testimony: **Mr Igor Koruga**

Current Challenges and Opportunities in Infection in Immune Deficiency – **Dr David Lowe**

Poliovirus and the IEIs – Where are we today? – **Prof Surjit Singh**

Case study: Refractory Non-tuberculosis Mycobacteria Infections in Patients with IFNg Antibodies – **Prof Jettanong Klaewsongkram**

Case study: Lesions from Infections of Helicobacter In X-linked Agammaglobulinemia – **Prof Charlotte Cunningham-Rundles**

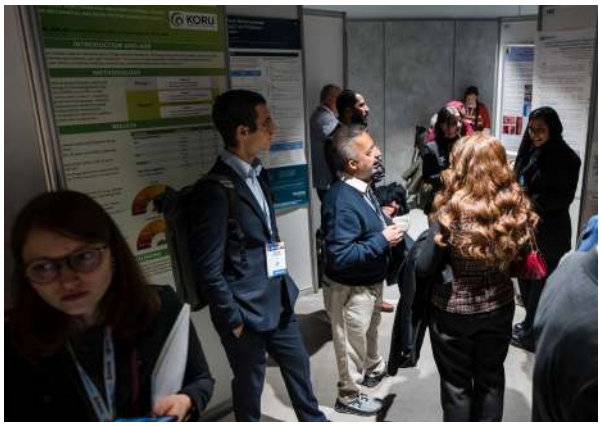
- There's an urgent need to develop better screening tools, treatment guidelines, and understanding surrounding chronic, complex infections associated with highly refractory and burdensome infections in patients with immunodeficiencies.
- Proactive, adaptive, and innovation-driven infection management strategies tailored to the unique risks faced by immunodeficient populations, as opposed to standard treatment regimens, are a must to provide better care to patients with PIDs and protect the general population.
- Polio is a flight away – surveillance of circulating viruses, even those deemed mostly eradicated, is essential to safeguard public health, and it depends on coordinated eradication strategies.

Igor Koruga, a 40-year-old patient with XLA from Serbia, opened the session with a powerful testimony illustrating the reality of living with a chronic infection. Despite IgRT and multiple antibiotic combinations, Igor experienced prolonged and relapsing Helicobacter cinaedi infection. His account exemplifies the difficulty of identifying bacteria with current diagnostic techniques, which took three years. Relapses and ongoing infection were associated with significant burden, including cellulitis, erythema nodosum, swelling, headaches, fatigue, low-grade fever, and elevated inflammatory markers, affecting him physically and psychologically. Importantly, the testimony highlighted the value of patient engagement, trust-based clinician–patient relationships, and international collaboration in identifying and managing rare and persistent infections. Igor reinforced the need for improved diagnostic infrastructure, clearer clinical pathways, and greater recognition of patient expertise, saying, *"It is my hope that [by sharing my story], I can bring more awareness to the improvements that will allow patients like me to not only survive, but to also live with dignity and stability."*

Dr David Lowe built on the patient testimony by emphasising many of the challenges identified and proposing recommendations. Chronic and persistent infections, particularly viral and antimicrobial-resistant bacterial infections, are common and often inadequately addressed with standard treatment regimens, endangering not only patients with PIDs but also the general public due to ongoing transmission and the difficulty of eradicating pathogens prone to rapid resistance development. Thus, immunodeficient patients with chronic infections need adapted diagnostics and treatment schedules and combinations, including the use of host biomarkers and host-directed therapies to reduce inflammation in a true personalised approach. Travel and the lag between pathogen evolution and immunoglobulin products were also identified as challenges in the management of patients. Overall, Dr Lowe argued for proactive, adaptive, and innovation-driven infection management strategies tailored to the unique risks faced by immunodeficient populations.

Prof Surjit Singh focused on poliovirus, a very contagious and under-recognised threat to patients with PIDs, despite global progress toward eradication. Two key reasons were highlighted: continued use of the oral polio vaccine leading to ongoing circulation of vaccine-derived polioviruses, and immunodeficiency-associated vaccine-derived poliovirus. In the latter, immunodeficient individuals act as reservoirs for viral transmission, and in both cases, this may lead to the development of infection. These strains can regain neurovirulence and cause paralysis indistinguishable from wild poliovirus infection. International spread, outbreaks, and re-emergence in polio-free regions are therefore slowly rising, warranting systematic screening, long-term monitoring, and coordinated vaccination strategies to safeguard public health. Prof Singh presented India's national surveillance programme experience, demonstrating the advantages of proactive screening and advocating for coordinated eradication strategies.

Prof Jettanong Klaewsongkram presented the complexity of a rare, adult-onset immunodeficiency with marked regional prevalence in Southeast Asia. Characterised by the presence of anti-interferon-γ autoantibodies, patients are selectively vulnerable to intracellular microorganisms, unlike in other immunodeficiencies. Diagnosis of the condition is often delayed due to preserved standard immune parameters, while patients become increasingly susceptible to opportunistic pathogens, such as non-tuberculous mycobacteria, and to the development of reactive and infectious skin lesions. Disease management is complex, requiring prolonged antimicrobial therapy combined with immunomodulatory treatment to reduce autoantibody production, but necessary given the relapsing nature of the syndrome. Late diagnosis, persistent and recurrent severe infections, and the lack of standardised treatment are factors contributing to significant mortality. Prof Klaewsongkram underscored that regional awareness, early diagnosis, titre monitoring, immunomodulation combinations and interdisciplinary care are crucial to improve the outcomes of these patients.



The session concluded with **Prof. Charlotte Cunningham-Rundles** presenting cases closely aligned with the patient's testimony. Using illustrative cases spanning more than two decades, she emphasised the correlation between Helicobacter infections and progressive leg ulcers and XLA, and the difficulty in diagnosing, treating, and understanding this phenotype. One proposed mechanism was a disruption of the Bruton's tyrosine kinase (BTK) pathway, since patients on BTK inhibitors display the same lesions, and patients with other PIDs leading to hypogammaglobulinemia, such as CVID, do not have these infections. These lesions are frequently misdiagnosed as venous disease or inflammatory skin disorders, leading to inappropriate therapies and prolonged diagnostic delays. Similar to what the patient described in the session opening, pathogen identification proved to be a major hurdle, as these organisms are highly fastidious and often undetectable using standard culture techniques. Moreover, despite aggressive and prolonged antimicrobial therapy, including multi-year treatment courses, infections were often refractory, leading to systemic disease with significant morbidity. Prof Cunningham-Rundles concluded by underscoring the need to increase clinical awareness of this complication, to use molecular diagnostics earlier, to investigate BTK-related pathways more deeply, and to develop targeted treatment strategies.

SESSION 5: BREAKING TOPICS FROM AROUND THE WORLD

Chaired by **Dr Anne Barasa** and **Mr Dimas Sugiharto**

Asia Pacific Society for Immunodeficiencies (APSID) – XLA HSCT vs IgRT – **Prof Pamela Lee**

African Society for Immunodeficiencies (ASID) – Haploidentical HSCT in Tunisia – **Prof Monia Ouederni**

Latin American Society for Immunodeficiencies (LASID) – Newborn Screening – **Dr Lorena Regairaz**

Clinical Immunology Society (CIS) – The Impact of Newborn Screening on Racial and Ethnic Disparities in SCID HSCT Outcomes – **Prof Elie Haddad**

European Society for Immunodeficiencies (ESID) – Challenges of Access to Gene Therapy for Primary Immunodeficiencies – **Prof Fabio Candotti**

- Current treatment options across regions depend on cost, availability, accessibility, phenotype, and clinical history.
- Equality starts with newborn screening – racial disparities in SCID outcomes are not biologically driven and can be reduced through universal newborn screening diagnosis.
- Despite gene therapy evolution and efficacy, challenges to access need to be addressed to ensure this technology is available to patients with PIDs.

Prof Pamela Lee opened the session with a critical comparison between lifelong IgRT and hematopoietic stem cell transplantation (HSCT) as therapeutic strategies for XLA. Data from multiple cohorts worldwide show that lifelong IgRT improves survival but does not prevent disease progression, particularly chronic lung disease, which remains a leading cause of premature mortality for these patients. This can be linked to a few limitations of this therapy, namely that IgRT only replaces IgG and does not restore B cells or their functional role. As such, an alternative could be HSCT due to its capability to restore B-cell development and function. Recent studies evaluating this option in XLA patients have demonstrated improved survival and acceptable graft-versus-host disease rates, but longer follow-up is needed. Economically, Prof Lee argued that HSCT could become cost-competitive if transplant-related morbidity decreases and survival improves. Therefore, in the future, for as long as gene therapy is not an option, HSCT is increasingly a realistic corrective option for selected XLA patients, requiring individualised decision-making that accounts for donor availability, patient age, disease burden, and socioeconomic context.

Prof Monia Ouederni presented the expansion of Tunisia's HSCT programme, focusing on the current rationale for haploidentical HSCT in children with PIDs. The adoption of haploidentical HSCT using post-transplant cyclophosphamide (PTCy) enabled timely transplantation for patients lacking matched donors, emphasizing their cost-effectiveness, feasibility, and suitability in settings without access to complex graft manipulation technologies. Prof Ouederni illustrated the advantages of implementing this technique with multiple clinical cases and a cohort study, including patients with SCID, Omenn syndrome, Wiskott–Aldrich syndrome, and chronic granulomatous disease, among others, all with encouraging engraftment rates, immune reconstitution, and survival, particularly in SCID patients. Some highlighted challenges included CMV reactivation and veno-occlusive disease, with factors such as malnutrition and pre-transplant viral infections playing significant roles in survival. Prof Ouederni concluded that haploidentical HSCT using PTCy can serve as a widely applicable, life-saving strategy for patients with PIDs in low- and middle-income countries.

Dr Lorena Regairaz reviewed the development and implementation of newborn screening (NBS) for PIDs in Brazil, offering a perspective from a developing country with a nationwide public health program. To date, Brazil is the only Latin American country with a public NBS policy for PIDs, using T-cell receptor excision circles (TRECs) and kappa-deleting excision circles (KRECs) to detect newborns at risk before confirmatory diagnosis is performed in PID centres. It took over a decade to implement the programme, with long-term pilot data, multidisciplinary collaboration, and sustained advocacy by patient organizations all playing crucial roles in achieving legislative change. Screening outcomes demonstrated early identification of SCID, agammaglobulinemia, and other combined or intermediate immunodeficiencies, enabling timely referral, definitive diagnosis, and curative treatment. Dr Regairaz concluded by emphasizing the gradual expansion of screening programs across Brazilian states and positioning Brazil's experience as a model for broader implementation of NBS for immunodeficiencies in Latin America and other resource-constrained regions.

Prof Elie Haddad critically examined the role of NBS in addressing racial and ethnic disparities in outcomes for patients with SCID undergoing HSCT in North America. Drawing on large retrospective and prospective multicentre cohort studies, Prof Haddad argued that race and ethnicity have historically been independent predictors of survival, with non-Hispanic Black and Asian patients experiencing significantly poorer outcomes compared to non-Hispanic White patients. Importantly, these disparities were not attributable to differences in donor availability, SCID phenotype, or genotype, as Black patients often had genotypes associated with better prognosis and comparable donor options. When evaluating the impact of NBS diagnosis compared with clinical diagnosis, NBS was associated with earlier diagnosis, younger age at transplantation, reduced infection burden, and significantly improved survival. Most notably, NBS diagnosis showed no racial or ethnic disparities in survival, with equivalent outcomes across groups. Thus, Prof Haddad emphasized the role of NBS as a powerful public health equalizing intervention, ensuring equality of access to early diagnosis and treatment and reducing systemic inequities in SCID care.

Prof Fabio Candotti concluded the session by exploring the challenges currently limiting access to gene therapy for PIDs. Despite substantial scientific and clinical progress in the field, with more than 30 PIDs being the focus of gene therapy development, the technology remains not widely accessible. ADA-SCID gene therapy was presented as an example of success, with durable immune reconstitution and clinical benefits spanning 30 years, leading to its approval by the EMA in 2016. However, the lack of financial sustainability and small patient populations led to industry withdrawal, revealing the vulnerability of ultra-rare disease therapies to market forces and, consequently, the significant barriers to accessing these therapies. Key barriers outlined included the complexity and cost of vector manufacturing, high upfront treatment costs, reimbursement challenges, limited long-term data, and fragmented regulatory frameworks across countries. As a result, access to gene therapy remains largely restricted to clinical trials or compassionate use. Prof Candotti emphasized the need for alternative, sustainable models to tackle these challenges, including innovative reimbursement strategies, streamlined regulatory pathways, and strong patient advocacy. Foundations like AGORA, a non-profit international initiative supporting gene therapy access, along with coordinated global efforts, were highlighted as solutions to ensuring equitable and sustainable access to gene therapy for patients with rare immunodeficiencies.

SESSION 6: THE CURRENT STATUS OF GENE THERAPY IN PID

Chaired by **Prof Fabio Candotti** and **Ms Otilia Stanga**

Harnessing the Power of Gene Addition: a Vintage Tool for Contemporary IEI Cure – **Prof Marina Cavazzana**

Can We Cure Genetic Diseases by Rewriting DNA? – **Prof Ayal Hendel**

CAR T and CAR NK Approaches in Immune Diseases – **Dr Thanyavi Chinsuwan**

New Avenues for Gene Editing / Genomic Medicine in PIDs (New Technologies) – **Prof Claire Booth**

- Gene editing is emerging as a complementary tool to gene addition strategies, opening the door to personalised gene therapies in the future.
- New techniques in the field of genomics, such as T-cell editing and CAAR-T (chimeric autoantibody receptor T) strategies, offer new potential targeted therapies for PIDs.
- Long-term clinical use of genomic medicine to cure patients with PIDs and associated conditions depends on optimising safety, manufacturing scalability, and cost-efficiency, and ensuring equitable patient access.

Prof Marina Cavazzana opened the session by positioning gene therapy as an alternative to allogeneic HSCT to avoid donor-related complications such as graft-versus-host disease and conditioning toxicity. In this context, lentiviral vectors have become the preferred tool for gene addition, eliciting efficient transduction of non-dividing stem cells, improved safety through self-inactivating designs, and efficacious polyclonal engraftment and multilineage reconstitution. Lentivirus platforms are not without limitations, including the associated high cost, the need for good manufacturing practice (GMP) facilities and specialised personnel, a lengthy vein-to-vein process, and limitations for autosomal recessive diseases. Still, multiple clinical trials in PIDs using lentiviral gene therapy are underway, with strong evidence that survival and immune reconstitution rates are comparable to those of transplantation. Conditions such as ADA-SCID, SCID-X1, RAG1-SCID, Artemis-SCID, leaky SCID, Wiskott–Aldrich syndrome (WAS), chronic granulomatous disease (CGD), and severe forms of Leukocyte Adhesion Deficiency Type 1 (LAD1) have demonstrated clinical benefit from gene therapy, justifying expanding the application of this technology after further studies. Indeed, Prof Cavazzana explained that only 10 PIDs out of over 500 had patients treated in Phase I/II trials, leading to only 4 treatment protocols currently approved or under review: 2 for ADA-SCID, 1 for WAS, and 1 for LAD1. To improve accessibility to gene therapy, innovations in non-genotoxic conditioning, scalability, and sustainable access models are needed.

Prof Ayal Hendel explored the potential of CRISPR-based genome editing as a next-generation therapeutic approach for PIDs. Gene editing may offer advantages in diseases that require precise physiological regulation of gene expression, where gene-addition strategies may be insufficient. Using multiple SCID models, including RAG1, RAG2, Artemis, and IL7R, Prof Hendel's team showed that CRISPR-mediated correction of patient-derived hematopoietic stem cells restored T-cell development and function in vitro. Given the technique's genotoxicity, strategies were proposed to address it, including minimizing donor DNA exposure, optimizing guide RNA design, and using small molecules to enhance homologous recombination efficiency. The optimisation of this technique has allowed for patient-tailored editing, in which correction strategies are customised to individual mutations using patients' cells, enabling early intervention post-NBS detection. While the potential for personalised gene editing therapy for PIDs rises, some challenges remain, such as reducing costs, scaling production, conducting comprehensive off-target safety studies, and establishing regulatory pathways for individualised therapies before this therapy can be widely used in the clinical setting.

Dr Thanyavi Chinsuwan provided a comprehensive overview of the evolution and future potential of CAR-based cellular immunotherapies. The development of CAR-T cells involved successive design innovations until a clinically effective therapy was achieved, and CAR-NK will likely need to follow a similar approach. Currently, seven CAR-T cell products are approved (EMA/FDA), the majority targeting B-cell malignancies, while current strategies in autoimmune disease remain in early stages of development, mainly mirroring haematological approaches of global B-cell depletion rather than selective targeting. Meanwhile, CAR-NK cell approaches are developing, with fewer clinical trials and data available compared to CAR-T. Current studies point to lower risks of graft-versus-host disease and cytokine release syndrome with CAR-NK cells, but to more challenging in vitro expansion and shorter persistence in vivo, necessitating further development and larger clinical trials to mature. While current strategies lead to global B-cell depletion, increasing the risk of infections, Dr Chinsuwan proposed a shift toward selective targeting of pathogenic immune clones in autoimmunity, demonstrating the example of an innovative Taiwanese CAAR-T (chimeric autoantibody receptor T) strategy in which engineered CAR-T cells expressed modified interferon-γ to selectively eliminate autoreactive B-cell clones with in vivo efficacy. As CAR-T technologies continue to evolve rapidly, more can still be expected in the field of immune diseases.

Prof Claire Booth closed the session by giving the audience an overview of the new technologies and avenues for genomic medicine in PIDs. Lentiviral gene addition therapies have a transformative clinical impact and long-term durability, and are effective for many PIDs. Gene editing is emerging as a complementary, rather than replacement, technology, particularly valuable when physiological regulation of gene expression is required, with advantages over stem cell editing, such as easier cell harvest and manipulation, and less toxic conditioning. T-cell editing is moving toward clinical trials for Hyper-IgM syndrome, Cytotoxic T-lymphocyte associated protein 4 (CTLA4), and XLA. While currently gene editing is best suited for hotspot mutations, the future will be to target patient-specific variants, making this technology truly personalised. To achieve this, safety, scalability, and cost need to be optimised, with not-for-profit academic manufacturing models potentially being critical for this development in PIDs. Lastly, Prof Booth emphasised that the long-term clinical use of genomic medicine depends on safety, durability, and equitable patient access, saying, *"We need to work together to ensure patients can receive sustainable access to effective therapies and so that we can continue to develop new cures."*

SESSION 7: ETHICS SESSION: PHILOSOPHICAL AND ETHICAL CONSIDERATIONS TO CLINICAL BOUNDARIES IN GENOMICS

Chaired by **Dr Lizzy Rivers** and **Ms Roberta Anido**

Invited panellists:

Prof Claire Booth

Dr Martin Zach

Prof James Taylor

Prof Adli Ali

Nurse Rosalind Fisher

Dr Věra Franková

- Despite the clinical potential of genomics, there is no ethical 'one size fits all' rule – instead, each case should be considered individually.
- "Non-curable" is ethically insufficient as an exclusion criterion when early diagnosis can improve quality of life and allow for proper monitoring.
- Although genetic diagnosis is important in the diagnosis of PIDs, genetic information may not correlate to disease presentation or progression or the necessity for therapy, requiring careful, case-by-case interpretation.

In this session, the panel discussed the ethical, clinical, and societal challenges that arise from the expanding use of genomic technologies in immunology and rare disease diagnosis. Drawing on real and adapted cases, the panel explored how genetic knowledge intersects with patient autonomy, psychological well-being, cultural context, and health-system responsibility, and invited the audience to engage in the discussion.

The first case examined the ethical complexities surrounding genetic carrier status testing and disclosure to minors. The case focused on a male patient with an X-linked PID, which guarantees that his two daughters, ages 10 and 12, are obligate carriers. The PID presented in adulthood, and when a genetic diagnosis was made, the patient experienced strong guilt and anxiety about the implications of his daughters being carriers. Panellists explored the balance between potential medical benefit, psychological harm, and respect for future autonomy regarding functional testing and reproductive counselling for the children. While parental guilt and emotional burden might be significant, impacting family dynamics and potentially being transmitted to children, other factors, such as the children's current well-being, cultural and social consequences, and what could be medically achieved with additional genetic information, should also be considered. Carrier status and functional testing do not predict symptom presentation; therefore, there is no direct medical benefit to early testing in this case, as there is no treatment or preventive benefit. Moreover, matters of reproductive health require maturity and autonomy, which the carriers might not yet have as children. According to the European Society of Human Genetics, in such a case, counselling and testing should be performed only once the daughters are of age and have inquired about it themselves. In the meantime, it is crucial to address the father's guilt first by supporting the family emotionally so they have the tools to live with the condition and the unknown peacefully.

The second case focused on the early diagnosis of ataxia telangiectasia (AT) as a secondary finding in NBS-SCID. AT is a neurodegenerative syndrome with systemic manifestations, including immunodeficiency and malignancy, diagnosed early in life, and non-curable/actionable. NBS-SCID can detect immunodeficiencies other than SCID, raising the ethical question of whether other diagnoses should be pursued and, if so, whether non-curable PIDs should be included in this secondary screening. NBS screening programmes are highly variable globally, but still rely on Wilson–Jungner criteria, which support screening only when treatment is available. The ethical implications mentioned include the psychological burden and impact on the family of early diagnosis when treatment is not an option, and the child is still asymptomatic, versus the potential benefits of early diagnosis, without forgetting the healthcare system's capacity to support non-curable diseases. Multiple points were raised regarding the pursuit and disclosure of non-curable incidental findings. Inequitable access to diagnosis and treatments globally means that, even for curable diseases, not every patient has access to treatment. Therefore, inequity shouldn't justify withholding information where testing and clinical care are available. Knowledge can feel empowering for families and help them prepare psychologically and practically, and they should be given the choice to know if their child has a non-curable condition. Additionally, having no cure today doesn't mean there won't be one tomorrow, so early diagnosis may give the patient and family more long-term options. From a clinical standpoint, early diagnosis can improve the patient's quality of life by preventing infections and malignancies. Moreover, preventing morbidity is also in the interest of the healthcare system, as the costs increase when a diagnosis is made later. An important underlying issue concerned consent to NBS – consent is often requested immediately post-partum, and evidence shows that a significant proportion of parents don't recall consenting. The panel argued that meaningful consent depends on understanding the tests and potential results across languages and literacy levels and proposed that

antenatal consent, in addition to postnatal consent, could be beneficial. Overall, the discussion emphasised the importance of pre-test counselling, expectation-setting, and shared decision-making to help patients understand the potential and limitations of genomic knowledge and how it can affect their newborns' lives.

The final case touched on a new and increasingly clinically significant aspect of genetic diagnosis – variants. The retrospective genetic study identified a patient with a de novo variant with functional evidence supporting the diagnosis of a PID, raising the question of whether treatment should be started, depending on symptomatology, or if monitoring and prophylaxis are a better option. There was no consensus among the panellists, except that genetic diagnosis should not automatically imply therapy; rather, clinical history and symptomatology should guide the clinical approach. Clinical outcomes rely on shared understanding and decision-making between patient and physician, and justify withholding treatment in light of risks associated with overtreatment (e.g., side effects or masking symptoms). Best ethical practice encompasses monitoring, transparency, and joint clinician–family decision-making, particularly when there are no functional data to inform risk of new variants.

Overall, the session highlighted that ethical decision-making in genomics cannot be anchored to fixed rules or purely technical considerations, as genetic information does not inherently translate into clear clinical actionability. Panellists emphasised the importance of contextual factors—including developmental stage, family dynamics, cultural norms, and long-term psychosocial consequences—in shaping ethically responsible care. The discussions reinforced the central role of genetic counselling, multidisciplinary collaboration, and sustained clinician–family relationships in supporting shared decision-making. There was broad agreement against an immediate shift towards genetic diagnosis alone, based on concerns about infrastructure demand and cost, and current challenges in data interpretation, including varying penetrance and variants of unknown significance. Ethics in genomic medicine was thus framed as a dynamic, case-by-case process requiring nuanced judgment and flexibility, particularly as genomic technologies become increasingly embedded in routine clinical practice.

YOUNG PID INVESTIGATORS: POSTER WINNERS' SESSION

Chaired by **Dr Lorena Regairaz** and **Ms Martine Pergent**

1st place: "Analysis of Genetic Overlap Between Inborn Errors of Immunity and Neurodevelopmental Disorders."– **Dr Inés Serra**

2nd place: "Machine Learning-Driven Analysis of Epigenetic Signatures in Primary Immunodeficiency Disorders: Investigating Histone Modification Dynamics" – **Dr Rohit Rajput**

3rd place: "Clinical Trial Design and Safety Profile of HDR-Edited CD4 T Cells for the Treatment of Hyper IgM1" – **Dr Daniele Canarutto**

This session aims to highlight research excellence by rewarding upcoming PID investigators who submitted exceptional abstracts, giving them the opportunity to present their work to the audience in addition to a poster presentation during IPIC.

Dr Ines Serra won first place and presented research on the emerging intersection of immunogenetics and neurodevelopment, examining the shared genetic architecture of PIDs and neurodevelopmental disorders (NDDs). Using PIDs and NDDs databases, Dr Serra conducted a comprehensive bioinformatic analysis to investigate the risk genes in the two disease groups. Results revealed that one-third of IEI-causing genes were also linked to NDD symptomatology independently of infection, challenging traditional assumptions about neurological involvement in immunodeficiency. Functional and expression analyses demonstrated that while PID-unique genes are predominantly expressed in immune tissues, a subset of shared genes shows distinct expression within specific central nervous system cell populations. These findings suggest a biological basis for overlapping clinical phenotypes observed in some patients with PIDs, underscoring the need for integrated immunological and neurological phenotyping to better inform clinical screening and management strategies.

Dr Rohit Rajput, the second winner, presented a study on the application of machine learning techniques to investigate the role of histone modifications in the pathophysiology of primary immunodeficiency disorders. The study utilised data from neuronal precursor cells derived from 250 PID patients and matched healthy controls to detect significant differences and identify epigenetic biomarkers. Distinct histone modification patterns pertaining to neural signalling and immune regulation were observed in PID patients with early disease onset and more aggressive progression. This study highlighted the potential to use machine learning techniques to uncover biomarkers that may inform future diagnosis and therapeutic strategies for patients with primary immunodeficiency disorders.

Lastly, **Dr Daniele Canarutto** presented his work on homology-directed repair (HDR) gene editing for treating Hyper-IgM 1 as the third winner. A CRISPR-mediated homology-directed repair approach was described that restores physiological CD40L expression by integrating a promoterless donor cassette capable of correcting the majority of known pathogenic mutations. The strategy was designed to maximise editing efficiency while minimising oncogenic risk, with preclinical results showing high levels of targeted correction, restoration of normal protein expression kinetics, and reassuring genome integrity profiles, including minimal off-target activity. Following these promising results, Dr Canarutto's team designed the first-in-human, open-label, phase I/II clinical trial to evaluate the tolerability and efficacy of this innovative treatment, expected to begin early 2026 following regulatory approval. By enrolling patients with a mutation amenable to correction for which HSCT is considered high risk and using tools developed to monitor single-cell HDR editing outcomes, this new approach shows promise for improving gene editing outcomes in clinical settings.

SESSION 8: "MYSTIC LIVER" – MANAGEMENT OF HEPATIC MANIFESTATIONS

Chaired by **Prof Martin Van Hagen** and **Ms Tracy Shaw**

Video – Patient testimony: **Ms Fani Eliades**

Introduction – **Prof Martin Van Hagen**

Liver Manifestations in CVID – Clinical Cases – **Dr Leif Hanitsch**

Assessment and Management of Liver Abnormalities in PID – **Dr Neil Halliday**

New Developments in Liver Regeneration Therapies, Stem Cells, Organoids – **Prof Luc van der Laan**

- Clinical evidence strongly supports that liver disease is common, heterogeneous in presentation, often under-recognised, and prognostically significant in PID patients.
- Liver pathogenesis in patients with PIDs remains poorly understood, limiting current therapy options and necessitating proactive, multidisciplinary assessment strategies and guidelines.
- More research to develop screening methods, diagnosis tools and targeted therapies is needed, with liver organoids presenting potential as a research platform, regenerative therapy and model to optimise personalised therapies.

Fani Eliades, the mother of a young girl with a STAT1 GOF mutation, opened the session. In her video testimony, she described the strenuous journey toward a diagnosis, starting with recurrent infections not long after birth, which were initially underestimated, leading to eventual diagnosis of autoimmune hepatitis, autoimmune thyroiditis and adrenal insufficiency, highlighting the cumulative burden of multisystem autoimmunity and the impact of frequent relapses requiring hospitalisation, intravenous steroids, and repeated liver biopsies. Referral to a specialised centre led to the diagnosis of STAT1 GOF, a turning point for the family and the patient's clinical prognosis. Fani described the introduction of targeted therapy with the JAK inhibitor baricitinib as transformative, resulting in sustained disease stability and improved quality of life, including normal school attendance and reduced infection frequency. However, she noted that she was informed about the lack of data on long-term treatment safety and that, in the future, HSCT could be an option depending on the evolution of her daughter's clinical state.

Prof Martin Van Hagen provided a brief follow-up and introduction to the session, explaining the mechanism of STAT1 GOF and its correlation with increased susceptibility to infections and autoimmunity. Importantly, Prof Van Hagen highlighted the dual role of the liver as both a metabolic and immune organ, emphasising that liver involvement in PIDs is likely underestimated and linked to autoimmune hepatitis, lymphoproliferation, granulomas, fibrosis, cirrhosis, and portal hypertension, often asymptomatic. This variety of presentations, along with the genetic overlap between PID and liver disease-associated genes, warrants a more systematic evaluation in patients with complex immunological phenotypes.

Dr Leif Hanitsch presented two cases to illustrate the diagnostic complexity of liver complications in patients with CVID. In the first case, a normal ultrasound failed to detect non-cirrhotic portal hypertension, an easily missed liver complication that may lead to ascites, splenomegaly, oesophageal varices, and hepatopulmonary syndrome, illustrating how liver disease can masquerade as pulmonary or systemic pathology. The following treatment with the placement of a shunt was done carefully to avoid infections while accounting for altered drug metabolism post-treatment. In the second case, a CVID patient with unexplained hypoxemia was ultimately diagnosed with hepatopulmonary syndrome following an echo, changing the treatment from lung to liver-focused. Both cases highlighted how liver disease can cluster with other inflammatory and non-infectious complications, and that while clinically significant, it is frequently overlooked. Dr Hanitsch concluded by offering recommendations for non-invasive screening and monitoring of biomarkers, underscoring that liver pathogenesis in patients with PIDs remains poorly understood, limiting current therapy options and necessitating proactive, multidisciplinary assessment strategies.

Dr Neil Halliday offered a comprehensive hepatology perspective on liver disease in PIDs. While liver disease can present acutely or chronically and be drug-induced, have infectious, metabolic and immune-mediated causes, presentation in patients with PID can also vary between abnormal liver enzymes, portal hypertension with ascites or variceal bleeding, and hepatopulmonary complications. Cohort data presented showed that up to 40% of adult CVID patients develop liver disease, with XLA, Hyper-IgM syndrome type 1, ADA-SCID and AT patients showing more than 20% of liver involvement. Despite evidence that liver disease has a substantial impact on morbidity and markedly increased mortality risk, no protocols for diagnosis, management and treatment of these patients are available. Current approaches rely on treating complications, and current studies on liver transplantation reveal difficulties in long-term recovery, depending on careful patient selection and combined approaches (e.g. HSCT). Dr Halliday concluded by emphasising the need for coordinated immunology–hepatology care and collaborative research efforts to improve understanding and outcomes in this high-risk patient population.

Prof Luc van der Laan concluded the session by presenting the state of the art of liver regeneration therapies with a focus on organoid technology in immune-mediated disease. Liver organoids—self-organising, patient-derived structures that recapitulate key features of hepatic architecture and function—were presented as a transformative platform to develop disease modelling, drug screening, toxicology testing, and personalised therapeutic exploration. Prof van der Laan presented data on the integration of organoids with macrophages to study antiviral and inflammatory responses, successfully demonstrating functional immune responses, including cytokine production following inflammatory stimulation. Proof-of-concept data from bile duct repair using organoid-derived cells in ex vivo perfused livers suggest that this technology may eventually serve both as a research tool and as a regenerative therapy. Additionally, these platforms can be used to test antiviral, anti-inflammatory, and combination therapies in the selection of personalised therapies.

CLOSING SESSION: INCLUDING CLOSURE TALK

Chaired by **Dr Nizar Mahlaoui**

Closure Talk: Seeing the Whole Picture: A Comprehensive Approach to Genetic Evaluation – **Prof Stuart Tangye**

Closing Remarks – **Ms Martine Pergent**

Prof Stuart Tangye delivered a comprehensive overview of the role of genetic evaluation in the diagnosis and management of PIDs. The rapid expansion of known PIDs over the past two decades, driven by the affordability and accessibility of next-generation sequencing technologies, has transformed how PIDs are treated and managed through the identification of the causative gene. Diagnostic rates have significantly improved, with evidence indicating that approximately 50% of patients experience meaningful changes in clinical management that positively affect their clinical outcomes and quality of life. Prof Tangye presented data from the Clinical Immunogenomics Research Consortium Australasia supporting this finding across 30 centres, demonstrating a 70% rate of major management change following diagnosis. Outcomes included a 48% and 47% increase in access to HSCT and targeted therapies, respectively, and cascade testing of family members, with 16% of patients having family members diagnosed who might otherwise not have been detected. Despite these incredible improvements, it is estimated that 60–70% of patients remain without a molecular diagnosis, with the major bottleneck being data interpretation and not sequencing itself, particularly for variants of uncertain significance and non-coding genetic changes. These require functional validation and careful contextual interpretation, for which methodologies still need to be developed. To demystify the notion that variants are rare, Prof Tangye presented the case of IFNAR1 and IFNAR2 deficiencies, which are prevalent in Polynesian and Arctic populations with extensive geographic distributions. This case also exemplified the importance of collaboration in validating variants, accelerating diagnosis, guiding therapy, and ultimately reaching patients.

Prof Tangye underscored the need for multidisciplinary expertise and international collaboration to resolve complex cases involving challenges in genetic data interpretation, concluding that comprehensive genetic evaluation is essential to advancing precision medicine and improving outcomes for patients with IEI.

The conference was closed by Ms Martine Pergent, who expressed gratitude to all involved in the success of the event. She highlighted the scientific quality, collaborative spirit, and dynamic exchanges that characterised the congress, emphasising the importance of integrating basic science, clinical practice, and ethical reflection in the evolving field of PIDs and associated conditions.

Finally, the next IPIC edition was announced to take place in Mallorca, Spain, on 3-5 November 2027. See you there...!

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CATEGORIES

LEVERAGING AI AND DISRUPTIVE TECHNOLOGIES FOR DATA-DRIVEN ADVANCES IN PID CLINICAL CARE

DIAGNOSIS AND NEWBORN SCREENING ADVANCES

AUTOINFLAMMATION, AUTOIMMUNITY AND PRIMARY IMMUNE REGULATORY DISORDERS (PIRDS)

PID FUNDAMENTAL RESEARCH
(BASIC AND TRANSLATIONAL RESEARCH FINDINGS)

LIFE WITH PID – INSIGHTS AND QUALITY OF LIFE

SECONDARY IMMUNODEFICIENCIES

PID MANAGEMENT OF COMORBIDITIES AND ORGAN COMPLICATIONS, INCLUDING THE LIVER

PID TREATMENT ADVANCES
(PERSONALISED TREATMENTS, TARGETED THERAPIES, GENE THERAPIES, NOVELTIES IN IG REPLACEMENT THERAPY…)

MANAGEMENT OF INFECTIONS IN PID

OTHER TOPICS

POSTER WINNERS

1ST PLACE: Dr Inés Serra (Erasmus MC, Rotterdam, the Netherlands) for *"Analysis of Genetic Overlap Between Inborn Errors of Immunity and Neurodevelopmental Disorders."*

2ND PLACE: Dr Rohit Rajput (F H Medical College & Hospital, Agra, India) for *"Machine Learning-Driven Analysis of Epigenetic Signatures in Primary Immunodeficiency Disorders: Investigating Histone Modification Dynamics"*

3RD PLACE: Dr Daniele Canarutto (IRCCS San Raffaele Hospital, Milan, Italy) for *"Clinical Trial Design and Safety Profile of HDR-Edited CD4 T Cells for the Treatment of Hyper IgM1"*

POSTER 13

AUTHORS

Dr. Ines Serra1, Mr. Mick de Koning1, Prof. Dr. Peter J. van der Spek2, Dr. Virgil A. S. H. Dalm3, Dr. Aleksandra Badura1. *"Analysis of Genetic Overlap Between Inborn Errors of Immunity and Neurodevelopmental Disorders."*

AFFILIATIONS

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Objective:
Inborn errors of immunity (IEI), formerly known as primary immune deficiencies (PID), are a group of genetic disorders that affect the immune system, leading to increased susceptibility to infections, autoimmunity, allergy, and cancer. So far, 449 IEI-causing genes have been identified with more likely to be discovered with the rapid adoption of whole genome sequencing in clinical practice. Patients with IEI often present with neurological symptoms such as cognitive impairments, neurodevelopmental delay and even seizures. These clinical features could be indicative of an increased risk of neurodevelopmental disorders (NDDs) in IEI patient population. However, to date, no exhaustive study has been done on the genetic overlap between NDDs and IEIs.

Design and Method:
Publicly available NDD and IEI variant databases were used to identify risk genes belonging to the two groups of diseases and gene ontology, machine learning, and protein-network clustering analysis was employed to analyse gene function and group prediction.

Results:
Our analysis shows that one-third of IEI-causing genes were also linked to NDD symptomatology (Figure 1). These genes were primarily involved in immune development and DNA repair pathways. In contrast, genes causing exclusively IEIs were enriched in immune response functions (Figure 2). Additionally, while IEI genes were enriched in immune cells, genes associated with both IEIs and NDDs presented a clear signature of expression in distinct brain cells (Figure 3). Functional connectivity analysis revealed that NDD-risk genes integrated immune-related networks, including those involved in DNA repair, highlighting immune-NDD interactions (Figure 4).

Conclusion:
Altogether, this work demonstrates a molecular and protein-network level overlap between NDD and IEI-causing genes. Our analysis strongly suggests that NDD phenotypes in IEI patients could be underreported in both IEI patients and in NDD-related databases.

POSTER 243

AUTHORS

Dr. Rohit Rajput1, Dr DK Khatri1. 1F H Medical College & Hospital, Agra, India. *"Machine Learning-Driven Analysis of Epigenetic Signatures in Primary Immunodeficiency Disorders: Investigating Histone Modification Dynamics"*

Objective:
This study aims to investigate the role of histone modifications in the pathophysiology of Primary Immunodeficiency Disorders (PIDs), an emerging yet underexplored area of epigenetic research. The primary goal is to identify epigenetic biomarkers associated with disease onset and severity, using machine learning techniques to uncover regulatory patterns that may inform diagnosis and therapeutic strategies.

Background:
PIDs are a diverse group of inherited immune disorders often linked to monogenic mutations. However, clinical heterogeneity among patients with similar genetic defects suggests that non-genetic factors, such as epigenetic modifications, may also play a role in disease progression. Histone modifications are key regulators of gene expression, and their dysregulation may influence immune cell function, inflammatory pathways, and susceptibility to immune-related complications. Despite their relevance, the epigenetic landscape of PIDs—particularly histone modifications—remains poorly characterized.

Methods:
The study utilized chromatin immunoprecipitation sequencing (ChIP-seq) data from neuronal precursor cells derived from 250 PID patients and matched healthy controls. Analysis focused on key histone modifications (e.g., H3K4me3, H3K27ac) at regulatory immune-related gene loci. These datasets were integrated with whole-genome sequencing and clinical metadata. Convolutional Neural Networks (CNNs) were applied to detect spatial patterns of histone modification peaks, while a Random Forest (RF) model was used to predict disease onset and severity by integrating epigenetic, genomic, and clinical variables. Stratified cross-validation was used to evaluate model performance and ensure reproducibility.

Results:
Distinct histone modification patterns were observed in PID patients with early disease onset and more aggressive progression. These alterations were especially pronounced near genes involved in neuronal signaling and immune regulation. The combined CNN-RF model achieved 88% accuracy in distinguishing early- from late-onset PID, with an area under the curve (AUC) of 0.94 and a mean absolute error of 2.3 years in predicting disease onset. A subset of patients with specific epigenetic signatures exhibited a 30% higher rate of disease progression.

Conclusion:
This study highlights the potential of machine learning tools to decode the epigenetic architecture of PIDs. Histone modification profiles may serve as early biomarkers and therapeutic targets, offering new avenues for personalized immunological care and advancing our understanding of PID pathogenesis.

POSTER 65

AUTHORS

Dr. Daniele Canarutto “Clinical trial design and safety profile of HDR edited CD4 T-cells for the treatment of Hyper IgM1”

AFFILIATIONS

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Objective:
We report progress of our academic clinical trial using homology-directed repair (HDR) gene editing for treating Hyper-IgM 1 (HIGM1).

Design and Methods:
HIGM1, an X-linked immunodeficiency caused by CD40LG mutations, impairs CD4+ T cell function and has a median survival of 25 years. We developed FT018, an autologous CD4+ T-cell product that was HDR-edited at the CD40LG locus using Cas9 and an integrase-defective lentiviral vector (IDLV) encoding the corrective template and a LNGFR selector. Edited cells restore physiological CD40LG expression, CD40 binding, and signaling.

Results and conclusions:
GLP biodistribution study showed normal behavior of edited cells. No off-target effects were detected by CAST-Seq, Optical Mapping, or target sequencing. Targeted nanopore sequencing revealed a majority of precise intended HDR events and the rest accounted by on-target concatemers not compromising functionality. Conventional single cell tracking tools, such as scRNA-seq, cannot capture genomic outcomes at single cell level, that are mostly transcriptional silent. Therefore, we developed a novel single cell DNA sequencing assay for characterization of editing outcomes at single cell level. We designed an amplicon panel covering the X chromosome, including the target Cas9 site, the donor IDLV template, and nominated off-targets. Three clusters were present in the cell product: 1. Unedited cells, with preservation of the amplicon covering the nuclease target site 2. Precisely edited cells, with no amplification of the nuclease target site and amplification of the repair template 3. Imprecisely edited cells, with

no amplification of the nuclease target site and amplification of the repair template and other amplicons mapping onto the donor IDLV, compatible with previously characterized template concatemers. No off-target integrations or on-target large deletions were detected.

We designed a first-in-human, open label, phase I/II clinical trial to evaluate the tolerability and efficacy of FT018 for the treatment of Hyper IgM1, and is anticipated to start at the end of 2025/early 2026, following regulatory approval. We'll enroll patients with a mutation amenable to correction (95% of known mutations) for which HSCT is considered to be high risk. The first patients will be treated with a trial-boost regimen, without lymphodepletion. Dosing adjustments will be considered after treatment of the initial cohort. Endpoints include engraftment, CD40LG restoration, and clinical benefit.

In summary, we report on the advancement of our trial for the treatment of HIGM1 due to start enrolment soon, and present a novel technology for assessment of single cell HDR editing outcomes in clinical settings.

POSTER 3 - REPORT OF 14 PATIENTS WITH INHERITED ARPC1B DEFICIENCY: EXPLORING FOUNDER GENE EFFECT IN RARE DISEASE

AUTHORS

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Background and aims:
Inherited ARPC1B deficiency (ARPC1BD) is a rare combined immunodeficiency with a myriad of infective, allergic, and inflammatory features. Very few cases have been reported in the literature. We describe 14 patients with ARPC1BD with unique features from Nepal.

Methods:
Data on clinical-epidemiological features, immuno-hematological parameters, treatment, and outcome were included in the analyses. Homozygosity mapping and haplotype analysis were also done.

Results:
Similar to previous reports, we noted infective and autoimmune/allergic manifestations in all of our patients. Unique features noted in our study include rheumatoid factor (RF) positive chronic arthritis (mimicking RF+ juvenile idiopathic arthritis), significantly elevated anti-tissue transglutaminase antibody titers, generalized skin hyperpigmentation, distal phalangeal enlargement, frontal bone hypertrophy, hypertrophic skin scars, and hyperkeratosis. Twelve cases harbored the founder splice-site variant c.64+2T>A in the ARPC1B gene. Two cases have unique compound heterozygous mutations. Long-term outcomes in our patients were significantly worse than reported previously. Comparative phenotypic analysis showed significantly greater proportions of otitis, gastroenteritis, lymphadenopathy, arthritis, inflammatory bowel disease-like manifestations, and elevated IgA.

Conclusions:
This is the first report on ARPC1BD from Nepal and largest cohort of A1BD ever reported from a single center. c.64+2T>A is a founder variant in Nepalese patients with ARPC1BD.

POSTER 4 - A RARE CASE OF DİGEORGE SYNDROME WİTH ATYPİCAL COURSE

AUTHORS

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Introduction:
DiGeorge Sydrome (DGS) is a rare disease associated with 22q11.2 chromosomal microdeletion, also known as a velocardiofacial syndrome, based on the frequent involvements of the palate, facial, and heart problems. Hematologic autoimmunity is rare in DGS but presents with a refractory course and poor prognosis. Herein, we report a case of partial DGS in a patient with refractory immune cytopenia and autoimmune lymphoproliferative syndrome (ALPS)-like manifestations.

Case:
A 9-year-old girl with growth retardation was first diagnosed with DiGeroge during the antenatal period and was followed up by pediatric cardiology with tetralogy of Fallot (TOF) after birth. She underwent TOF surgery at the age of 19 months, and from about this age onwards, her motor development regressed. When the patient was followed up for immunodeficiency, immunoglobulin (IVIG) treatment was given at 2-month intervals and simultaneous trimethoprim sulfamethoxazole and then triflucan prophylaxis was given. The patient suffered from thrombocytopenia since the age of 5 years. One year later, he developed multiline cytopenias including thrombocytopenia, neutropenia and anemia. On clinical follow-up, splenomegaly was noted on splenic palpation and abdominal ultrasonography revealed massive splenomegaly. Whole exome sequencing revealed the presence of a de novo heterozygous 1.91 Mb deletion on chromosome 22q11.21. Furthermore, a decrease in the proportion of naive T cells and an increase in double negative T cells were detected. In the follow-up of the patient, no regression of cytopenias and persistence of splenomegaly were observed. The patient was planned to be treated with sirolimus without adding other immunosuppressive agents. If splenomegaly does not resolve with sirolimus, the surgical procedure will be dropped.

Conclusions:
In this case, we wanted to present an atypical course of DGS with ALPS-like features and rare association.

Key words:
DiGeorge sysndrome, ALPS, DVTs, İmmundeficiency.

POSTER 5 - THE DIAGNOSTIC SIGNIFICANCE OF DETERMINING THE NUMBER OF TREC AND KREC FOR MONITORING THE EARLY NEOGENESIS OF T AND B LYMPHOCYTES AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS

AUTHORS

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Background and aims:
After hematopoietic stem cell transplantation(HSCT), the key aspect is the restoration of T- and B-lymphocytes from primary lymphoid organs,which is vital for the rapid restoration of lymphocytic response and increased patient survival. Assessment of lymphocyte neogenesis and identification of subpopulations of naive cells are traditionally carried out using the flow cytofluorometry method. However, there is a more cost-effective alternative: determining the absolute number of circles of DNA fragments of T- (TREC) and B-cell(KREC) receptors. Methods.DNA samples from healthy individuals(n=98) aged 0.0(0-15.0) years and patients after HSCT(n=41) aged 6.4(0.3–14.8) years were used as the study material.

Reconstitution of T- and B-cell immunity after HSCT was studied in 3 groups of patients:
acute lymphoblastic leukemia(ALL) (n=15), aplastic anemia(AA)(n=15), primary immunodeficiency(PID)(n=11). The number of TREC and KREC in recipients was determined at 30,45,60,100,145,180,245,365 days after HSCT. The validity of the method was assessed by constructing ROC curves.

Results:
TREC reached the threshold of normal values on day 180 in 12/15 in the ALL group, in 9/15 in the AA group, and in 7/11 recipients in the PID group. In the ALL group 13/15 recipients KREC exceeded the lower threshold of normal values on day 100. In addition, on day 100, such data were observed in 12/15 recipients with AA and in 8/11 with PID(p=0.024). Starting from day 365, KREC values did not differ significantly from those in the control group. However, up to day 365, TREC/KREC levels in all recipient groups were significantly lower compared to the control group(p=0.021;p=0.024), respectively. We did not find any significant differences between the three nosological groups at any time. Due to the lack of statistical differences in the number of TREC and KREC between the groups, further reliability assessment was carried out jointly. To assess the validity of determining TREC after HSCT, parameters were selected at all time points. AUCTREC according to ROC analysis was 0.98±0.01(p<0.001) with a diagnostic sensitivity of 88.1% and specificity of 92.8%. To assess the diagnostic informativeness of determining KREC after HSCT, parameters were selected that significantly differed from the control group from day +30 to day +245. According to the results of the ROC analysis, AUCKREC was 0.92±0.02(p<0.001) with a diagnostic sensitivity of 85.8% and specificity of 82.5%.

Conclusions:
The data obtained demonstrate the high diagnostic significance of the TREC/KREC determination method and is an effective for monitoring thymus and bone marrow production after HSCT in children with oncohematological and immunopathological diseases.

POSTER 6 - CLINICAL CASE OF PRIMARY IMMUNODEFICIENCY STATE: X-LINKED AGAMMAGLOBULINEMIA

AUTHORS

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CLINICAL CASE OF PRIMARY IMMUNODEFICIENCY STATE: X-LINKED AGAMMAGLOBULINEMIA

Objective:
Primary immunodeficiency states (PIDS) are genetically determined defects of one or more links of the immune system that prevent the normal implementation of immune functions. Agammaglobulinemia may be a consequence of defects in genes linked to the X chromosome or inherited as an autosomal recessive trait. This sex-linked, recessive disease occurs predominantly in boys.

Methods:
A 4-year-old boy with primary immunodeficiency state (PIDS) - X-linked agammaglobulinemia was examined. This patient underwent studies of general blood test parameters, immune profile, universal markers of T-cell immunodeficiencies - TREC and KREC in dry spots of neonatal screening, molecular genetic testing.

Results:
Analysis of a clinical case of primary immunodeficiency state (PIDS) - X-linked agammaglobulinemia in a 4-year-old boy showed that at the age of 1 month the child suffered from an acute respiratory infection (ARI) with purulent conjunctivitis, since 5 months there have been signs of impaired anti-infective protection (frequent ARIs accompanied by purulent discharge from the ears, enterocolitis, 8 months - balanoposthitis). Since the age of two there have been episodes of a widespread ulcerative form of pyoderma, recurrent bronchitis with prolonged cough and mucopurulent sputum, purulent otitis, sinusitis. Three episodes of middle and lower lobe pneumonia on the right, as well as convulsions and fever. A complete blood count revealed severe leukopenia (1.2 × 109 /l) with neutropenia (2%), promyelocytes (3%), and ESR of 40 mm/hour. Immunophenotyping of peripheral blood lymphocytes revealed a sharp decrease in the number of B-lymphocytes (CD19+, % – 0.1; CD19+, 109 /l – 0.0028; normal values – 12-22%; 0.3-0.5, respectively). Serum immunoglobulin levels: IgA – 0.0 mg/ml; IgG – 0.0 mg/ml; IgM – 0.03 mg/ml; IgE – 2.4 mg/ml. Molecular genetic testing: mutation in the BKT gene c.383T>C (p.Leu128Pro) in exon 5. TREC - 182 copies / 10^5 cells, KREC - 2 copies / 10^5 cells in neonatal screening dried spots.

Conclusions:
Thus, a child with agammaglobulinemia from the age of one month showed a very low degree of resistance, which is confirmed by the data of general clinical and immunological examination. It is necessary to conduct population screening in a timely manner for children with suspected pathology, which is recognized as the only means of early diagnosis of many primary immunodeficiencies before the onset of serious infections. This will allow timely administration of adequate replacement and antimicrobial therapy to sick children, thus improving their quality of life.

POSTER 8 - FACTORS WHICH AFFECT SHARED DECISION-MAKING IN THE TREATMENT OF PRIMARY IMMUNODEFICIENCY

AUTHORS

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Objective:
To identify and examine the factors which may aid or hinder Shared Decision-Making in the treatment of adults with a diagnosis of Primary Immunodeficiency. A secondary aim was to contribute to the existing research in this area and to inform contemporary evidence-based practice. Shared decision-making is a collaborative process involving a patient and their clinician working together to reach a joint decision about treatment. Shared decision-making has been internationally recognised as a key element of quality healthcare, particularly in the area of chronic disease management. Primary immunodeficiency is a chronic disease which affects approximately 6 million people globally.

Design and method:
A Qualitative Systematic review of four electronic databases (CINHAL, MEDLINE, PubMed, PsycINFO) was conducted up to June 2024, with supplemental Grey literature searching. Meta analysis of findings was conducted using JBI SUMARI software. Owing to the nature of research undertaken no ethical approval was necessary.

Results:
Three themes emerged from meta-analysis of the data; factors affecting shared decision-making which are outside of the clinicians' control, factors affecting shared decision-making which are within the clinicians' control and thirdly, factors which may be used to promote shared decision-making in the treatment of primary immunodeficiency. Factors included organisational issues, socio-economic factors, personality traits & characteristics and the use of decision aids. Compelling evidence was additionally found for the incorporation of shared decision-making into practice when examined in the wider context of health policy and chronic disease.

Conclusions:
A greater awareness and understanding of the many factors which affect shared decision-making in the treatment of primary immunodeficiency identified by this systematic review would be advantageous to the delivery of effective patient-centred care. The additional identification of a dearth of research in this area indicates the need for further robust research studies to address the knowledge gap, and to inform evidence-based practice for the management of this patient cohort in the future.

POSTER 9 - MANNOSE-BINDING LECTIN 2 (MBL2) VARIANT DD (RS5030737) AND ITS ASSOCIATION WITH INCREASED SUSCEPTIBILITY TO COVID-19 IN THE INDIAN POPULATION

AUTHORS

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Background:
Mannose-Binding Lectin (MBL) is a key protein in the innate immune system, playing a vital role in first-line defense against pathogens. It activates the lectin complement pathway in conjunction with Mannose-Binding Lectin-Associated Serine Proteases (MASPs), specifically MASP-1 and MASP-2. This activation leads to opsonization and elimination of infectious agents, including viruses such as SARS-CoV-2. Variability in MBL and MASP-2 plasma levels, often due to genetic polymorphisms, can influence an individual's immune response, potentially impacting susceptibility to infections and disease severity. Given the crucial role of MBL in immune defense, this study investigates its plasma levels and genetic variations in COVID-19 patients compared to healthy controls.

Objectives:
The primary objective of this study was to assess the plasma levels of MBL and MASP-2 in COVID-19 patients and compare them with those of healthy individuals. Additionally, we aimed to evaluate the association between genetic polymorphisms in the MBL2 gene and susceptibility to SARS-CoV-2 infection. By identifying genetic variants that may predispose individuals to COVID-19, this study contributes to understanding the genetic basis of immune response variation and disease progression.

Methods:
A case-control study was conducted in the urban population of Patna, India. Blood samples were collected from confirmed COVID-19 patients and age-matched healthy controls. Plasma levels of MBL and MASP-2 were measured using enzyme-linked immunosorbent assay (ELISA). Genetic polymorphisms in the MBL2 gene were analyzed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) techniques to identify specific variants associated with infection susceptibility.

Results:
The study revealed that median serum levels of MBL and MASP-2 were significantly lower in COVID-19 patients compared to controls. However, these levels normalized upon recovery, suggesting a transient immune suppression during active infection. Genetic analysis showed that individuals carrying the D allele of the MBL2 gene were at a higher risk of contracting COVID-19. Notably, the DD genotype (rs5030737) was found to be significantly associated with increased disease prevalence. Despite lower serum MBL and MASP-2 levels, the severity of mild to moderate cases appeared independent of genotype.

Conclusion:
This study provides evidence for a genetic predisposition to COVID-19, with the MBL2 variant DD (rs5030737) associated with increased infection risk. The findings emphasize the role of MBL in antiviral immunity and highlight the potential of genetic screening as a tool for identifying individuals at higher risk of infection, thereby facilitating targeted preventive strategies.

POSTER 10 - INVISIBLE DEFENDERS: UNRAVELLING NEUTROPHIL DYSFUNCTION IN PEDIATRIC CHRONIC KIDNEY DISEASE

AUTHORS

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Background and aims:
In chronic kidney disease (CKD), neutrophils exhibit reduced capacity to phagocytize and eliminate bacteria. Underlying mechanisms remain poorly understood, particularly in pediatric CKD patients. We aimed to assess neutrophil phagocytic function in pediatric CKD patients, infections and hospital admissions.

Patients and Methods:
a cross-sectional study included CKD patients between 2 to 18 years, who were divided equally into: CKD group on conservative management, CKD on conventional type of hemodialysis (HD), and CKD on online hemodiafiltration (OL-HD). Patients with known primary immune deficiency, neutropenia were excluded. We obtained data of frequency and types of infection, hospitalization, and tested for neutrophil phagocytic function by Dihydrorhodiamine (DHR) test.

Results:
We included 66 comparable patients, with mean ± SD age of 10.46 ± 3.58 years, where 36.36% of them had infections an average of three times. Respiratory tract and bacterial infections were the most common (81.82%, 83.33% respectively. Hospitalization was reported in 68.18%, where catheter related blood stream infection (CRBSI) reported in 18.18%. DHR had a defective response in 3.03%. CKD stage, HD modality, had no significant influence on infection rate, or hospital admissions.

Conclusion:
Neutrophil phagocytic dysfunction is not uncommon in pediatric CKD patients. Bacterial and respiratory tract infections are common, and hospitalization is frequently reported due to CRBSI and sepsis. CDK stage, and HD modality had no significant association with infections, and hospitalization. These findings emphasize the need for vigilant infection prevention strategies in this vulnerable population.

POSTER 11 - THE ROLE OF COMPUTED TOMOGRAPHY AND LUNG FUNCTION TESTS IN THE DIAGNOSIS OF CHRONIC LUNG DISEASE IN PATIENTS WITH PRIMARY ANTIBODY DEFICIENCY

AUTHORS

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Background:
Common variable immunodeficiency (CVID) is characterized by impaired antibody production and immune system dysregulation. It clinically manifests with chronic or recurrent respiratory tract infections and non-infectious complications, including a broad spectrum of lung pathologies. Nevertheless, there is still low evidence on the prevalence and risk factors for lung involvement in CVID patients from prospective studies

Methods:
Multicentric prospective cross-sectional study including patients with fulfilled ESID diagnostic criteria for CVID upon written informed consent. Chest CT/HRCT, lung function tests (LFT), and immunological parameters were assessed.

Results:
In total, 88 patients (59% females, mean age 52.8 years, mean disease duration 11.9 years) were enrolled. Bronchial pathology (BP) was present in 51% of them. The most common patterns were bronchiectasis (40%), tree in bud (17%), and mucous plugs (14%). Mean bronchial Baumann´s score (BS) was 5.3 points, negatively correlated with FEV1, FVC, and TLC. BP was predicted by reduced serum IgA and IgG at the time of diagnosis. Parenchymal pathology (PP) was present in 72% of patients, including nodules (52%), linear scars (52%), lines (41%), and ground glass opacities (21%). Mean parenchymal BS was 5.12 points. It correlated with bronchial BS, higher age, and hilar/medistinal lymphadenopathy. Parenchymal pathology was also associated with higher counts of CD8+ T cells.

Conclusion:
PP and BP are frequent non-infectious complications in patients with CVID. While bronchial damage correlates with impaired LF T, parenchymal lesions have limited impact. The character of pathology may be predicted by the serum level of IgG, IgA, counts of CD8+ T cells, or lymphadenopathy.

POSTER 12 - NURSING CARE OF A PATIENT WITH MHC CLASS I DEFICIENCY DUE TO TAP1 MUTATION: A CASE REPORT

AUTHORS

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Introduction:
TAP1, TAP2, and Tapasin deficiencies cause Major Histocompatibility Complex (MHC) Class I deficiency syndrome, a rare autosomal recessive primary immunodeficiency disorder. MHC Class I molecules are expressed on all nucleated cells and are crucial for intracellular peptide antigen processing, thymic T cell development, and regulating natural killer (NK) and γδ T cell activities. Mutations in TAP1 or TAP2 proteins disrupt peptide transport to the endoplasmic reticulum, impairing MHC Class I-mediated antigen presentation. When peptides cannot enter the ER lumen, the MHC Class I/beta-2 microglobulin complex dissociates, resulting in reduced MHC Class I expression on the cell surface. This leads to recurrent sinopulmonary infections and skin lesions.

Case presentation:
A 34-year-old male patient was referred for immunodeficiency evaluation due to recurrent infections and bronchiectasis seen on chest CT. His medical history included recurrent oral ulcers and lower respiratory tract infections since childhood. Additionally, he had chronic rhinosinusitis, esophageal and colon ulcers, and an ulcerative lesion on his right heel. At age 15, subcutaneous nodules developed in his left elbow, and at age 22, progressive skin lesions appeared on his right foot. Skin biopsy revealed findings consistent with granuloma annulare/necrobiosis lipoidica, and MRI indicated osteomyelitis. Genetic and laboratory tests confirmed MHC Class I deficiency due to a TAP1 mutation.

Nursing care:
Wound care followed the TIME (Tissue, Infection, Moisture, Edge) method. Initially, the wound was debrided to remove necrotic tissue. The wound was cleaned with a 0.02% hypochlorous acid solution, and manuka honey was applied for healing. High zinc-content creams were used on the wound edges, and an oily dressing covered the wound. Dressings were changed three times a week. The wound was regularly assessed for infection and inflammation, and patient education on preventing contamination was provided. Excessive exudate was controlled, and a moist healing environment was maintained.

Oral supplements with Nitro, vitamins, antioxidants, omega-3, and vitamin D were administered. Adequate protein intake was ensured, and sugar was eliminated from the diet. Patient education focused on nutrition, hygiene, and avoiding pressure on the wound site. With consistent care and adherence to the treatment protocol, the wound healed completely within six months.

Conclusion:
This case demonstrates that appropriate nursing interventions can effectively manage wound healing in a patient with TAP1 mutation-induced MHC Class I deficiency, leading to positive clinical outcomes.

POSTER 13 - ANALYSIS OF GENETIC OVERLAP BETWEEN INBORN ERRORS OF IMMUNITY AND NEURODEVELOPMENTAL DISORDERS

AUTHORS

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Objective:
Inborn errors of immunity (IEI), formerly known as primary immune deficiencies (PID), are a group of genetic disorders that affect the immune system, leading to increased susceptibility to infections, autoimmunity, allergy, and cancer. So far, 449 IEI-causing genes have been identified with more likely to be discovered with the rapid adoption of whole genome sequencing in clinical practice. Patients with IEI often present with neurological symptoms such as cognitive impairments, neurodevelopmental delay and even seizures. These clinical features could be indicative of an increased risk of neurodevelopmental disorders (NDDs) in IEI patient population. However, to date, no exhaustive study has been done on the genetic overlap between NDDs and IEIs.

Design and Method:
Publicly available NDD and IEI variant databases were used to identify risk genes belonging to the two groups of diseases and gene ontology, machine learning, and protein-network clustering analysis was employed to analyse gene function and group prediction.

Results:
Our analysis shows that one-third of IEI-causing genes were also linked to NDD symptomatology (Figure 1). These genes were primarily involved in immune development and DNA repair pathways. In contrast, genes causing exclusively IEIs were enriched in immune response functions (Figure 2). Additionally, while IEI genes were enriched in immune cells, genes associated with both IEIs and NDDs presented a clear signature of expression in distinct brain cells (Figure 3). Functional connectivity analysis revealed that NDD-risk genes integrated immune-related networks, including those involved in DNA repair, highlighting immune-NDD interactions (Figure 4).

Conclusion:
Altogether, this work demonstrates a molecular and protein-network level overlap between NDD and IEI-causing genes. Our analysis strongly suggests that NDD phenotypes in IEI patients could be underreported in both IEI patients and in NDD-related databases.

POSTER 14 - ALLERGIC DISEASES MASKING PRIMARY IMMUNODEFICIENCIES

AUTHORS

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Introduction and Aim:
In Primary immunodeficiencies (PIDs) allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, and food allergies can present. This study aims to evaluate the frequency of allergic diseases accompanying PID patients and assess the impact of these comorbidities on the diagnostic and prognostic process.

Materials and methods:
Patients aged 0-18 years who were diagnosed with PID based on the diagnostic criteria of ESID and whose diagnoses were genetically confirmed were retrospectively evaluated.

Results:
Among the 252 patients diagnosed genetically, 109 patients (43.3%) were found to have allergic symptoms. For PID patients with allergic diseases, the median age of initial complaints was 12 months, the median age of allergic symptom onset was 30 months, the median age of PID diagnosis was 48 months, and the median diagnostic delay was 24 months. When the timing of allergic symptom onset was evaluated, it was observed that in 76.1% of cases, the symptoms began at or before the time of PID diagnosis. Based on the IUIS classification, the highest prevalence was observed in antibody deficiencies (67.1%), followed by combined immunodeficiency (51.2%). When the distribution of allergic diseases was evaluated, 31.3% of patients had asthma, 19.8% had allergic rhinitis, 11.1% had atopic dermatitis, and 6.7% had food allergy. Anaphylaxis, drug allergy, and chronic urticaria were detected at low rates. The risk of developing asthma and allergic rhinitis was found to be statistically significantly higher in patients with antibody deficiencies compared to other groups ($p<0.05$). The prevalence of atopic dermatitis was determined to be 41% in combined immunodeficiency (CID) patients and was significantly higher than in all other PID groups ($p<0.05$). Similarly, the prevalence of food allergy was significantly higher in the antibody deficiency and CID groups compared to the syndromic CID group ($p<0.05$). Among patients with allergic diseases, 30.4% experienced infectious complications, 9.8% had autoimmunity or inflammation, and 5.4% developed malignancies. The frequency of infectious complications was significantly higher in patients with allergic diseases compared to those without; however, no differences were observed in mortality rates. Among PID patients with allergic diseases, those with atopic dermatitis had the highest mortality rates, while patients with allergic rhinitis had the lowest ($p<0.05$).

Conclusion:
Allergic diseases are frequently observed in patients with PID, with symptoms beginning before the PID diagnosis in approximately three-quarters of cases. Therefore, early diagnosis of allergic diseases is crucial for preventing complications through appropriate treatment and improving the quality of life.

POSTER 15 - THE EFFECTIVENESS OF IMMUNOSUPPRESSIVE THERAPIES IN PATIENTS WITH ANTI-INTERFERON GAMMA AUTOANTIBODIES: A RETROSPECTIVE CASE SERIES

AUTHORS

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Objective:
Adult-onset immunodeficiency (AOID) due to anti-interferon gamma (IFN-γ) autoantibodies leads to recurrent and disseminated infections, especially with nontuberculous mycobacteria. Immunosuppressive therapies like intravenous cyclophosphamide (IVCY) and rituximab (RTX) have been used to suppress antibody production, but real-world data on their comparative effectiveness remain limited. This study evaluates the outcomes of IVCY and RTX in AOID patients at a tertiary center.

Design and Methods:
We conducted a retrospective analysis of 12 patients diagnosed with AOID and positive anti-IFN-γ autoantibodies. Patients were initially treated with IVCY (7–15 mg/kg/every 3-4 weeks for 6 cycles) or RTX (500 mg for single dose or 500 mg every 2 weeks for 2 doses). Demographic data, autoantibody titers, and clinical outcomes were collected. Treatment success was defined as absence of infection recurrence or clinical improvement within six months.~

Results:
Among the 12 patients (mean age: 63.3 years; 10 females, 2 males), 6 received IVCY and 6 received RTX. The mean IFN-γ autoantibody titer was 2.99. Overall, 5 patients (41.7%) experienced recurrence, while 7 patients (58.3%) remained recurrence-free at 6 months.

• In the IVCY group, 3 out of 6 (50 %) experienced recurrence.
• In the RTX group, only 2 out of 6 (33.3 %) experienced recurrence.

Patients treated with RTX showed a higher rate of sustained remission at six months. No serious adverse events were reported with either treatment.

Conclusion:
This case series suggests that rituximab may offer better recurrence prevention compared to cyclophosphamide in patients with anti-IFN-γ autoantibodies. While both regimens were well tolerated, RTX was associated with higher effectiveness. Further prospective studies are needed to determine optimal immunosuppressive strategies for this rare but serious condition.

POSTER 17 - CLINICAL AND GENETIC CHARACTERISTICS OF THE AGAMMAGLOBULINEMIC TYPE OF PID

AUTHORS

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Introduction:
Agammaglobulinemia or hypogammaglobulinemia is the most common type of congenital immunodeficiency, characterized by a persistent decrease or complete absence of immunoglobulins in the blood serum and secretory fluids as a result of impaired immunoglobulin synthesis. One of the main causes is genetic mutations affecting the maturation of B-lymphocytes in the bone marrow. Deficiency of IgG and IgM leads to a serious weakening of bacterial protection.

Material and methods:
In the Research Laboratory of Immunology of the AMU, 169 patients with primary immunodeficiency (PID) aged 2 to 16 years were observed. The patients underwent clinical examination, laboratory and instrumental studies, extended immunological and genetic analyses.

Result:
Antibody-dependent type of PID was confirmed in 58 children, including agammaglobulinemia – in 10, CVID in 36, selective sIgA deficiency in 10, and hyper IgM in 2 patients. Agammaglobulinemia was recorded in all 11 boys born on time with normal height and weight, of which 6 (60%) were born from consanguineous marriages. These children developed normally in infancy, but from 6-9 months, recurrent bronchopulmonary and gastrointestinal infections, purulent wounds on the skin, etc. were more often observed. After 24 months' pain in the joints and abdomen were appear. Immunological examination revealed B-lymphocytes ≤2%, absence of IgA and IgM antibodies, the level of IgG was reduced by 5-10 times. In genetic analysis, the most frequently detected mutations were the BTK gene - in 7 boys, the DNAH5 gene in 1 patient and the BLNK gene - in 1 patient. All these patients receive replacement therapy with IVIG, which fully recovered the level of IgG in serum and stopped the frequent bacterial infections.

Conclusion:
Thus, the antibody-dependent type of PID, manifested by the same clinical symptoms, can be associated with different genetic mutations. Early diagnosis leads to the choice of the correct treatment tactics and improves the patient's quality of life.

POSTER 18 - CLINICAL AND IMMUNOLOGICAL PROFILES OF INFECTION-PRONE CHILDREN WITH SUSPECTED PRIMARY IMMUNODEFICIENCY

AUTHORS

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Background:
Primary immunodeficiency diseases (PIDs) pose significant health, economic, and psychosocial challenges, often exacerbated by diagnostic delays. This study aimed to estimate the burden of PID in Kerala, India, and assess the impact of early diagnosis and therapy.

Methods:
We conducted an observational, longitudinal, and comparative study involving 44 patients diagnosed with PID based on the latest classification. Data on healthcare utilization and functional outcomes were collected before and after diagnosis.

Results:
The median diagnostic delay was 2.17 years (IQR = 6.44). Prior to diagnosis, patients reported a median of 0.86 hospitalizations/year (IQR = 2.28), 0.92 emergency visits/year (IQR = 1.77), 15 doctor visits/year (IQR = 11.25), and 52.72 school/work absence days/year (IQR = 56.35). After diagnosis, 45.45% (n = 20) received IVIG therapy, resulting in statistically significant reductions across all metrics ($p < 0.05$). Despite treatment, the disease burden remained elevated compared to healthy controls. Complications were noted in 43.18% (n = 19), with a mortality rate of 6.82% (n = 3).

Conclusions:
PID imposes a high but potentially modifiable disease burden. Timely diagnosis and access to therapies like IVIG significantly improve patient outcomes. Our findings underscore the need for early screening, public health planning, and integration of primary care in PID management strategies.

POSTER 19 - DISEASE BURDEN AMONG PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISEASES IN KERALA, INDIA: A COMPARATIVE STUDY

AUTHORS

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Background:
Primary immunodeficiency diseases (PIDs) pose significant health, economic, and psychosocial challenges, often exacerbated by diagnostic delays. This study aimed to estimate the burden of PID in Kerala, India, and assess the impact of early diagnosis and therapy.

Methods:
We conducted an observational, longitudinal, and comparative study involving 44 patients diagnosed with PID based on the latest classification. Data on healthcare utilization and functional outcomes were collected before and after diagnosis.

Results:
The median diagnostic delay was 2.17 years (IQR = 6.44). Prior to diagnosis, patients reported a median of 0.86 hospitalizations/year (IQR = 2.28), 0.92 emergency visits/year (IQR = 1.77), 15 doctor visits/year (IQR = 11.25), and 52.72 school/work absence days/year (IQR = 56.35). After diagnosis, 45.45% (n = 20) received IVIG therapy, resulting in statistically significant reductions across all metrics ($p < 0.05$). Despite treatment, the disease burden remained elevated compared to healthy controls. Complications were noted in 43.18% (n = 19), with a mortality rate of 6.82% (n = 3).

Conclusions:
PID imposes a high but potentially modifiable disease burden. Timely diagnosis and access to therapies like IVIG significantly improve patient outcomes. Our findings underscore the need for early screening, public health planning, and integration of primary care in PID management strategies.

POSTER 20 - ABERRANT B AND T CELL DEVELOPMENT AND DIFFERENTIATION CORRELATE WITH THE SEVERITY OF CLINICAL COMPLICATIONS IN SIGAD PATIENTS

AUTHORS

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Background:
Selective IgA deficiency (SIgAD) is the frequent common inborn error of immunity, characterized by low or absent immunoglobulin A (IgA) levels. The pathogenesis of SIgAD remains unclear. This study aimed to evaluate B and T cell immunophenotyping, as well as T cell function, and their correlation with clinical manifestations in symptomatic SIgAD patients.

Methods:
B and T cell subsets were assessed by flow cytometry in 30 symptomatic SIgAD patients and 30 age- and sex-matched healthy controls. T cell proliferation was evaluated using the CFSE assay.

Results:
In symptomatic SIgAD patients, late-stage B cell subsets, including marginal zone-like and switched memory B cells, were significantly reduced, whereas early-stage subsets, such as naïve and transitional B cells, were increased. CD4+ T cell subsets, including naïve, central memory, Th1, Th2, and regulatory T cells, were significantly decreased, along with central and effector memory CD8+ T cells. In contrast, terminally differentiated effector memory T cells (TEMRA) in both CD4+ and CD8+ populations were elevated. Categorization of patients by clinical severity revealed a higher proportion of CD21low B cells and reduced marginal-zone and switched memory B cells in severe cases. Severe patients also exhibited elevated TEMRA cells and reduced regulatory T cells compared to mild cases. T cell proliferation was significantly impaired in severe patients, while no differences in T cell responses were noted between patients and controls.

Conclusions:
Symptomatic SIgAD patients display profound abnormalities in B and T cell subsets, resembling those observed in CVID. Severe phenotypes are associated with higher CD21low B cell levels and impaired T cell proliferation. These findings highlight the potential of CD21low B cells and T cell proliferation as diagnostic biomarkers for predicting disease severity in SIgAD patients.

POSTER 21 - HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISEASE: A REVIEW OF PATIENT REPORTED OUTCOMES

AUTHORS

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Background:
Primary Immunodeficiency Diseases (PIDs), particularly those involving hypogammaglobulinemia, are associated with recurrent and severe infections that significantly impact patients' daily lives. While immunoglobulin G (IgG) replacement therapy is the cornerstone of management, its effect on health-related quality of life (HRQOL) is increasingly recognized as a critical outcome in both clinical care and research.

Objective:
To evaluate existing evidence on HRQOL in patients with PIDs and to identify how treatment modalities influence patient satisfaction and well being.

Methods:
A comprehensive literature review was conducted to identify studies using standardized HRQOL measurement tools in PID patients. Instruments included the Child Health Questionnaire Parent Form-50, Short Form-36 (SF-36), PedsQL 4.0, Lansky Play-Performance Scale, and the Life Quality Index (LQI). Comparative analyses were made between PID patients, healthy controls, and patients with other chronic diseases. Patient preferences for intravenous (IVIG) versus subcutaneous (SCIG) and home-based versus hospital-based therapy were also assessed.

Results:
Patients with PIDs consistently scored lower on multiple HRQOL domains compared to healthy populations. While SCIG and home-based therapy were often associated with higher satisfaction and greater flexibility, treatment satisfaction varied depending on clinical status, frequency of administration, and individual preferences.

Conclusion:
HRQOL is significantly compromised in patients with PIDs. Incorporating patient-reported outcomes into routine care can help tailor immunoglobulin therapy, enhance satisfaction, and improve overall disease management. Future research should focus on longitudinal assessment of HRQOL to guide patient-centered interventions.

POSTER 22 - FLUOXETINE SUCCESSFULLY TREATS INTRACRANIAL ENTEROVIRUS E18 INFECTION IN A PATIENT WITH CD79A DEFICIENCY ARISING FROM SEGMENTAL UNIPARENTAL DISOMY OF CHROMOSOME 19

AUTHORS

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Objective:
Mutations in the gene CD79A, which encodes the Igα component of the Pre-BCR, can lead to autosomal recessive agammaglobulinemia (ARA). Here, we present a case of a patient with a homozygous CD79a mutation, exhibiting recurrent respiratory infections, diarrhea, growth and development delay, unique facial abnormalities and microcephaly, as well as neurological symptoms including tethered spinal cord, sacral canal cyst, and chronic enteroviral E18 meningitis. It is the 9th reported case of ARA with a CD79A mutation.

Design and Method:
Clinical data of the patient were collected regularly, and the CD79A gene mutation was initially identified through whole-exome sequencing (WES). Bioinformatics analysis was used to assess the pathogenicity of the mutation and chromosomal variations. The homozygous mutation and its pathogenicity were further validated at the genetic, mRNA, and protein levels using Sanger sequencing, quantitative polymerase chain reaction (qPCR), and flow cytometry. qPCR was used to quantify concentration of enterovirus in the plasma.

Results:
The patient presented with recurrent fever and cough, and cerebrospinal fluid mNGS indicated an Echovirus 18 (E18) infection. There was a 19.20 Mb heterozygous deletion (LOH) on chromosome 19, which included a homozygous mutation in the CD79A gene (CD79A-H36Q*). After treatment with fluoxetine combined with IVIG, the patient's plasma E18 virus CT values gradually increased, fever subsided, and blood routine results tended to normalize.

Conclusions:
Complete blockade of the early B cell development in the bone marrow of the patient results in the absence of peripheral circulating mature B cells. Whole exome sequencing revealed a Loss of Heterozygosity (LOH) of approximately 19.20Mb containing CD79a on chromosome 19 in the patient. This is the first case of a homozygous CD79a mutation caused by segmental uniparental diploid (UPD). Another key outcome of this study is the effective management of long-term chronic enteroviral meningitis using a combination of intravenous immunoglobulin (IVIG) and fluoxetine. This approach offers compelling evidence of fluoxetine's utility in treating enteroviral meningitis, particularly in immunocompromised patients.

POSTER 23 - UNIDENTIFIED FEVER AND PERSISTENT LIVER DYSFUNCTION IN A PATIENT WITH X-LINKED AGAMAGLOBULINEMIA

AUTHORS

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Objective:
Mutations in the BTK gene can lead to X-linked agammaglobulinemia (XLA). This article reports the first case of Helicobacter bilis infection primarily manifesting as cholestatic hepatitis in a patient diagnosed with XLA. This study aims to provide important reference for the diagnosis and treatment of Helicobacter bilis infection secondary to XLA.

Design and method:
A retrospective analysis of the patient's clinical data was conducted. The PubMed database was utilized to search for literature from January 1999 to September 2024 using the keyword "Helicobacter bile", and the case data from the literature were summarized.

Results:
The 15-year-old boy admitted to the hospital due to "generalized jaundice for 5 days." He was diagnosed with XLA at 1 year old. Liver tissue and blood mNGS indicated an infection with Helicobacter bilis, and pathological analysis suggested cholestatic hepatitis. After 2 weeks of combined treatment with meropenem and metronidazole, followed by 3 months of oral levofloxacin and metronidazole, the blood mNGS results turned negative, and liver function recovered. A total of 8 cases of Helicobacter bilis infection have been reported previously, of which 1 case presented as suppurative cholangitis, and the rest primarily manifested as skin cellulitis.

Conclusions:
Based on our case study, the intravenous administration of carbapenem antibiotics combined with metronidazole, followed by sequential oral administration of levofloxacin and metronidazole, can effectively control Helicobacter bile infections rapidly. Immunocompromised patients are at increased risk for infections caused by opportunistic and zoonotic pathogens. Due to deficiencies in antibody production and the challenges associated with culturing rare pathogens, traditional pathogen identification methods based on antibody detection and cultures are limited in immunodeficient patients. Therefore, mNGS of tissue pathogens as well as peripheral blood may prove to be highly effective.

POSTER 24 - FROM HIDDEN CLINICAL CLUES TO GENETICS: UNMASKING ARPC1B DEFICIENCY

AUTHORS

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A one-year-old female patient (P1), born to consanguineous parents, presented with a history of recurrent attacks of bloody diarrhea and facial eczema since birth. At the age of 9 months she was hospitalized with pneumonia complicated by lung abscess. Lower GI endoscopy results showed ulcerated mucosa of the rectosigmoid part, moderate colitis, duodenitis with preserved villi. Immunological workup including complete blood picture ALC 5300 cells/ul, eosinophilia 10%. The patient had elevated immunoglobulin levels IgG 1080mg/dl, IgA 365 mg/dl, IgE 1130 IU/ml and normal IgM level 71 mg/dl and normal DHR test. Lymphocyte subsets percentages showed reduced CD3 (37%) and CD8 (3%) T cells, CD4 (30.7%) T cells, CD19 B cells (39%) and NK cells (13%), HLA-ABC 99%. The patient had a 3-year-old female sibling (P2) who had been suffering since infancy from diarrhea that was diagnosed as cow mild protein allergy. She had attacks of vasculitis/purpuric-like skin lesions over upper and lower limbs diagnosed as dysfibrinogenemia and partially improved on cryoprecipitate and anticoagulation therapy. The patient continued to have chronic bloody diarrhea, lower GI endoscopy results revealed marked inflammation, suspected vasculitis with colonic wall perforation, colostomy was done with very poor wound healing, wound dehiscence and stoma site infection. Patient had elevated CRP, ESR Amyloid A levels, autoimmune panel including ANA, ANCAs, ASCA, Anti-cardiolipin antibodies was negative. The patient had low CD3, CD4, CD8 T cells, normal CD19 B cells and NK cells and normal Immunoglobulins levels. Unfortunately, the patient died without a definitive diagnosis with severe abdominal wound infection, peritonitis and septic shock. WES results of P1 identified a homozygous variant of uncertain significance in ARPC1B gene. She was started on antimicrobial prophylaxis, IVIG replacement therapy and directed to HSCT. ARPC1B deficiency is a recently described inborn error of immunity. To date, only a few individuals have been diagnosed worldwide. It has a wide spectrum of presentations including infections, allergy, autoinflammation and immune dysregulation. Herein, we report this family to highlight the presentations that should never be overlooked or missed, as early diagnosis will definitely alter treatment strategies and patient outcome.

POSTER 25 - FIRST DESCRIPTION OF NEUTRALIZING AUTOANTIBODIES AGAINST IFN- A AND IFN- Ω IN A PATIENT WITH A HETEROZYGOUS FOXN1 VARIANT

AUTHORS

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Objective:
To identify neutralizing autoantibodies against IFN-I in a pediatric patient with severe varicella and history of severe pneumonias. Design and Methods. Anticytokine autoantibodies were detected using multiplex particle-based flow cytometry. Their neutralizing activity was assessed via STAT1 phosphorylation in PBMCs and IFN- α2a reporter HEK 293 cells. Flow cytometry and spectrophotometry were used for analysis. Data were processed with Bio-Plex manager and FlowJo software. Results. Bio-Plex analysis detected anti-IFN-α autoantibodies in the patient's serum. Functional assays showed these autoantibodies inhibited STAT1 phosphorylation and SEAP production in response to IFN-α2a and IFN-ω but not IFN-β. These findings confirm the presence of neutralizing autoantibodies against IFN-α2a and IFN-ω in the patient's plasma.

Conclusion:
Neutralizing autoantibodies against IFN-I may play a significant role in the pathogenesis of severe viral infections. Their detection could serve as a biomarker for disease severity in FOXN1 defects and other thymopathies and guide personalized treatment strategies. Further studies are needed to elucidate the genetic and immunological factors underlying susceptibility to severe viral infections in children.

POSTER 26 - HETEROZYGOUS MUTATIONS IN COPA GENE MASQUERADING AS RHEUMATOID FACTOR POSITIVE JUVENILE IDIOPATHIC ARTHRITIS (JIA) – A REPORT FROM NORTH INDIA

AUTHORS

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Introduction:
Inborn errors of immunity (IEIs) often result in immune dysregulation, in addition to immunodeficiency,which may manifest as autoinflammation, autoimmunity or malignancy. One of the recently discovered monogenic disorders of immune dysregulation is COPA (Coatomerprotein subunit alpha) syndrome. COPA syndrome is an autosomal dominant disorder caused by mutations in COPA gene which is associated with defective protein sorting to endoplasmic reticulum. Case report: An 11-year-old boy presented to us with symmetrical,additive anddeforming polyarthritis involving small as well as large joints. Initial possibility of rheumatoid factor positivepolyarticular JIA was considered and he was treated with subcutaneous methotrexate, and tapering doses of oral prednisolone. However in view of strong family history of similar arthritis,markedly symmetrical joint involvement, reticulonodular pattern on chest X-ray and normal inflammatory markers possibilities of pseudorheumatoid chondrodysplasia and familial arthropathies like COPA syndrome wereconsidered. Genetic analysis revealed 2variants in exon 9 of COPA gene – heterozygous c.757T>A (p.Ser253Thr)mutation and heterozygous c.841C>T (p.Arg281Trp)mutation. Both the variant types are predicted to be pathogenic on in-silico analysis (Mutation Taster, Provean, SIFT and Polyphen). Although the disease is inherited in an autosomal dominant pattern with variable penetrance, our case is unique in documenting compound heterozygous mutations in COPA gene.

Conclusion:
Our clinical case reiterates the need to suspect and evaluate for monogenic defects in children presenting with autoimmunity and a strong family history.

POSTER 27 - ITPR3 VARIANT IN AN IMMUNODEFICIENT PATIENT RESULTS IN A LEAKY DEFECTIVE IP3R3 CALCIUM CHANNEL

AUTHORS

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Introduction:
Calcium ions play a vital role as a second messenger in various cell types including immune cells. It is involved in lymphocyte activation, and disruption in the mechanisms governing Store Operated Calcium Entry (SOCE) can lead to immunodeficiency with severe clinical phenotypes. The inositol 1,4,5 triphosphate receptor (IP3R), comprising homo/hetero tetramers of the IP3R1, IP3R2, and IPR3R3 isoforms, induces the signaling of lymphocyte activation by releasing Ca2+ from endoplasmic reticulum (ER) stores upon T-cell receptor (TCR) antigen stimulation. Human diseases are linked to mutations that are associated with all subtypes of the inositol 1,4,5-trisphosphate receptor Ca2+ release channel.

Methods:
To evaluate the impact of the detected ITPR3 variant and its association with the clinical phenotype of the patient, first, sanger sequencing was done to validate the ITPR3 variant detected in the whole genome sequencing. Second, western blotting and quantitative real-time PCR were performed to assess the effect of the ITPR3 variant on the level of protein and transcripts respectively. Next, we further assessed the role of the detected ITPR3 variant and its impact on immune responses by evaluating lymphocyte proliferation, lymphocyte subsets and the calcium signaling pathway upon TCR stimulation. Carboxyfluorescein succinimidyl ester (CFSE) cell division assay was performed to evaluate the proliferation rate of the T-cell population stimulated with anti-CD3/anti-CD28 antibodies.

Results:
In this study, we identified a de novo heterozygous variant for p.R2524C of ITPR3 (encoding IP3R isoform 3) in a patient of Egyptian Arab descendant with immunodeficiency. Functional analysis revealed that c.7570C>T mutation does not alter the expression of ITPR3 at the transcript and the protein levels. Calcium level was significantly reduced in the patient's lymphocytes endoplasmic reticulum (ER) store, which was associated with impaired T cell proliferation. The patient exhibited a significant decrease in the naive compartment of both CD4+ and CD8+ T-cells, accompanied by an elevation in naive B-cells and a reduction in memory B-cells, correlating with reduced immunoglobulin levels compared to healthy controls. Consequently, the patient is receiving monthly Intravenous Immunoglobulins (IVIG).

Conclusion:
We conclude that these findings establish a functional association between the defective IP3R3 Ca2+ channels and immunodeficiency. Moreover, these results extend our understanding of the specific inborn errors of immunity that are associated with impaired Ca2+ mobilization from the ER stores, highlighting the increased sensitivity of lymphocytes to Ca2+ signaling defects. Conclusion:
Our clinical case reiterates the need to suspect and evaluate for monogenic defects in children presenting with autoimmunity and a strong family history.

POSTER 28 - COMPLETE LOSS OF TRPM4 CAUSES IMMUNE DYSREGULATION DUE DEFECTIVE MONOCYTE MIGRATION

AUTHORS

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Introduction:
Transient receptor potential melastatin subfamily member 4 (TRPM4) is a broadly expressed, calcium-activated, monovalent cation channel that has been shown to play a role in regulating immune function in mice and cell lines. Clinically however, partial loss or gain of function mutations in TRPM4 lead to arrythmia and heart disease, with no documentation of immunological disorders. In the present study, we describe the first human cases of a homozygous complete loss of TRPM4 channel. The TRPM4 deficiency causes immune dysfunction with increased susceptibility to fungal and bacterial infections requiring hospitalization. The aim of this study is to characterize the functional cellular mechanisms underlying the immune dysregulation phenotype in the proband and his siblings affected by the same TRPM4 mutation.

Methods:
Bulk RNA-seq was performed on patient activated T-cells, which suggested altered expression of genes involved in cell migration. Single cell RNA-seq was performed to validate and further map these results to monocytes. Functional migration assays and single cell tracking were performed to show that inhibition of TRPM4 function in T cells and monocytes reduces their migration potential. Monocyte function was assessed by LPS activation and cytokine expression was measured using flow cytometry. To confirm TRPM4 as the causative mutation leading to defective monocyte migration, we generated TRPM4 knockout monocyte cell lines using the CRISPR/Cas9 technique by indels frameshift.

Results:
We report the first human cases with complete loss of the TRPM4 channel leading to immune dysregulation. Affected individuals present with immune dysregulation with frequent bacterial and fungal infections. Single cell and bulk RNA-seq point to altered expression of genes affecting cell migration, specifically in monocytes. Inhibition of TRPM4 in T cells and the THP1 monocyte cell line reduces migration. More importantly primary T cells and monocytes from the TRPM4 patients migrate poorly. Finally, CRISPR knockout of TRPM4 in THP1 cells greatly reduces their migration potential.

Conclusion:
Our results demonstrate that TRPM4 plays a critical role in regulating immune cell migration, leading to increased susceptibility to infections.

POSTER 29 - CD25 DEFICIENCY: REPORT OF TWO CASES, THE FIRST IDENTIFIED IN MOROCCO

AUTHORS

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Introduction:
CD25, the alpha subunit of the interleukin-2 receptor, is highly expressed on the surface of regulatory T cells. It plays a key role in immune homeostasis and tolerance. CD25 deficiency is an infrequent genetic disorder inherited in an autosomal recessive manner. We report here the clinical, immunological, and genetic features of the first two diagnosed cases of CD25 deficiency in Morocco.

Methods:
Both cases were investigated using two complementary approaches: flow cytometry, with a panel of surface markers including CD45, CD3, CD4, and CD25, was used to assess CD25 expression. Genetic analysis was performed using next-generation sequencing (NGS).

Results:
Both patients exhibited autoimmune manifestations. Flow cytometry revealed a complete absence of CD25 expression on the patients' cell surfaces. In contrast, their parents showed intermediate CD25 expression levels, between those observed in patients and healthy controls, suggesting a heterozygous carrier phenotype. Genetic analysis identified a homozygous mutation in the IL2RA gene (encoding CD25) in each patient, not previously reported in public genetic databases. The first patient carried the c.65-2A>G mutation, affecting the intronic splice acceptor site. The second patient exhibited a large deletion encompassing exons 5 to 7 and part of exon 4 (c.557_795-1625del). Both mutations disrupt alternative splicing of the gene, thereby impairing the functional expression of the CD25 protein.

Conclusion:
A clearer clinical and immunophenotypic characterization of CD25 deficiency syndrome will facilitate early molecular diagnosis and the timely initiation of appropriate treatment.

POSTER 30 - CONSANGUINITY AND INHERITED IMMUNODEFICIENCY: LESSONS FROM FOUR CGD FAMILY CASES

AUTHORS

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Introduction:
Chronic granulomatous disease is a genetic disorder caused by mutations in the gene encoding the NADPH oxidase enzyme, exposing patients to potentially life-threatening infections. Consanguinity, a widespread practice in certain regions, is a key factor in its occurrence, raising medical and genetic interest due to its impact on the health of descendants.

Objective:
The objective of this study is to highlight the importance of prenatal and neonatal diagnosis in consanguineous marriages.

Patients and Methods:
We report four cases of children diagnosed in the pediatric department of the Abderrahim Harouchi Mother-Child Hospital. The diagnosis was confirmed by NBT and DHR tests, followed by genetic analysis to identify the responsible mutation.

Results:
The family comes from a consanguineous marriage, with all members affected by CGD. Among the children, two have passed away. The first, an 11-year-old boy, died due to cerebral aspergillosis, and genetic analysis revealed a deficiency in the p67phox subunit. The second, an 8-month-old girl, died in a context of severe diarrhea and septic shock. The two other children include a 14-year-old who was diagnosed at 3 months of age and suffers from refractory inflammatory colitis, and a 9-year-old who was diagnosed on the third day of life and experiences recurrent pulmonary infections and frequent hospitalizations.

Discussion: In populations where consanguinity is widespread, the prevalence of autosomal recessive diseases, such as CGD, is significantly higher. In response to this challenge, prenatal and neonatal diagnosis helps anticipate these risks, enabling the identification of conditions that may benefit from appropriate treatment and allowing timely intervention.

Conclusion:
This study contributes to a better understanding of the challenges associated with this phenomenon and highlights the importance of an adequate medical approach.

POSTER 31 - UNVEILING NOVEL ZNF341 MUTATIONS IN AUTOSOMAL RECESSIVE HYPER-IGE SYNDROME

AUTHORS

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Introduction:
Autosomal recessive hyper-IgE syndrome (AR-HIES) due to ZNF341 deficiency is a rare primary immunodeficiency characterized by markedly elevated IgE levels, chronic eczema, recurrent skin and respiratory infections, and mucosal candidiasis. The clinical and immunological spectrum remains incompletely defined. Here, we report two Moroccan patients with genetically confirmed ZNF341-related AR-HIES, each carrying novel pathogenic variants.

Objective:
To describe the clinical, immunological, and genetic features of two pediatric patients with autosomal recessive hyper-IgE syndrome (AR-HIES) caused by novel ZNF341 mutations, and to highlight the importance of molecular diagnosis in rare primary immunodeficiencies.

Methods:
We conducted a retrospective analysis of two pediatric patients followed at the Mother and Child Hospital El Harrouchi. Clinical, immunological, and genetic data were collected. The diagnosis was confirmed by whole-exome sequencing (WES).

Results:
The two patients, aged 6 and 9 years, presented with severe atopic dermatitis, recurrent respiratory tract infections, chronic mucocutaneous candidiasis, and multiple skin abscesses. Both had significantly elevated serum IgE levels with normal other immunoglobulins. Immunophenotyping showed normal T cell subsets (CD3, CD4, CD8), low NK cell counts, and elevated PNE levels. WES identified two novel, likely pathogenic homozygous mutations in ZNF341, not previously reported in public databases.

Conclusion:
These two cases expand the genotypic and phenotypic spectrum of ZNF341-associated AR-HIES. The identification of novel mutations underscores the importance of early genetic testing for precise diagnosis, allowing tailored management and genetic counseling in affected families.

POSTER 32 - PRIME EDITING ENABLES PRECISE CORRECTION OF TIM3 MUTATIONS IN T CELLS FOR VIRUS-FREE GENE THERAPY IN MONOGENIC IMMUNE DISORDERS

AUTHORS

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Objective:
To develop a virus-free prime editing approach for correcting pathogenic mutations in T cells from patients with inborn errors of immunity (IEIs), specifically targeting HAVCR2 (TIM3) mutations associated with Subcutaneous panniculitic T-cell lymphoma (SPTCL-HLH).

Design and Method:
Patient T cells with confirmed HAVCR2 mutations were isolated, activated, and edited using in vitro transcribed (IVT) mRNA encoding PE7 and dnMLH1, together with synthetic pegRNAs and nicking guide RNAs. Editing was performed via nucleofection using the Lonza 4D system. Edited cells were analysed using flow cytometry, amplicon sequencing, RNA-seq, and CIRCLE-seq to evaluate editing efficiency, functional restoration, and off-target effects.

Results:
Prime editing achieved a 20–30% correction efficiency of the Tyr82Cys HAVCR2 mutation across three patient samples. Restoration of surface TIM-3 expression was confirmed by flow cytometry. RNA-seq analysis revealed no significant changes in the transcriptome between edited and unedited cells. Genome-wide off-target profiling using CIRCLE-seq detected no editing in known oncogenes and <1% unintended editing at any locus.

Conclusions:
We demonstrate that prime editing can correct disease causing mutations in human T cells without the need for viral vectors or double-strand breaks. This strategy restores immune function with high precision and safety, supporting its potential as a therapeutic platform for monogenic immune disorders.

POSTER 33 - HENOCH-SCHOENLEIN PURPURA(HSP) LIKE LESIONS IN IL12RB1 AND IL12B DEFECTS- OUR EXPERIENCE FROM NORTH INDIA

AUTHORS

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Objective:
Mendelian susceptibility to mycobacterial disease (MSMD) is a rare group of human inborn error of immunity. Here we describe a cohort of children with underlying IL12RB1/ IL12B defects who had skin vasculitis resembling Henoch-Schoenlein purpura (HSP).

Design and methods:
Of the 21 patients with pathogenic homozygous IL12RB1/IL12B defects (19 IL12RB1 and 2 IL12B), 4 of them (19%) (IL12RB1-3; IL12B-1) developed HSP-like lesions [Table 1]. All had maculopapular purpuric rash in lower limbs, predominantly in the anterior aspect of legs and posterior thighs resembling the rash of HSP. Two children had multiple recurrences of the skin lesions and were thought to have an underlying autoimmune/ autoinflammatory disease before a diagnosis of MSMD was made. All of them had associated bacterial infections along with rash that include Salmonella sp. and Pandorea apista. None had recurrence following treatment of underlying infections. Out of all the 4 patients IgA levels were elevated in 3 patients and no one developed nephritis.

Results:
The HSP-like vasculitic rash usually occurred in setting of underlying bacterial infections in these patients and treatment of underlying infections usually resulted in complete remission of vasculitic lesions. Presence of such vasculitis–like lesions suggest underlying immune dysregulation in IL12RB1/ IL12B defects. These skin lesions can also be considered as one of the potential clinical clues for underlying IL12RB/IL12B defects.

Conclusion:
Our report shows that patients with IL12RB1/IL12B defects can present with cutaneous vasculitis resembling HSP. These lesions are usually associated with underlying bacterial infections, an important clinical clue for underlying IL12RB/ IL12B defects, and are likely to be much more common in developing countries as compared to West.

POSTER 34 - COMPLEMENT DEFICIENCIES IN MOROCCO: 6 CONFIRMED CASES AND IDENTIFIED GENETIC VARIANTS

AUTHORS

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Introduction:
Complement Deficiencies (CD) are immune disorders where certain complement system proteins are absent or dysfunctional. They are often linked to recurrent invasive infections, renal diseases, and autoimmune conditions. In Morocco, these deficiencies are not well known.This study aims to identify Moroccan patients with CD, diagnosed locally or reported in the international literature.

Methods:
Data were collected from the Moroccan PID registry, Moroccan published cases, and patients who underwent genetic testing

Results:
Among the 831 patients registered in the Moroccan Primary Immunodeficiency Registry, only 7 had CD (2 patients with C5 deficiency, 1 with C7 deficiency, 1 with C4 deficiency, 1 with C8b deficiency, 1 with C6 deficiency and 1 with C3 deficiency). In the literature, 3 patients with C5 deficiency and 3 with C7 deficiency were identified. Additionally, out of 300 genetically tested patients, 85 had homozygous and heterozygous variants in different complement fractions.

Conclusion:
CD do exist in Morocco due to the population's high rate of consanguinity, which also explains the high prevalence of variants related to the disorder. The need to improve awareness and diagnosis of CD is crucial in order to prevent severe complications and enhance the quality of life for the patients.

POSTER 35 - HEREDITARY ANGIOEDEMA WITH UNCOMMON GENETIC MUTATIONS: THREE CASE REPORTS INVOLVING ANGPT1 AND PLG

AUTHORS

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Introduction:
Hereditary angioedema is a rare autosomal dominant disorder that can be either histaminergic or non-histaminergic in origin. The hereditary, non-histaminergic forms are most frequently associated with mutations in the SERPING1 gene, which encodes the C1 inhibitor. In recent years, additional genes have been identified as contributors to the disease phenotype, including ANGPT1 (angiopoietin 1), PLG (plasminogen), KNG1, F12, MYOF, and HS3OST6. This work presents three clinical cases involving pathogenic variants in the ANGPT1 and PLG genes, illustrating the genetic diversity of hereditary angioedema.

Methodology:
The genetic variants were unexpectedly identified during a diagnostic assessment for suspected immunodeficiency. All three patients underwent a targeted gene panel analysis focused on immunodeficiencies and cytopenias, which included the SERPING1, ANGPT1, and PLG genes. The pathogenic nature of the detected mutations was established through a combination of clinical and biological data, along with in silico predictive analyses using tools such as CADD, PolyPhen, REVEL, and Alpha Missense.

Results:
The first case involves a 2.5-year-old child presenting with recurrent conjunctivitis, bronchitis, and episodes of epistaxis. Genetic analysis revealed a heterozygous pathogenic variant in the ANGPT1 gene. The second patient, aged 18, has atopic dermatitis within a personal and family history of atopic conditions, including asthma and allergic rhinitis. The third patient, an 8-year-old child, experiences isolated recurrent fever and abdominal pain without a clear etiology.

In both the second and third cases, heterozygous mutations in the PLG gene were identified: PLG c.2134G>A and PLG c.112A>G—variants that have already been described in previous studies. In contrast, the ANGPT1 variant found in the first patient is novel and has not been reported in the literature.

Conclusion:
Given the young age of the patients, it is expected that more specific clinical features associated with these genetic variants may manifest progressively over time.

POSTER 36 - ANTI IL-17 TREATMENT RESPONSE IN TWO PATIENTS WITH NETHERTON SYNDROME

AUTHORS

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Objective:
Netherton syndrome is a rare form of congenital ichthyosis caused by homozygous mutations in the gene encoding the serine protease inhibitor Kazal type 5 and characterized by early hypernatremic dehydration, food allergy and growth retardation. It is characterized by diffuse erythroderma that begins at birth and peels all over the body, ichthyosis linearis circumflexa and trichorexis invaginata. It has been shown that an increase in the T helper 17 signaling pathway and IL-17 production may also play a role in the pathophysiology. Secukinumab is a human monoclonal antibody developed against IL-17A that has been shown to be useful in the treatment of Netherton syndrome in a small number of cases.

Design and method:
In this report, we will report on two pediatric patients with Netherton syndrome who were followed up in our clinic and benefited from treatment with secukinumab.

Results:
A 2-month-old female patient (P1) was referred to our outpatient clinic with a preliminary diagnosis of primary immunodeficiency. This was due to skin redness, peeling, growth retardation, frequent mucous stools and recurrent moniliasis since birth. Detailed immunological examinations were carried out. A mutation in the SPINK5 gene was found (c238dupG (p. Ala80Glyfs*19) c.1888-1G>A).

A 3-month-old E patient (P2) was referred to our outpatient clinic due to skin redness, peeling, growth retardation, chronic mucous diarrhea, recurrent moniliasis, hypernatremic dehydration and recurrent otitis, which had been present since birth. A frameshift mutation in the SPINK5 gene was detected.

Both patients were started on skin care recommendations, local steroids, IVIG (0.5 g/kg every 3 weeks), TMP-SMZ and fluconazole prophylaxis. Secukinumab 75 mg was administered subcutaneously once weekly for the first month and once monthly for the next 6 months. Active symptoms, physical examination results and SCORADs were recorded at the monthly patient assessment. Th17 levels were analyzed at baseline and at follow-up.

Conclusions:
The use of the monoclonal IL-17 antibody secukinumab in patients with Netherton syndrome improves cutaneous manifestations and improves quality of life and sleep. By reducing the need for local steroids, it prevents the development of symptoms such as growth retardation and Cushing's syndrome. Although an increase in the incidence of mucocutaneous candidiasis and upper respiratory tract infections due to IL-17 blockade has been reported with long-term use, no side effects were observed in our patients. Although there is insufficient data in the literature on long-term results, this treatment is promising in patients with Netherton's syndrome.

POSTER 37 - DETECTION OF BRONCHIECTASIS IN PATIENTS WITH X-LINKED AGAMMAGLOBULINEMIA USING AI-DRIVEN AUTOMATED CHEST CT QUANTIFICATION TOOLS

AUTHORS

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Objective:
X-linked Agammaglobulinemia (XLA) patients are at risk for progressive structural lung abnormalities (SLAs), including bronchiectasis (BE) secondary to recurrent chest infections. Little is known about the nature and extent of SLAs in XLA patients. We aimed to quantify SLAs in XLA patients using a manual and an artificial intelligence-based automated algorithm.

Design and method:
Chest CT scans from XLA patients in whom BE was mentioned in the radiology report were manually annotated using the validated Bronchiectasis Scoring Technique for CT (BEST-CT). Atelectasis/consolidation, BE with and without mucus plugging (MP), airway wall thickening, MP, ground-glass opacities, and bullae are annotated using a grid-based approach and expressed as percentage of total lung volume. Composite scores include total BE (BE with and without MP), total MP (BE with MP plus MP alone), and total disease (all abnormalities). Secondly, automated LungQ bronchus-artery (BA) and MP analysis (version 3.1.0.8, Thirona, Nijmegen, Netherlands) were used to segment bronchial and arterial trees. BA algorithm measures bronchial outer diameter (Bout), bronchial inner diameter (Bin), bronchial wall thickness (Bwt) and artery diameter (A) to calculate BA-ratios for bronchial dilatation or bronchiectasis (Bout/A, Bin/A) and for bronchial wall thickening (Bwt/A), as well as the artery independent measure for wall thickening bronchial wall area/bronchial outer area (Bwa/Boa). MP algorithm automatically detects the number and volume of airway obstructing MPs. Results from the manual and automated annotation tools were compared using Pearson's correlation coefficient.

Results:
Chest CT scans of 10 XLA patients with BE were analyzed. Median BEST-CT subscores were 3.0 (IQR, 0.6–9.1) for total BE, 0.5 (0.0–2.9) for total MP, and 7.6 (2.9–12.5) for total disease. These percentages are aligned with data from the EMBARC registry of non-CF bronchiectasis patients. Automated LungQ algorithm detected 1806 BA pairs, detected widened airways in all patients and classified a median of 13% of airways as bronchiectatic (conservative BA ratio cut-off >1.5). MP algorithm detected 38 airway obstructing MPs. Manual and automated outcomes showed significant correlations of varying strength: BEST-CT total BE vs Bout/A (r=0.5), BEST-CT total BE vs Bin/A (r=0.4), BEST-CT total MP vs LungQ total volume of MPs (r=0.8).

Conclusions:
Manual BEST-CT and automated LungQ BA and MP algorithms can be used to quantify SLAs in XLA patients. These algorithms have the potential to measure bronchial dimensions and MPs in large numbers of chest CTs without interobserver variability and could be valuable in early detection and prevention of SLAs in XLA patients.

POSTER 39 - SEE THE UNSEEN: A LATE-ONSET GRISCELLI SYNDROME TYPE 2 DIAGNOSIS WITHOUT HYPOPIGMENTATION

AUTHORS

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Objective:
Autosomal recessive mutations in the RAB27A gene lead to Griscelli syndrome type 2 (GS-2), characterized by hypopigmentation and development of early-onset, potentially fatal hemophagocytic lymphohistiocytosis (HLH). Recently, GS-2 cases, both late onset and sine albinism, have been reported in the literature.

Design and method:
Here, we present a pediatric patient diagnosed as late-onset GS-2 without hypopigmentation.

Results:
A fourteen-year-old boy was admitted to the pediatric emergency department in his hometown due to fever. After receiving ceftriaxone, he had a sudden loss of consciousness and cardiac arrest. After resuscitation, he was intubated. Laboratory tests revealed haemolytic anemia and thrombocytopenia. He received erythrocyte and platelet transfusions, inotropes, intravenous immunoglobulin (IVIG), and pulse-steroid. On follow-up, he was referred to our pediatric intensive care unit (PICU) in need of plasmapheresis and continuous renal replacement therapy. On PICU admission, physical examination revealed splenomegaly, nonspecific rashes, and extensive mucosal bleeding. Laboratory tests revealed anemia, thrombocytopenia, low haptoglobin, and elevated ferritin, triglyceride levels, positive direct Coombs, elevated liver enzymes, supporting HLH. Because of his complicated clinical course, an immunology consultation was planned. Background history revealed that he was born to non-consanguineous parents and over the last two years, he has been followed by splenomegaly and intermittent pancytopenia/ bicytopenia. Myelodysplastic syndrome, paroxysmal nocturnal hemoglobinuria, Gaucher, and Niemann Pick disease were excluded. Immunologic work-up revealed EBV viremia, low Ig M level, and low absolute lymphocyte subsets counts. He received rituximab, anakinra, IVIG, and steroid for treatment. Exome sequencing (ES) was performed and identified compound heterozygous [c.488G>T (p.Ser163Ile), and c.-3A>C] variants of unknown significance in the RAB27A gene (NM_183235.3). Sanger sequencing validated that the c.488G>T (p. Ser163Ile) variant is maternally and the c.-3A>C variant is paternally segregated and found to be in trans configuration. After discharge from PICU, steroid treatment was tapered. He was treated according to HLH 94:2018 consensus recommendations. After HLH treatment, he was transplanted from his 10/10 HLA- matched elder sister. He is now well at post-transplant 3.5 months with 100 % chimerism.

Conclusions:
RAB27A mutations should be investigated in patients with suspected HLH disease, even if lacking hypopigmentation.

POSTER 40 - NOVEL STAT3 MUTATION IN A PATIENT WITH HYPER-IGE SYNDROME PRESENTING WITH RECURRENT PULMONARY INFECTIONS (JOB SYNDROME)

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Background:
Autosomal dominant hyper-IgE syndrome (AD-HIES) caused by STAT3 mutations is a rare primary immunodeficiency disorder characterized by recurrent eczema-like rashes, skin and pulmonary abscesses, and significantly elevated serum IgE levels. The purpose of this article is to highlight the distinct clinical presentation, the importance of genetic studies in diagnosing AD-HIES and the role of bronchoscopy lavage in managing pulmonary complications.

Case report:
Herein, we report a 9-year-11-month-old girl of Chinese origin who presented with recurrent eczema-like rashes, fingertip abscesses, and recurrent pulmonary infections. In her past medical history, she experienced with severe allergies to seafood and peanuts, and frequent infections such as congenital pneumonia, recurrent bacterial and viral pneumonias, and cutaneous abscesses. The immunological workup revealed normal TBNK panel, normal general immunology results, and an increase in IgE level > 5000 IU/mL. The genetic testing confirmed a heterozygous STAT3 mutation (autosomal dominant) while NIH AD-HIES score was 45 (> 40, highly suggestive of Job Syndrome). She underwent extensive immunological and genetic workups, including STAT3 expression testing via flow cytometry, which showed normal expression despite the detected pathogenic variant. Bronchoscopy lavage was performed as part of her pulmonary infection management, which was preferred over surgical intervention.

Conclusion:
Further studies on STAT3 mutations are required to better understand genotype-phenotype correlations in HIES. Bronchoscopy lavage should be considered over invasive procedures for managing pulmonary infections in pediatric patients with HIES.

POSTER 41 - INSIGHTS INTO 24 PATIENTS WITH X-LINKED CHRONIC GRANULOMATOUS: A DUAL FOCUS ON CLINICAL MANIFESTATIONS AND GENETIC MUTATIONS

AUTHORS

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Objective:
This study aims to evaluate the clinical manifestations and genetic mutations in 24 patients diagnosed with X-CGD to provide insights into genotype-phenotype correlations and improve patient care strategies.

Design and method:
A retrospective analysis were conducted on 24 male patients diagnosed with X-CGD between 2014 and 2024. Diagnosis was confirmed using the Nitroblue Tetrazolium (NBT) slide test or Dihydrorhodamine (DHR) flow cytometric assay, followed by genetic analysis of the CYBB gene using next-generation sequencing (NGS) and Sanger sequencing. Clinical data were collected to evaluate infection patterns, inflammatory manifestations, and organ involvement.

Results:
NBT and DHR tests were found to be within the abnormal range in these patients, confirming the diagnosis of CGD. The most common clinical manifestations included purulent abscesses (78%), lymphadenopathy (69%), pulmonary involvement (52%), BCGosis (39%), hepatosplenomegaly (34%), gastrointestinal symptoms (30%), osteomyelitis (26%), and oral manifestations (17%). Genetic analysis revealed diverse mutations in the CYBB gene: nonsense mutations (11 cases), deletions (4 cases), missense mutations (3 cases), duplications (3 cases), and splicing site defects (3 cases). These findings demonstrated significant clinical heterogeneity and genetic diversity among X-CGD patients.

Conclusions:
This study highlights the clinical heterogeneity and genetic diversity of X-CGD. The high prevalence of infections and systemic complications underscores the need for early diagnosis, regular monitoring, and appropriate prophylactic treatments. Genetic testing is crucial for confirming the diagnosis and guiding treatment decisions. Further studies are needed to explore genotype-phenotype correlations and optimize individualized management approaches for X-CGD patients.

POSTER 42 - NATURAL KILLER AND ADOPTIVE MEMORY T-CELL THERAPY FOR INFECTION MANAGEMENT IN PRIMARY IMMUNODEFICIENCIES: PROPHYLACTIC AND THERAPEUTIC APPLICATIONS AFTER ALLOGENEIC HSCT

AUTHORS

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Objective:
Primary immunodeficiency patients undergoing allogeneic HSCT are at high risk for severe infections.

Design and method:
We report three cases in which NK and donor-derived memory T-cell infusions were successfully used for prophylaxis and viral and fungal post-HSCT complications therapy.

Results:
The first case involves an 18-month-old male with SCID-ARTEMIS who received a second TCRαβ/CD19-depleted haploidentical graft after losing the first graft. On day +16, he experienced EBV reactivation with a viral load of 23,137 copies/mL and a deep lymphodepletion. By day +17, he developed PTLD with the appearance of clonally restricted B-cells. The EBV load increased to 91,614 copies/mL by day +22. Rituximab and cidofovir treatments were ineffective. By day +26, he developed ARDS and cytokine release syndrome, requiring ICU support with intubation and administration of tocilizumab and anakinra. On day +28, he received an infusion of 36.2 × 10^6 CD45RO+/kg memory T-cells, followed by 85.7 x 10^6/kg NK cell infusion on day +29. Within days, his lymphadenopathy resolved, hepatomegaly decreased, and EBV DNA became undetectable by day +40, with anti-EBNA IgG levels reaching 236 U/ml.

The second case is a 9-month-old girl with chronic granulomatous disease who received a TCRαβ-depleted haploidentical graft. On day +6, she received a prophylactic infusion of 1.08 × 10^6/kg donor memory T-cells (CD45RA-/CD45RO+). By day +22, she developed EBV positivity, while CD3+ T-cells were <80 cells/mm³. The child rapidly mounted an effective antiviral response. Total lymphocyte count rising to 4,560 cells/mm³ by day +32, driven by a CD8+ T-cell expansion. EBV viral load peaked at 34,520 copies/mL, but she remained asymptomatic, and viral load spontaneously cleared within two weeks. By day +39, anti-EBNA IgG was 481 U/ml.

The third case involves a 14-month-old boy with SCID who underwent a second haploidentical rescue HSCT. On day +2, he developed multiple organ complications and severe Adenovirus infection, pulmonary Aspergillosis, and acute renal insufficiency due to the drug's toxicity. The viral load has grown from 71,743 copies/mL on day +2 to 26,250,000 copies/mL on day +44, causing life-threatening enteritis. Pulmonary Aspergillosis is complicated by ARDS, requiring ICU support and intubation. On day +52, he received an infusion of 41.3 x 10^6 CD45RO+ memory T-cells/kg, followed by 5.61 x 10^6 NK cells/kg. The child had a rapid and complete immunological reconstitution, with viral and fungal clearance.

Conclusions:
These cases demonstrate that NK and memory T-cell infusions effectively and safely manage post-HSCT viral and fungal complications.

POSTER 43 - NIJMEGEN BREAKAGE SYNDROME – A RARE CLINICAL CASE IN KAZAKHSTAN

AUTHORS

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Nijmegen syndrome is a rare primary immunodeficiency marked by chromosomal instability, microcephaly, physical retardation, specific facial skeletal disorders, and increased cancer risk. It often results from a homozygous del5 mutation in the NBS gene, particularly common among Slavic populations. This is the first report of Nijmegen syndrome in Kazakhstan, aiming to provide initial data on this condition in the region.

An 8-year-old girl complained of cough, lag in physical development, lack of nasal conchae, facial skin lesions, purulent discharge from the nose and ears, pain, swelling in the left knee joint and diarrhea. She has been ill since the age of 1.6 with manifestations of purulent otitis media, febrile fever, frequent streptococcal tonsillitis, stomatitis, recurrent respiratory infections. During an examination delayed physical development, protein and energy deficiency of 3 degrees. Microcephaly. Chronic bilateral otitis media. Chronic rhinopharyngitis in remission, bacilli bearing. Anemia of mild severity. At the age of 7 there took a skin biopsy atypical cells (granulomatous inflammation and T-cell lymphoproliferative neoplasm) were detected for the second time. Conclusion of the molecular histological test dated : does not confirm the possibility of a tumor process of lymphocytes. After sequencing of whole exome, the Nijmegen syndrome was detected: the result is a pathogenic variant in the NBS gene according to the autosomal recessive type of inheritance.

When examined according to immunophenotyping data, the child has an incomplete defect of the cellular and humoral links of immunity. Immunophenotyping: leukocyte count 9.76 10^9/L, lymphocyte count 27.22%, cd3- HLA-DR lymphocytes+ 7.23% , B-lymphocytes cd19+cd3- abs 0.17 x10^9/L , B-lymphocytes cd19+cd3- 6.41 %, mature cd3+cd19 T-lymphocytes- abs 2.08 x10^9/L , mature cd3+cd19 T-lymphocytes- 78.44% , NK cells cd3-cd16+/cd56+ abs 0.31 x10^9/L , NK cells cd3-cd16+/cd56+ 11.73% , Immunoregulatory index (cd4+/cd8+) 0.75 Immunoglobulin A 0.00 g/L , Immunoglobulin G 3.14 g/L Immunoglobulin M 0.23 g/L .

At age of 8 there made CT scans revealed intrathoracic lymphadenopathy and bilateral subclavian and axillary lymphadenopathy, raising concerns about possible lymphoma. Histological examination showed: The morphological picture and immunophenotype correspond to ALK-(negative) anaplastic large cell lymphoma.

In conclusion, early detection and proper treatment of Nijmegen syndrome can help avoid a number of complications. Timely stem cell transplantation can help delay complications in the form of cancer. Therefore, it is very important to inform primary and secondary care physicians about such rare pathologies more often.This case highlights Nijmegen Syndrome as a previously unreported genetic anomaly in the Kazakh population.

POSTER 45 - CLINICAL AND GENETIC OF CERNUNNOS DEFICIENCY: INSIGHTS FROM A NATIONAL COHORT OF INBORN ERRORS IF IMMUNITY

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Object:
Non-homologous end-joining (NHEJ) is a pivotal DNA repair pathway essential for V(D)J recombination during the development of antigen receptors in T and B lymphocytes. Cernunnos deficiency, caused by deleterious mutations in one of the NHEJ components, has been rarely reported. This study aims to broaden the clinical, immunological, and molecular insights into Cernunnos deficiency through a retrospective analysis of genetically diagnosed individuals within our national registry of inborn errors of immunity.

Design and methods:
We investigated a cohort of 10 individuals (50% female) with confirmed biallelic mutations in the Cernunnos gene. The condition exhibited an autosomal recessive inheritance pattern, commonly associated with neurological impairments, T cell lymphopenia, and heightened radiosensitivity. Although most subjects fulfilled the clinical criteria for severe combined immunodeficiency (SCID), a subset demonstrated an atypical presentation with preserved growth, normal head circumference, and adequate antibody production.

Results:
A recurrent splice-site mutation (c.390+1G>T) was found in 80% of patients, suggesting it as a prevalent pathogenic variant within our population. These individuals exhibited features of a hypomorphic or "leaky" phenotype, indicating partial preservation of B cell development and function.

Conclusions:
Cernunnos deficiency should be considered in the differential diagnosis of children presenting with recurrent bacterial infections, microcephaly, and growth failure, even when humoral immunity appears intact.

POSTER 46 - TARGETED THERAPY FOR CD 20-POSITIVE LYMPHOPROLIFERATIVE DISORDER IN A PATIENT WITH X-LINKED SEVER COMBINED IMMUNODEFICIENCY

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Object:
Severe Combined Immunodeficiency (SCID) is a rare but life-threatening condition marked by profound T-cell lymphopenia, often accompanied by B-cell and/or NK-cell deficiencies. This immunodeficiency renders patients highly vulnerable to recurrent and opportunistic infections. Lymphoproliferative disorders (LPDs), characterized by aberrant lymphocyte proliferation, may emerge in immunocompromised hosts. Among these, CD20-positive LPDs respond favorably to rituximab therapy. We present the case of an infant with SCID who developed a CD20-positive lymphoproliferative lesion in the distal femur following a minor trauma.

Design and method:
The patient, a 6-month-old boy born to consanguineous parents with a familial history of SCID, was identified through newborn screening using the T-cell receptor excision circles (TREC) assay, which revealed undetectable TREC levels. Further immunophenotyping showed profound T and NK cell lymphopenia with a relative increase in B-cell count. Whole exome sequencing confirmed a diagnosis of X-linked SCID, subsequently validated via Sanger sequencing. At six months, the patient sustained a femoral fracture with associated erythema and swelling. Imaging and histopathological evaluation of the lesion revealed a CD20-positive lymphoproliferative infiltration at the fracture site.

Results:
Given the dominance of B cells in the biopsy sample, rituximab was initiated, leading to rapid clinical improvement. The patient successfully underwent hematopoietic stem cell transplantation (HSCT) at nine months of age.

At his most recent follow-up, the patient—now three years old—demonstrated complete (100%) donor chimerism. He is in excellent overall health, with no evidence of post-transplant complications observed to date.

Conclusion:
This case highlights the rare occurrence of LPD in the context of SCID, particularly following bone trauma. The development of a localized CD20-positive lymphoproliferative lesion in such patients underscores the importance of prompt immunopathological assessment. Targeted therapy with rituximab proved effective in controlling the disorder prior to definitive treatment with HSCT. Our findings support the role of immunophenotyping and monoclonal antibody therapy in managing lymphoproliferative manifestations in immunodeficient individuals.

POSTER 47 - FROM GENES TO INFECTIONS: A COMPLEX CASE OF LEAKY SCID WITH DUAL OPPORTUNISTIC INFECTIONS DISSEMINATED TUBERCULOSIS AND RENAL FUNGAL BALL

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Objective:
To report a rare and complex case of disseminated mycobacterial and fungal infections in a pediatric patient with leaky severe combined immunodeficiency (SCID) caused by a homozygous JAK3 mutation, and to highlight the diagnostic and therapeutic challenges in managing such immunodeficiencies in tuberculosis-endemic regions.

Design and methods:
We present the case of a 2.5-year-old boy, the first child of distantly related parents, born at 36 weeks gestation and admitted to the NICU after birth. He had recurrent infections since early infancy, including persistent oral thrush, fever, diarrhea, vomiting, and multiple episodes of pneumonia.

Results:
Genetic testing was performed due to clinical suspicion of SCID confirming a homozygous mutation in the JAK3 gene, and confirmed the diagnosis.

The patient developed disseminated BCG infection with osseous involvement of the upper limb following routine neonatal BCG vaccination. This condition necessitated surgical intervention and abscess drainage.

Subsequently, at 20 months of age, the patient developed a renal abscess during evaluation for persistent high-grade fever. Despite receiving broad-spectrum anti fungal therapy, the lesion showed no significant reduction in size, and the renal fungal ball remained unchanged.

The patient is a candidate for hematopoietic stem cell transplantation (HSCT) with a fully matched unrelated donor available. However, due to ongoing active infection and poor response to treatment, transplantation has been postponed despite six months of hospitalization.

Conclusion:
Leaky SCID due to JAK3 mutations may present with atypical and severe infections including disseminated tuberculosis and invasive fungal disease, especially in TB-endemic settings. Early recognition, molecular diagnosis, and multidisciplinary management—including infection control and preparation for definitive treatment via stem cell transplantation—are critical for improving patient outcomes. Unfortunately, severe and treatment-resistant infections can occasionally occur in patients with primary immunodeficiency, posing significant therapeutic challenges. These infections not only delay hematopoietic stem cell transplantation but also adversely affect post-transplant prognosis.

POSTER 48 - DIVERSE CLINICAL PRESENTATIONS AND DIAGNOSTIC CHALLENGES OF ACTIVATED PI3K DELTA SYNDROME (APDS): A COHORT FROM IRAN

AUTHORS

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Objective:
Activated PI3K Delta Syndrome (APDS) represents a dominantly inherited primary immunodeficiency caused by gain-of-function mutations in the PIK3CD gene (APDS1) or loss-of-function variants in PIK3R1 (APDS2). This genetic condition manifests through a broad spectrum of clinical problems, including immune dysregulation, repeated infections, lymphoproliferative disorders, heightened cancer susceptibility, and autoimmune complications. Despite increasing global awareness, APDS remains underrecognized in Iran, where high rates of consanguineous marriages and significant genetic heterogeneity may influence its prevalence.

Design and method:
Following ethical approval and obtaining informed consent, we conducted a retrospective study involving nine pediatric patients diagnosed genetically with APDS (seven with APDS1 and two with APDS2) at Mofid Children's Hospital. Data collection was based on detailed family interviews and thorough review of medical records, emphasizing clinical presentation, immunological assessments, genetic results, and therapeutic approaches. Genetic diagnosis was confirmed via whole-exome sequencing and validated by Sanger sequencing.

Results:

• **Demographic and Genetic Features:** The patient ages ranged from 6 months to 10 years (median age: 5 years), with symptom onset varying from 4 months to 6 years. Consanguinity was reported in four families, and three patients had a positive family history of immunodeficiency or APDS. The PIK3CD c.3061G>A (p.E1021K) mutation was the most common, whereas two patients carried splice-site mutations in PIK3R1.

• **Clinical Manifestations:** Recurrent respiratory infections dominated the clinical picture (89%), followed by lymphoproliferation (78%), autoimmune disorders (44%) including Crohn's disease, immune thrombocytopenic purpura, autoimmune hepatitis, systemic lupus erythematosus, and CMV/EBV infections (22%). One patient developed lymphoma.

• **Immunological Profile:** Common laboratory findings included a Hyper-IgM phenotype, decreased switched memory B cells, reversed CD4/CD8 ratios, and suboptimal responses to vaccinations.

• **Therapeutic Outcomes:** All patients received intravenous immunoglobulin therapy alongside antimicrobial prophylaxis. Five patients with lymphoproliferation showed partial response to sirolimus. Two patients required additional immunosuppressive treatments, including rituximab for hemolytic anemia and hydroxychloroquine for lupus.

Conclusion:
This case series is among the first detailed reports from Iran, underscoring the clinical diversity of APDS and emphasizing the urgent need for improved regional recognition, availability of molecular diagnostics, and implementation of targeted treatment strategies. Our observations align with data from European and international cohorts, reinforcing the importance of early diagnosis and integrated multidisciplinary management. Advancing global outcomes for APDS demands collaborative international efforts and enhanced awareness across diverse population.

POSTER 49 - FIRST CASE SERIES OF DIGEORGE SYNDROME IN KAZAKHSTAN: CHALLENGES IN THE DIAGNOSIS AND MANAGEMENT OF CHILDREN WITH PARTIAL AND COMPLETE GENETIC CONFIRMATION

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Introduction:
DiGeorge syndrome is a syndrome caused by a microdeletion of chromosome 22 at a location known as 22q11.2. with a broad phenotypic presentation, abnormal facies, congenital heart disease, frequent infections, intellectual disability, cleft palate, thymic hypoplasia or aplasia, developmental delay, and hypocalcemia. The aim of this study is to present cases of 20q11.2 microdeletion with complete and partial syndrome, to describe clinical manifestations and the importance of early diagnostics and treatment.

Case Presentation:
A 4-year-old female and a 4- year-old male patients, genetically confirmed with DiGeorge syndrome (partial and complete deletions, respectively), were diagnosed at 32 weeks gestation and 2 years old. In a case of female patient, she underwent Ventricular Septal Defect and repair of patent ductus arteriosus at 7 days old age, with an absent thymus noted during surgery. 1 month later, she had been diagnosed for primary immunodeficiency, DiGeorge syndrome that was confirmed at our hospital in Astana and started SCIG therapy with positive effect. The male patient was diagnosed at 2 years with multiple complications: Hemorrhagic colitis, Protein-energy malnutrition, Intestinal lymphangiectasia, Severe anemia, Bacterial sepsis, Congenital anomalies of the urinary system, Agenesis of the right kidney, Nephromegaly on the left, congenital complete AV block. Biotronik pacemaker 4 SR. Initial and follow up immunologic analyses are presented in Figure 1 and Figure 2.

Discussion:
Complete DiGeorge syndrome presents with more severe symptoms compared to partial forms, emphasizing the critical importance of prenatal or early postnatal diagnosis. It provides timely surgical correction of congenital heart disease and prompt management, such as calcium and immunoglobulin G.

Conclusions:
These interventions and diagnosis significantly improve outcomes in both partial and complete DiGeorge syndrome, reducing complications associated with heart failure, hypocalcemia and immunodeficiency. Design and methods:
We present the case of a 2.5-year-old boy, the first child of distantly related parents, born at 36 weeks gestation and admitted to the NICU after birth. He had recurrent infections since early infancy, including persistent oral thrush, fever, diarrhea, vomiting, and multiple episodes of pneumonia.

POSTER 50 - A NOVEL HEMIZYGOUS NONSENSE VARIANT IN DOCK11 CAUSES SYSTEMIC INFLAMMATION AND IMMUNODEFICIENCY

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Background:
Hemizygous germline loss-of-function variants in DOCK11, the gene encoding the dedicator of cytokinesis 11 (DOCK11) have been recently identified to cause immunodeficiency and immune dysregulation. Features of immune dysregulation have been reported in all so far identified male patients with damaging variants in DOCK11, commonly manifesting with autoimmune cytopenias, inflammatory bowel disease, benign lymphoproliferation and systemic inflammation.

Methods:
Whole genome sequencing data were reevaluated for variants in DOCK11. The expression of DOCK11 was evaluated by Western blot analysis. Induced T cell polarization was evaluated by staining of the actin cytoskeleton. Clinical and immunological data of all so far known patients with damaging hemizygous mutation in DOCK11 were evaluated in available literature.

Results:
We identified a novel variant in DOCK11 (c.3754C>T, p.(Q1252*)), leading to loss of protein expression, in a patient with a history of recurrent pneumonia, bronchiectasis, infection-triggered hyperinflammation and persistent systemic inflammation.

Discussion:
Reevaluation of all previously identified patients and the current case, reveals that variants leading to the complete loss of DOCK11 expression and consequently function associate with autoinflammation and recurrent pneumonias, while missense variants, primarily associate with autoantibody-related autoimmune features.

POSTER 51 - PRESENTATION OF TWO NOVEL CASES OF ZNF341 DEFICIENCY FROM IRAN

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Objective:
The ZNF341 gene encodes a transcription factor that specifically binds to distinct DNA regions, thereby modulating the expression of target genes. It is postulated that the ZNF341 protein regulates the transcriptional activity of STAT1 and STAT3 genes, which encode proteins integral to immune system function. STAT1 and STAT3 play critical roles in cellular signaling pathways that orchestrate immune responses against pathogens including viruses, bacteria, and fungi. Notably, STAT3 is essential for the differentiation and maturation of immune cells, particularly T and B lymphocytes.

Mutations in ZNF341 leading to an autosomal dominant Hyper IgE Syndrome (AD-HIES)-like phenotype typically result in truncated or absent ZNF341 protein products. The consequent deficiency of functional ZNF341 disrupts STAT1 and STAT3 protein synthesis, impairing immune cell development, especially affecting the Th17 subset of T cells. This immunodeficiency predisposes affected individuals to recurrent bacterial and fungal infections, predominantly involving the pulmonary and cutaneous systems.

Clinically, patients with autosomal recessive (AR) ZNF341 deficiency exhibit a phenotype closely resembling that of AD STAT3 deficiency, albeit with a milder disease severity, as evidenced by a median NIH HIES score of 28.5 compared to 64 in AD STAT3 deficiency cases.

Design and method:
This report includes two additional Iranian patients diagnosed with ZNF341 deficiency, expanding the current understanding of the immunological and clinical spectrum associated with this disorder.

The first case is12-year- old male, born to consanguineous parents, presented with persistent cervical lymphadenopathy first noted at 6 months of age. His past medical history is notable for severe atopic dermatitis from early infancy. Additionally, he experienced four separate episodes of Staphylococcus aureus lung abscesses. The combination of recurrent bacterial infections and chronic skin inflammation raises suspicion for an underlying primary immunodeficiency, necessitating further immunologic assessment.

The second case is15-year-old girl, born to consanguineous parents, who developed severe, treatment-resistant atopic dermatitis starting at 6 months of age and recurrent skin abscess. Her clinical history includes multiple episodes of perforated otitis media and recurrent pneumonia. She has food allergy.

Result:
Although ZNF341 and STAT3 deficiencies share several overlapping biological characteristics, ZNF341-deficient patients frequently display reduced natural killer (NK) cell counts and exhibit more appropriate inflammatory responses both clinically and biologically.

Conclusion:
Given the limited number of reported cases, the full clinical and immunological profile of ZNF341 deficiency remains incompletely characterized. Therefore, the documentation of new cases is crucial to facilitate early diagnosis and guide effective therapeutic interventions.

POSTER 52 - OSTEOPOROSIS – AN IGNORED COMPLICATION OF PRIMARY IMMUNO-DEFICIENCIES IN ADULTS

AUTHORS

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Objective:
Primary immunodeficiencies (PID) may compromise bone health. This study aimed to evaluate bone mineral density (BMD), trabecular bone score (TBS), and appendicular lean mass index (ALMI) in adults with PID.

Design and Methods:
Fifty adult PID patients: 20 females, 30 males; mean age 40.3 ± 14,6 years; 20 common variable immunodeficiency (CVID), 9 agammaglobulinemia, 7 dysregulation disorders, 10 undifferentiated hypogammaglobulinemia and 4 others were evaluated. Dual-energy X-ray absorptiometry (DXA) scans of the proximal femur, lumbar spine, and total body were performed (Lunar Prodigy, GE). Osteoporosis was diagnosed based on T-score ≤ -2.5 in postmenopausal women and men >50, or Z-score < -2 with risk factors in younger individuals. TBS was assessed via TBS iNsight software; values <1.2 and 1.2–1.349 indicated deteriorated or partially deteriorated bone microarchitecture, respectively. ALMI was calculated from total body DXA and adjusted for height; values <5.5 kg/m² in women and <7.0 in men indicated sarcopenia. Laboratory tests included serum 25(OH) vitamin D, calcium and phosphorus were performed. Clinical data on glucocorticoid therapy (GC), physical activity, low-energy fractures, lung involvement (GLILD, bronchiectasis), enteropathy, and lymphoproliferative disease were collected.

Results:
Most patients (94%) were on subcutaneous immunoglobulin replacement. PID was diagnosed before age 18 in 36% of cases. Osteoporosis was found in 11 patients (22%; 8 men, 3 women), with DXA indicating involvement of the proximal femur in 9 (18%) and lumbar spine in 4 (8%). Osteopenia was present in 11 (22%) patients, and 2 (4%) had low-energy fractures. TBS showed deteriorated microarchitecture in 3 (6%) and partially deteriorated in 9 (18%). Sarcopenia was found in 12 (24%) patients. Vitamin D levels were <30 ng/mL in 38%.

No significant differences in bone parameters were found between GC-treated vs. non-treated, with currently normal vs. low/deficient vitamin D, with vs. without lymphoproliferative disease and physically active vs. inactive groups. However, osteoporosis was significantly more frequent in patients with lung involvement (9/24 vs. 2/26, p=0.0164), sarcopenia was more common in those with enteropathy (6/9 vs. 8/41, p=0.0043) and deteriorated or partialy deteriorated microarchitecture was more prevalent in patients diagnosed after the age of 18 vs before (11/32 vs 1/18, p=0.036).

Conclusions:
Osteoporosis is a frequent complication in PID, particularly in younger men, and is best detected via proximal femur DXA. The cortical bone may be more affected than trabecular bone. Lung involvement increases osteoporosis risk, while enteropathy is associated with sarcopenia.

POSTER 53 - CLINICAL IMMUNOLOGY SERVICE DISRUPTION AMIDST SUDAN CONFLICT: PERSPECTIVE FROM A REAL EXPERIENCE

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The armed conflict that erupted in Sudan on April 15, 2023, has led to a catastrophic collapse of the country's centralized healthcare system, disproportionately affecting vulnerable groups such as patients with primary immunodeficiency (PID) and other immune-mediated diseases. This perspective, authored by Sudanese clinical immunologists, documents the war's devastating impact on clinical immunology services, including the loss of diagnostic infrastructure, disruption of care continuity, and critical shortages of lifesaving treatments such as intravenous immunoglobulin (IVIG). Drawing on field experiences, patient case stories, and efforts by professional and patient advocacy organizations, this paper highlights the urgent need for decentralized healthcare systems, strengthened telemedicine capacity, and international solidarity. It concludes with lessons learned and a call to global health actors to prioritize and protect immune-compromised populations in conflict settings.

POSTER 54 - MOLECULAR DIAGNOSIS OF WHIM SYNDROME AND CONGENITAL NEUTROPENIAS: RESULTS FROM PATH4WARD, A SPONSORED GENETIC TESTING PROGRAM

AUTHORS

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Patients with suspected WHIM (Warts, Hypogammaglobulinemia, Infections, Myelokathexis) syndrome and other forms of severe congenital neutropenia (SCN) often present with heterogeneous clinical phenotypes, making early diagnosis challenging. X4 Pharmaceuticals partnered with Labcorp Genetics (formerly Invitae) on PATH4WARD, a sponsored genetic testing program designed to facilitate early and accurate molecular diagnosis of primary immunodeficiencies (PIDs) associated with neutropenia.

Eligibility criteria were progressively refined over time, and as of April 2023 included suspicion of PID or congenital neutropenic disorder, history of absolute neutrophil count ≤ 1,000/µl on multiple occasions not related to drugs or chemotherapy or secondary to viral infection, and one or more of the following: personal history of recurrent and/or severe infections, lymphopenia, hypogammaglobulinemia, warts or family history of recurrent and/or severe infections or neutropenia.

The program, active from July 2019 to April 2025, employed a next-generation sequencing panel that expanded from an initial SCN panel (23 genes) in 2019, to PID panel (407 genes) in 2021, and to a comprehensive 574-gene PID and Cytopenias panel in 2022. Genetic variants were interpreted using Sherloc, an evidence-based classification framework based on the ACMG-AMP criteria.

As of the May 19, 2025 data cutoff, 3,088 individuals underwent testing, with 51% aged ≤10 years. Among these, 355 (11.5%) received a positive molecular diagnosis—93 with severe congenital neutropenia (SCN) and 267 with another type of PID (5 patients had a positive test for both SCN and other PID). Notably, 18 patients had a positive genetic test for WHIM syndrome with pathogenic or likely pathogenic variants in CXCR4, and an additional 8 patients had variants of uncertain significance in the same gene.

Genetic testing for PIDs, including neutropenia, can facilitate the diagnosis of specific clinical disorders (e.g., WHIM syndrome). Their identification may enable opportunities for appropriate clinical management, early treatment with approved therapy or participation in interventional trials.

POSTER 55 - IDENTIFIED CLINICAL CASES OF ATAXIA TELANGIECTASIA AT ONE IMMUNOLOGY CENTER IN KAZAKHSTAN

AUTHORS

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Introduction:
Ataxia Telangiectasia (A-T) is a rare inherited neurodegenerative disorder marked by neurological impairment and immune deficiency. The condition is caused by mutations in the ATM gene, leading to deficiencies in DNA repair mechanisms, which manifest as motor, immune, and other systemic dysfunctions. This study aimed to investigate the clinical and immunological features of A-T in a series of patients followed at a tertiary clinical immunology center from 2020 to 2024.

Case Presentation:
The study involved a case series of 7 patients diagnosed with A-T which were referred to the center for clinical immunology. The patients ranged in age from 4 to 16 years, with a slightly higher male prevalence (5 males, 2 females). Ataxia (loss of coordination and balance) and unsteadiness of gait was present in all patients (100%), which is a hallmark feature of A-T.

Immunological Findings:
Decreased B-cell and T-cell numbers were noted in all 7 patients, pointing to immune system dysfunction. This immunodeficiency is a significant aspect of A-T, contributing to increased vulnerability to infections and other complications. It is also noted that 5 patients had a decrease in the level of immunoglobulin IgA.

Discussion:
Ataxia telangiectasia (Louis-Bar syndrome) is a rare hereditary disease. The diagnosis is based on the clinical picture of the disease, laboratory and instrumental research methods. Detection of mutations in the ATM gene confirms the diagnosis. The study reinforces that A-T is a progressive disorder with no current cure, whichmakes early diagnosis and continuous clinical follow-up essential.

Conclusions:
This study contributes to enhancing diagnostic awareness and management strategies for A-T, underscoring the need for early intervention and monitoring to address both neurological and immune system complications.

POSTER 56 - SHINE INITIATIVES: ACTIONABLE PATHWAYS FOR SCID, SMA AND XLA FROM POSITIVE SCREENING TO MANAGEMENT CLINICAL CARE FOR NEWBORNS IN MALAYSIA

AUTHORS

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This pilot project under the SHINE initiative aims to assess the feasibility of implementing newborn screening for Severe Combined Immunodeficiency (SCID), Spinal Muscular Atrophy (SMA), and X-linked Agammaglobulinemia (XLA) in Malaysia. It also aims to outline a structured clinical pathway for positive screening results, emphasizing early diagnosis, timely intervention, and coordinated care. A total of 400 dried blood spot (DBS) samples were collected via heel prick test from Malaysian newborns. DNA extraction from DBS cards was performed following standard laboratory procedures, including punching using the Revvity DBS puncher, sample sealing, mixing, and centrifugation. Molecular analysis was conducted using the QuantStudio™ Dx Real-Time PCR system to detect gene targets associated with SCID, SMA, XLA, and IEM. Out of 400 samples screened, three (0.75%) were identified as presumptive positive for SCID. No positive cases were detected for SMA, XLA, or IEM in this cohort. For each positive SCID case, a coordinated response was initiated, involving immediate communication with pediatric immunologists, retesting, and confirmatory diagnostic procedures such as lymphocyte subset analysis using flow cytometry and targeted genetic testing from whole blood samples. Although no SMA or XLA positives were detected in this pilot, protocols are in place for confirmatory testing, including SMN1 gene deletion analysis for SMA and flow cytometry and BTK gene analysis for XLA. This study demonstrates that screening using DBS samples and real-time PCR is a feasible approach for early identification of SCID and other rare but serious conditions in newborns. Positive screening results should trigger immediate communication with relevant specialists, followed by confirmatory testing and condition-specific management. These include hematopoietic stem cell transplantation (HSCT) for SCID, gene therapy or pharmacologic treatment for SMA, and immunoglobulin replacement therapy for XLA. Long-term follow-up and family counseling are critical components of care. The findings underscore the need for structured clinical pathways as a key future direction to ensure timely and effective interventions for newborn screening.

POSTER 57 - MALIGNANCY AND AUTOIMMUNE SUSCEPTIBILITY IN ADULT PATIENTS WITH HUMAN INBORN ERRORS OF IMMUNITY

AUTHORS

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Objective:
Clinical features of inborn errors of immunity (IEI) patients are dominated by susceptibility to a spectrum of infectious diseases, as well as autoimmune, autoinflammatory, allergic and malignant phenotypes that usually appear in childhood, which is when the diagnosis is typically made. However, some IEI patients are identified in adulthood due to symptomatic delay of the disease or other reasons that prevent the request for a molecular study.

Methods:
The application of next-generation sequencing (NGS) as a diagnostic technique has given rise to an ever-increasing identification of IEI-monogenic causes, thus improving the diagnostic yield and facilitating the possibility of personalized treatment. This work was a retrospective study of 173 adults with IEI suspicion who underwent genetic sequencing between 2005 and 2023.

Results:
Disease-causing variants were identified in 44 of 173 (25.43%) patients. The clinical phenotype of these 44 patients was mostly related to infection susceptibility (63.64%). An enrichment of immune dysregulation diseases was found when cohorts with molecular diagnosis (w_MolDx) were compared to those without (wo_MolDx) (Figure 1). A significant increase of malignancies was observed in patients w_MolDx compared to those wo_MolDx (Figure 2). Notably, hematologic malignancies were predominant in the w_MolDx cohort, whereas solid tumors were more frequently observed in the wo_MolDx group. In contrast, the correlation between autoimmune diseases and molecular diagnosis was less evident when comparing w_MolDx and wo_MolDx patients (Figure 2). In this cancer cohort, we observed that the median age of appearance of cancer among w_MolDx patients was 34.31 years, lower than 50 years, and significatively younger than the wo_MolDx cohort (46.76 years) (Figure 3). This suggests the importance of malignancy as a warning sign in young adults.

Conclusions:
These findings could be useful for diagnosing IEI in adulthood, particularly in patients with a clinical history of infection susceptibility or other JMF-modified warning signs, in addition to hematological neoplasms. Understanding the complex relationship between IEI, malignancies and autoimmunity is crucial for optimizing patient management. Early diagnosis of IEI allows for timely interventions, including hematopoietic stem cell transplantation, gene therapy and targeted immunomodulatory therapies, which can mitigate the risk of both malignancies and autoimmune complications.

POSTER 58 - ELAPEGADEMASE IN PATIENTS WITH ADENOSINE DEAMINASE-SEVERE COMBINED IMMUNODEFICIENCY PREVIOUSLY TREATED WITH PEGADEMASE: A CASE SERIES

AUTHORS

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Objective:
Elapegademase (Revcovi®), a PEGylated recombinant bovine adenosine deaminase (ADA), is the only FDA-approved enzyme replacement therapy (ERT) for ADA-severe combined immunodeficiency (SCID), replacing pegademase (Adagen®) since 2018. Elapegademase is typically used from diagnosis until hematopoietic stem cell transplant (HSCT) or gene therapy (GT) can be performed, or as a bridge therapy if failed HSCT/GT, or continued long-term if neither option is feasible. In a Phase 3 trial (NCT01420627), patients maintained metabolic detoxification, improved/stabilized lymphocyte counts and tolerated elapegademase. Given the rarity of ADA-SCID, real-world data are crucial for evaluating the long-term effectiveness and safety of elapegademase; here we report long-term data from a case series of four patients.

Design and method:
This analysis included four patients from four US sites who started elapegademase in the Phase 3 trial and continued treatment in the US registry (NCT03878069). The exposure periods for the case series spanned: trial, February 2015–May 2019; registry, April 2019–January 2023. All four patients received pegademase for 15–25 years before starting elapegademase. Assessments included plasma ADA activity, erythrocyte deoxyadenosine nucleotide (dAXP) levels, and safety outcomes.

Results:
Four patients with ADA-SCID, diagnosed in infancy (two males) or early childhood (two females), began ERT (pegademase) within a year of diagnosis (Table). One patient (patient 4) with unsuccessful GT continued ERT. For the other three, HSCT was not an option. Mean (range) age at elapegademase initiation was 21 years (16–31 y). Mean (standard deviation) total duration of elapegademase, including in the Phase 3 trial, was 69.5 (22.6) months (range, 40.1–95.1 m). At registry end, ADA activity levels were numerically higher than at elapegademase baseline and also exceeded levels at Phase 3 trial end. Additionally, all four patients were considered metabolically detoxified as satisfactory dAXP levels were maintained (≤ 0.02 mmol/L). Two patients required dose adjustments based on clinical assessments. Three patients experienced eight infections that resolved without sequelae and required no treatment interruption. No patients had any elapegademase-related adverse events.

Conclusions:
Long-term elapegademase was well tolerated with patients achieving stable plasma ADA and dAXP levels and maintaining metabolic detoxification for up to 8 years. This cohort received long duration ERT for ADA-SCID, with up to 30 years of treatment, remaining clinically stable without any new safety concerns.

POSTER 59 - SELECTIVE PHOSPHATIDYLINOSITOL-3 KINASE DELTA (PI3KΔ) INHIBITOR BEYOND ACTIVATED PHOSPHOINOSITIDE 3-KINASE SYNDROME (APDS): SUCCESSFUL COMPASSIONATE-USE EXPERIENCE OF LENIOLISIB IN PROTEIN KINASE C DELTA DEFICIENCY

AUTHORS

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Objective:
Leniolisib is a selective inhibitor of phosphoinositide 3-kinase delta (PI3Kδ), currently approved for the treatment of activated PI3Kδ syndrome (APDS), a well-characterized inborn error of immunity (IEI). Here, we describe the first documented case of leniolisib being used on compassionate grounds in a patient with protein kinase C delta (PKCδ) deficiency—a distinct IEI with no approved targeted therapy. This report aims to highlight the rationale, safety, and observed efficacy of leniolisib in this novel clinical context.

Design and method:
The off-label use of leniolisib was considered in a patient with genetically confirmed PKCδ deficiency who presented with progressive multiorgan involvement and was unresponsive or poorly responsive to standard immunomodulatory therapies. The decision to initiate leniolisib treatment was grounded in several converging factors: the clinical and immunological overlap with APDS, evidence of dysregulated mTOR signaling in PKCδ deficiency (S6 hyperphosphorylation and ex- vivo normalization after addition of PI3K-selective-inhibitor), and the absence of viable therapeutic alternatives. Clinical monitoring included safety assessments, laboratory parameters (cytopenias, liver enzymes, etc.), imaging studies (lymphadenopathy, splenomegaly, thymic size), pulmonary function tests, immunologic parameters and extent of S6 phosphorylation.

Results:
Leniolisib was well tolerated, with no adverse events reported during the treatment period. Clinically, the patient exhibited a significant reduction in lymphoproliferation, with measurable decreases in lymph node size, splenic volume, and thymic hyperplasia. Hematological abnormalities, including cytopenias, improved progressively. Immunophenotypic anomalies in peripheral blood normalized to a considerable extent. An optimal control of infectious and autoimmune manifestations was obtained together with the absence of newly emerging autoimmune manifestations. Surprisingly, pulmonary function tests including carbon monoxide diffusion, and pulmonary volumes demonstrated objective improvement, together with imaging improvement of tree-in-bud appearance, air-trapping and bronchiectasis.

Conclusions:
These findings provide preliminary evidence that PI3Kδ inhibition may be beneficial beyond its current indication, particularly in IEIs characterized by pathological activation of the PI3K-AKT- mTOR axis. Although this single-patient experience cannot substitute for controlled clinical trials, it underscores the potential for leniolisib repositioning in select non-APDS immunodeficiencies and beyond.

POSTER 60 - UNMASKING INBORN ERRORS OF IMMUNITY: A PEDIATRIC CASE OF GRANULOMATOUS DISEASE REVEALING AUTOSOMAL DOMINANT STAT1 DEFICIENCY

AUTHORS

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Objective:
Granulomatous diseases in children arise from diverse etiologies, including infections, malignancies, systemic inflammation, and inborn errors of immunity (IEI). Conditions such as chronic granulomatous disease (CGD), common variable immunodeficiency (CVID), and Mendelian Susceptibility to Mycobacterial Disease (MSMD) may all present with granulomatous inflammation. Here, we report a diagnostically complex case of pediatric granulomatous disease mimicking sarcoidosis and Rosai-Dorfman disease, ultimately diagnosed as Mendelian Susceptibility to Mycobacterial Disease (MSMD), to highlight the importance of considering IEI in children with granulomatous inflammation.

Methods:
We conducted a comprehensive diagnostic assessment of previously healthy 7-year-old girl from a non-consanguineous Italian family who presented with persistent follicular papules.

Results:
Initial skin biopsy revealed nonspecific inflammation. At age 11, she developed erythematous plaques, cervical lymphadenopathy, and multifocal bone lesions visible on whole-body MRI. A new skin biopsy showed non-caseating granulomas with S100+ histiocytes and emperipolesis, raising suspicion for Rosai-Dorfman disease. Oral corticosteroid therapy resulted in partial improvement, but disease relapsed following tapering, with CNS involvement detected on MRI spectroscopy. Thus, a lymph node biopsy revealed non-necrotizing granulomas, with histological alterations supporting a diagnosis of sarcoidosis. A second course of steroids was initiated. Despite transient clinical responses, the disease recurred. Microbiological cultures, not performed initially, were later conducted due to relapse and atypical progression, and revealed Mycobacterium avium complex (MAC) in the granulomatous tissue. This prompted a thorough immunological workup. Functional studies demonstrated absent STAT1 phosphorylation in response to IFNγ stimulation. Targeted next-generation sequencing identified a known pathogenic heterozygous STAT1 variant, previously described in MSMD. Based on these findings, a diagnosis of MSMD with disseminated MAC infection was established. The patient was treated with antimycobacterial therapy, achieving sustained clinical and radiological improvement. Corticosteroids were discontinued, and the patient remained asymptomatic for over 18 months, with complete resolution of lesions and ongoing azithromycin prophylaxis.

Conclusion:
This case illustrates how sarcoid-like granulomas in pediatric patients may mask underlying mycobacterial infections, particularly in the context of IEI such as STAT1 deficiency. Microbiological cultures of biopsy material must be routine, even in histologically sarcoid-like cases. The absence of necrosis, poor steroid response, and atypical multisystem involvement should prompt timely immunologic and genetic evaluation. Failure to recognize underlying IEI may delay appropriate therapy and worsen prognosis. Multidisciplinary collaboration is essential to ensure accurate diagnosis and optimal management of pediatric granulomatous diseases with potential immunodeficiencies.

POSTER 61 - A COHORT STUDY OF IRANIAN PATIENTS WITH SCID FROM A TERTIARY REFERRAL CENTER

AUTHORS

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Objective:
Severe Combined Immunodeficiency (SCID) includes a group of life-threatening primary immunodeficiencies marked by profound T-cell dysfunction. Without treatment, affected infants face early mortality. Early diagnosis and timely hematopoietic stem cell transplantation (HSCT) are essential for survival. This study examines the clinical, immunological, and genetic characteristics of SCID patients referred to Mofid Hospital since 2022, along with treatment outcomes and the importance of neonatal screening

Design and method:
A retrospective review of 15 SCID patients diagnosed based on ECID 2019 criteria between 2022 and 2025. Clinical features, genetic mutations, treatment outcomes, and timing of HSCT were analyzed.

Results:
Patients were diagnosed at a mean age of 4 months. Common clinical features included severe infections (sepsis, CMV retinitis, fungal infections), chronic diarrhea, BCG-related complications, and failure to thrive. Genetic mutations were detected in 13 patients, most frequently in JAK3 (3 cases) and NHEJ1 (2 cases), with additional mutations in RAG1, IL7R, ADA, DCLRE1C, Cernunnos, and γc. Two patients had undetermined mutations despite SCID phenotype.

Only 3 (20%) underwent HSCT and survived—two transplants were performed locally and one abroad. Six patients (40%) died before transplantation due to severe infections. One patient died post-transplant due to cardiopulmonary complications. Three patients remain on the transplant list; only one currently has a matched donor.

Conclusion:
This cohort highlights the high mortality associated with delayed SCID diagnosis and transplantation, even when donors are available. The overall HSCT success rate was only 13%, emphasizing the urgency of early detection and timely intervention. Implementation of newborn screening programs, such as TREC assay, is critical to enable early diagnosis and reduce pre-transplant morbidity. Improved infection control and expedited referral pathways are essential to improving outcomes for SCID patients. Although early diagnosis is often achieved in our patients, clinical outcomes remain suboptimal. This is primarily due to unfavorable conditions for hematopoietic stem cell transplantation (HSCT) in the country. Major contributing factors include the absence of specialized transplant centers dedicated to patients with primary immunodeficiency (PID), limited availability of novel therapeutic agents commonly used in conditioning and post-transplant care, and insufficient national experience with PID-specific transplantation protocols. These limitations significantly impact the prognosis and long-term survival of affected patients. Therefore, substantial improvements in transplant infrastructure and access to modern therapies are urgently needed to enhance clinical outcomes for this vulnerable population.

POSTER 62 - NON-INFECTIOUS COMPLICATIONS IN COMMON VARIABLE IMMUNODEFICIENCY – EVALUATION OF NEW POTENTIAL BIOMARKERS, CZECH MULTICENTRIC STUDY

AUTHORS

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Objective:
Non-infectious complications in CVID patients are related to an unfavourable prognosis. Specific non-invasive markers are still missing. The aim of the presented pilot study was to evaluate the relation between oxidative stress markers and specific CVID complications.

Design and method:
A total of 122 patients from 5 national centres and 56 healthy controls were included in the study. Urinary neopterin (NEO), kynurenine (KYN), tryptophan (TRP), 8-hydroxyguanosine (8OHG) and 8-hydroxy 2-deoxy guanosine (8OH2DG) were measured as markers of oxidative stress using high selective and sensitive liquid chromatography mass spectrometry methods. The results were expressed as a ratio to creatinine (CREA), or TRP in urine.

Results:
Of the 122 CVID patients 73 (60%) suffered from at least one non-infectious complication, with predominant presentation of splenomegaly (37 %), enteropathy (27%), lymphadenopathy (20 %), and interstitial lung disease (ILD) (19 %). Enteropathy was histologically proven in 33 patients (17 coeliac-like enteritis, 9 IBD-like colitis, 7 nodular hyperplasia). NEO/CREA ratio, KYN/TRP, KYN/CREA, 8OHG and 8OH2DG were significantly higher in all general CVID patients group compared with healthy controls (all parameters $p<0.001$). NEO/CREA ratio in urine was significantly higher in patients with any dysregulatory complication ($p=0.008$), or specifically: ILD ($p=0.006$), enteropathy ($p=0.002$), splenomegaly ($p<0.001$) and lymphadenopathy ($p<0.001$). KYN/TRP and KYN/CREA were significantly higher only in patients with enteropathy and splenomegaly.

Further, logistic regression was used to predict dysregulation in CVID patients: after five iterations, it remained in the model as a reliable predictor NEO/CREA, whose OR = 2.832. Prediction of ILD: after four iterations, two predictors remained in the model as reliable: NEO/CREA (OR = 7.003) and KYN/TRP (OR = 0.387). Unfortunately, our model was insignificant for enteropathy. The summary F-score metric showed models for dysregulation and ILD as good (F > 50%). The best-balanced model was for immune dysregulation (sensitivity 0.838, specificity 0.327, precision 0.653, F-measure 0.734). In the model ILD, the lowest performance metric of average sensitivity was 0.435. However, specificity and precision are very good (value 1,000 for both) and with F-measure 0.606.

Conclusions:
All used markers indicate oxidative stress in CVID patients. Urinary neopterin and kynurenine seem to be promising predictors of dysregulatory complications, mainly ILD.

POSTER 63 - COMBINATION THERAPY WITH ABATACEPT AND RAPAMYCIN SIGNIFICANTLY IMPROVED INTERSTITIAL LUNG PATHOLOGY IN TWO PATIENTS WITH LRBA DEFICIENCY

AUTHORS

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Biallelic mutations in LRBA (lipopolysaccharide-responsive and beige-like anchor protein) gene result in inborn errors of immunity associated with hypogammaglobulinemia, recurrent infections and autoimmune manifestations. Previous studies showed that abatacept was effective in controlling lymphoproliferation and chronic diarrhea in these patients, but its efficacy on interstitial lung disease (ILD) has rarely been reported.

We described two cases of LRBA deficiency from China. One case involved an 11-year-old girl (P1) with immune thrombocytopenia as the predominant clinical manifestation; the other case was a 16-year-old boy (P2) presenting primarily with chronic diarrhea. Both patients exhibited frequent infections, lymphoproliferation, and reduced immunoglobulin levels. Chest CT scanning of the patients showed bilateral ground-glass opacities and honeycomb-like high density shadow in lungs. Genetic analysis identified novel compound heterozygous mutations in LRBA gene in both patients (P1: c.4339+1G>A and c.3241dupT; P2: c.2799dupC and c.3592delC). LRBA protein was completely abolished in this patient. Flow cytometry revealed decreased frequency of Treg cells and increased Tfh cells. Both patients started intravenous immunoglobulin replacement therapy since the diagnosis of Inborn Errors of Immunity(IEI), but severe pneumonia and interstitial lung pathology were progressing. Then they were treated with abatacept and rapamycin. Both patients showed favorable outcomes after several months of combined treatment with abatacept and rapamycin, particularly in terms of interstitial lung pathology.

ILD has a complex pathogenesis, and a proportion of patients with ILDs may develop a progressive-fibrosing phenotype. For genetically and immunologically defined CVID patients, we can choose more targeted immunotherapy to prevent progression of fibrosis according the immune mechanism.

POSTER 64 - ASSESSING PNEUMOCOCCAL IMMUNITY IN DOWN SYNDROME: A RETROSPECTIVE STUDY OF ANTIBODY TITERS AND CLINICAL OUTCOMES

AUTHORS

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Objective:
Children with Down syndrome (DS) are at increased risk of recurrent respiratory tract infections (RTIs), often resulting in prolonged antibiotic prophylaxis. Despite this burden, immunological evaluation is rarely performed. Pneumococcal polysaccharide conjugate (PnP-C) vaccines have been a part of the Dutch immunization programs since 2006. As a result, depending on year of birth, some individuals in our cohort were vaccinated as part of routine care, while others were not. This study aims to assess pneumococcal antibody titers in DS children and their association with clinical course. Additionally, we evaluated whether a 23-valent ELISA-based IgG test could serve as a practical screening tool to identify individuals with low pneumococcal antibody titers.

Design and method:
We conducted a retrospective cohort study including 62 individuals with DS (212 plasma samples) under the care of a single pediatrician at Máxima Medical Centre (MMC), the Netherlands. Vaccination status was inferred from birth year and clinical records. Pneumococcal IgG antibody titers were measured using a commercial 23-valent polysaccharide-based ELISA and an inhouse developed serotype-specific 23-valent Luminex assay on left-over serum samples. Clinical data on respiratory admissions, antibiotic prophylaxis, and recurrent infections were extracted after informed consent. Associations between antibody titers and clinical factors were analysed using multivariable logistic regression and linear mixed-effects models.

Results:
Of the 62 individuals, 28 had received PnP-C vaccination. Respiratory-related hospitalizations occurred in 22 individuals. Antibiotic prophylaxis was used in 34, including most of those hospitalized. ELISA yielded higher antibody titers than Luminex, especially in vaccinated individuals. Correlation between the assays was strong in unvaccinated participants (R = 0.86) but weaker in vaccinated ones (R = 0.67), suggesting method-dependent differences. Mixed-effects modelling showed that vaccination tended to be associated with higher titers, while history of respiratory admissions was associated with lower titers (Figure 1). These associations were not statistically significant but may reflect clinically relevant patterns.

Conclusions:
Children with DS generate measurable pneumococcal polysaccharide antibody titers, which vary widely and appear to be linked to the clinical course. The ELISA method may offer a cost-effective screening tool to assess immune status and identify individuals with low titers, aiding early identification and guiding targeted care. These findings contribute to optimizing patient stratification and proactive management.

POSTER 65 - CLINICAL TRIAL DESIGN AND SAFETY PROFILE OF HDR EDITED CD4 T-CELLS FOR THE TREATMENT OF HYPER IGM1

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Objective:
We report progress of our academic clinical trial using homology-directed repair (HDR) gene editing for treating Hyper-IgM 1 (HIGM1).

Design and methods:
HIGM1, an X-linked immunodeficiency caused by CD40LG mutations, impairs CD4+ T cell function and has a median survival of 25 years. We developed FT018, an autologous CD4+ T-cell product that was HDR-edited at the CD40LG locus using Cas9 and an integrase-defective lentiviral vector (IDLV) encoding the corrective template and a LNGFR selector. Edited cells restore physiological CD40LG expression, CD40 binding, and signaling.

Results and conclusions:
GLP biodistribution study showed normal behavior of edited cells. No off-target effects were detected by CAST-Seq, Optical Mapping, or target sequencing. Targeted nanopore sequencing revealed a majority of precise intended HDR events and the rest accounted by on-target concatemers not compromising functionality. Conventional single cell tracking tools, such as scRNA-seq, cannot capture genomic outcomes at single cell level, that are mostly transcriptional silent. Therefore, we developed a novel single cell DNA sequencing assay for characterization of editing outcomes at single cell level. We designed an amplicon panel covering the X chromosome, including the target Cas9 site, the donor IDLV template, and nominated off-targets. Three clusters were present in the cell product: 1. Unedited cells, with preservation of the amplicon covering the nuclease target site 2. Precisely edited cells, with no amplification of the nuclease target site and amplification of the repair template 3. Imprecisely edited cells, with no amplification of the nuclease target site and amplification of the repair template and other amplicons mapping onto the donor IDLV, compatible with previously characterized template concatemers. No off-target integrations or on-target large deletions were detected.

We designed a first-in-human, open label, phase I/II clinical trial to evaluate the tolerability and efficacy of FT018 for the treatment of Hyper IgM1, and is anticipated to start at the end of 2025/early 2026, following regulatory approval. We'll enroll patients with a mutation amenable to correction (95% of known mutations) for which HSCT is considered to be high risk. The first patients will be treated with a trial-boost regimen, without lymphodepletion. Dosing adjustments will be considered after treatment of the initial cohort. Endpoints include engraftment, CD40LG restoration, and clinical benefit.

In summary, we report on the advancement of our trial for the treatment of HIGM1 due to start enrolment soon, and present a novel technology for assessment of single cell HDR editing outcomes in clinical settings.

POSTER 66 - ASC SPECK DETERMINATION BY FLOW CYTOMETRY REVEALS CONSTITUTIVE INFLAMMASOME ASSEMBLY IN XIAP DEFICIENCY

AUTHORS

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Objective:
XIAP deficiency (XD) is an inborn error of immunity with clinical features of hyper-inflammation. Over the last years, some experimental evidence pointed towards NLRP3 inflammasome dysregulation as one of the main biological pathways that drives hyperinflammation in XD. In this regard, we decided to evaluate inflammasome assembly using a recently described flow cytometric technique in whole blood from a patient with XD. Materials and methods: 300 uL of whole blood from a XD patient and a healthy control (HC) were lysed with Versalyse reagent for 10 minutes. Cells were washed and divided in 4 tubes: one was left unstimulated while the other 3 were stimulated with LPS 20 ng/mL for three hours followed by stimulation with nigericin 10 mg/mL or ATP 5 mM for 1 hour. Afterwards cells were washed and stained with CD64-VioBlue/CD45-VioGreen/CD16-FITC/CD14-PerCP/HLA-DR-APC/CD19-PC7/CD1c-APC-Fyre770. Next, cells were fixed and permeabilized using Cytofix/Cytoperm/PermWash protocol. Permeabilized cells were stained with ASC-PE for 30 minutes at 4°C, washed and acquired in a FACS-CantoII cytometer. Results were analyzed using inficinicyt software. Results: XD patient showed increased basal ASC-specks in the monocytic/dendritic compartment with respect to the HC (6.22% vs 0.63%). No differences were observed between patient and HC after stimulation with LPS alone or LPS followed by ATP or nigericin. When analyzing the distribution of cells among those with basal inflammasome assembly it was noticed that most of them (64%) belonged to the CD1c+ compartment indicating high number of circulating myeloid dendritic cells with basal inflammasome activation in the patient. Conclusion: These results reveal the existence of a constitutive inflammasome activation in the patient. Moreover, flow cytometry allowed the characterization of these cells indicating that myeloid CD1c+ dendritic cells might play a crucial role in inflammasome activation in XD. Further studies with more XD patients will be needed to confirm these results.

POSTER 67 - EVALUATION OF INFECTIOUS AND INFLAMMATORY CENTRAL NERVOUS SYSTEM INVOLVEMENT IN SYNDROMIC AND NON-SYNDROMIC ADULT

AUTHORS

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Introduction:
CNS involvement is rarely observed in patients with primary immunodeficiency (PID). Ataxia-telangiectasia (AT), Nijmegen breakage syndrome (NBS) or purine nucleoside phosphorylase (PNP) deficiency may be a fundamental part of the syndrome, while CNS involvement secondary to infectious, autoimmune or malignant processes may develop in other PID cases.

Method:
The clinical, immunologic and microbiologic data of 9 cases with inflammatory and infectious involvement of the CNS were analyzed by retrospectively reviewing the files of adult PID cases followed up by Ege University Faculty of Medicine, Department of Adult Immunology.

Results:
The mean age was 35.78 years (±12.82), 6 were female and 3 were male. CNS involvement was presented as infectious in 4 and non-infectious in 5 patients. One of our patients had received anti-TB treatment for 2 years due to tuberculous meningitis at the age of 11. 1 patient was treated for intracranial cryptococcal infection with cryptococcal PCR positivity in CSF analysis. Stenotrophomonas maltophilia and Coagulase Negative Staphylococcus were detected in intraoperative cultures of a female patient with LRBA defect who had spondylodiscitis and paravertebral abscess. Among patients with non-infectious presentation, 1 patient had CNS malignancy (fibroblastic tumor), CNS inflammatory chronic disease (atypical demyelinating disease, Ataxia Telangiectasia, Neuromyelitis Optica, MNGIE syndrome (Mitochondrial neurogastrointestinal encephalomyopathy) and Guillain Barre Syndrome). In WES and CES analyses, COPG1, SLC37A4, ATM, CTLA4, LRBA, Thymidine phosphorylase and UNC119 mutations were detected. Detailed clinical, immunologic and genetic analysis of our patients are presented in Tables 1 and 2.

Conclusion and discussion:
CNS involvement in patients with PID can range from mild cognitive impairment to chronic inflammatory diseases and even malignancies. It is important to perform advanced viral and fungal PCR in CSF analysis in cases of suspected CNS infection; these cases may require lifelong prophylaxis treatment for the responsible infectious agents.

POSTER 69 - A NOVEL CD40L VARIANT PARTIALLY IMPAIRS T-B CELL COOPERATION IN A PRIMARY ATOPIC DISORDER

AUTHORS

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The CD40-CD40L axis is a key immune signaling pathway, whose alteration causes several conditions of inborn errors of immunity (IEI), mostly grouped as hyper-IgM syndromes. However, in accordance with recent reports, disruption of this pathway extends beyond this well-defined IEI. CD40L interacts with integrins-ike α5β1, which stabilizes the CD40/CD40L complex, enhancing downstream signaling and affecting cell adhesion, migration, and tissue remodeling. This interaction is key to immune cell trafficking and inflammation control.

We present the case of a 5-year-old-boy with severe atopic dermatitis since the age of 2 months, requiring both topical and systemic corticosteroids for adequate control. Skin lesions worsened upon several food introductions, leading to a strict elimination diet based on the identified allergens. Immunological work-up revealed mild eosinophilia(760/mcl) and high serum IgE(>2000 mg/dl). Ig levels, standard and extended T and B cell immunophenotype and specific antibody response were appropriate for age. In the investigation for a Primary Atopic Disorder (PAD), genetic analysis detected a hemizygous CD40L variant, the p.Q166R, located within a domain involved in the physical and functional interaction of CD40L protein with α5β1 integrin. Of note, Q166-residue plays a key role in CD154 binding to α5β1, as previously reported [PMID:25403978] and the interaction CD40L-integrin α5β1, in particular the one with the soluble form of CD40L (but also the membrane bound form of it in a cis manner), is involved in inflammation, autoimmunity and thrombosis[PMID:35681441].

We stimulated patient-derived peripheral blood mononuclear cells (PBMCs) to assess B and T cell activation. For direct B cell activation, we used IgM, CD40L+IL-4, or a combination of IgM, CD40L, and IL-4. For T cell activation, we utilized TransAct™, a colloidal polymeric nano matrix conjugated to humanized CD3 and CD28 agonists for optimal T cell activation and expansion. While direct B cell activation was normal, we found a two-fold reduction in T cell-mediated B cell activation and CD154 surface expression showed a one-fourth reduction compared to healthy controls. This case reveals the crucial function of CD40L with α5β1 integrin in T-B cell cooperation in the context of severe allergic manifestations as seen in PADs. Further, understanding of this intriguing interaction in immune regulation may extend the central role of CD40L to a wide range of immune processes, including allergy and inflammation. The early identification of monogenic atopic disorders through immunological, molecular, and functional analyses can significantly enhance patients outcomes and enable further development of targeted therapy in patients with atopic disorders.

POSTER 70 - MECHANICAL VERSUS ELECTRONIC SUBCUTANEOUS INFUSION SYSTEMS: PHASE I REAL-WORLD EVIDENCE ON MECHANICAL INFUSION SYSTEM USABILITY, SAFETY, AND PATIENT EXPERIENCE

AUTHORS

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Objective:
Subcutaneous (SC) infusion pumps are widely used for administration of high-volume therapies. The two primary infusion systems, electronic and mechanical, differ in functionality, training requirements, and user interaction. This study compares patient satisfaction between systems and evaluates ease of use, performance, and safety, including handling, instructions, troubleshooting, discomfort, and pain.

Design and method:
This ongoing, multi-phase, cross-sectional study includes adult and pediatric patients across Europe receiving SC immunoglobulin (IG) therapy for primary or secondary immunodeficiency (PID or SID). Structured questionnaires using a 5-point Likert scale (1 = negative; 5 = positive) are used to collect feedback from two groups: infusion pump-naïve patients (Group 1) and experienced electronic pump users (Group 2). In Phase I, Group 1 evaluated the mechanical system; in Phase II, Group 2 will first evaluate the electronic system and then switch to the mechanical system for comparison.

Results:
Preliminary data from 33 infusion pump-naïve participants using the mechanical system were analyzed. The largest patient group was under 18 years old (39%), followed by those over 55 years old (24%). Out of the 33 participants, most were male (58%), and 29 were diagnosed with PID and four (4) with SID. Almost half of the participants were diagnosed more than five (5) years ago (49%) and 25 participants (76%) had prior intravenous IG treatment. Ratings for set-up and ease of use ranged from 4 to 5 (e.g., simple to very simple) with narrow interquartile ranges, indicating high and consistent satisfaction. Device reliability was rated positively: 70% reported no issues, while 27% noted leakage. No malfunctions were reported.

Overall satisfaction scores were strong with ratings of 4 [4,5] or 5 [5,5] (satisfied to very satisfied). When asked for suggested improvements, 13% requested simplified instructions, while another 13 reported that no improvements were needed.

Regarding safety, several questions related to pain and discomfort during the infusion was asked and median scores for pain and discomfort ranged from 4 to 5 (mild to no pain or discomfort), indicating a favorable user experience and acceptance of the mechanical pump in this population.

Conclusions:
This first head-to-head, real-world comparison of electronic and mechanical SC infusion pumps provides key insights into user experience and satisfaction. Phase I results demonstrate high satisfaction and minimal issues with the mechanical pump. Results from Phase II will offer direct comparison and further inform healthcare providers and pharmaceutical manufacturers in selecting a patient-preferred, high-performing infusion system.

POSTER 71 - AUTOIMMUNE POLYENDOCRINE SYNDROME TYPE 1 ASSOCIATED WITH LARGE GRANULAR LYMPHOCYTIC LEUKEMIA AND GASTRIC NEUROENDOCRINE TUMOR

AUTHORS

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Objective:
To describe a rare association of Autoimmune Polyendocrine Syndrome Type 1 (APS-1) with two malignancies. The autoimmune regulator (AIRE) gene encodes a transcription factor that is crucial for the negative selection of self-reactive T cells in the thymus. When AIRE is mutated, this process is disrupted, leading to the survival of autoreactive T cells causing APS-1, also known as Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED).

Designe and method:
Direct sequencing of the AIRE gene in this patient revealed a homozygous R257X mutation resulting in a truncated, nonfunctional AIRE. Patient s parents had the same heterozygous mutation. In the patient's serum, we detected several autoantibodies by indirect immunofluorescence and ELISA (antiadrenal, antiparietal, antinuclear, liver-profile antibodies).

Results:
A 39-year-old female patient had a history of chronic bronchitis, onychomycosis, enamel hypoplasia, and oral candidiasis during childhood. At the age of 15 years, she developed hypoparathyroidism and autoimmune hepatitis which suggest possibility of APECED. At the age of 18 years, she was diagnosed with Addison's disease and pernicious anemia, while at 35 years, she developed a gastric neuroendocrine tumor which was surgically removed. At the of 37 years, the patient developed vaginal condilomas, labial herpes and transfusion-dependent macrocytic anemia (Hgb 84g/L, MCV 111fL) despite parenteral B12 supplementation, accompanied by severe leukolymphocytosis (Leukocytes 46.1×109/L, Lymphocytes 39×109/L). Peripheral blood lymphocyte immunophenotyping (T-Ly CD3+ 99%, T-Ly CD4+ 2%, T-Ly CD8+ 97%, CD4/CD8 index 0,02, NK-Ly CD3-56+ 0.2%, B-Ly CD19+CD20+ 0.5%), bone marrow biopsy and investigation of T-cell receptor clonality showed T-cell large granular lymphocytic leukemia (LGLL). The therapy with mycophenolate-mofetil (2x750 mg) and prednisone (10 mg/day) was introduced and led to significant clinical and laboratory improvement (Leu 11.9×109/L, Lymph 10×109/L, Hgb 104g/L, MCV 107fL).

Conclusions:
Mutations in the AIRE gene impair normal immune tolerance mechanisms, enabling the persistence of autoreactive T cells, which contribute to multiple organ-specific autoimmune diseases and malignancies. Permanent clonal expansion may drive hematologic malignancies, such as LGLL. Consequently, patient monitoring is mandatory and initiating immunosuppressive therapy on time is essential for the prognosis of malignancies in APS-1 patients.

POSTER 72 - INTRAVENOUS IMMUNOGLOBULIN (IVIG) REPLACEMENT THERAPY IN ASYMPTOMATIC PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY, YES OR NO?

AUTHORS

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Title:
Intravenous immunoglobulin (IVIG) replacement therapy in asymptomatic patients with common variable immunodeficiency, yes or no?

Objective:
Common Variable Immunodeficiency (CVID) is the most frequently diagnosed primary immunodeficiency. It is characterized by reduced serum levels of immunoglobulins in at least two classes, most commonly IgG and either IgA or IgM. The clinical picture is typically dominated by recurrent infections, but autoimmune, gastrointestinal, respiratory, and malignant complications are also common. The cornerstone of treatment is immunoglobulin replacement therapy. Genetic evaluation is essential for better understanding and targeted management of the disease.

Methods and results:
We report the case of a 13-year-old boy who presented with immune thrombocytopenic purpura. During evaluation in the hematology department, laboratory tests revealed low levels of immunoglobulins IgA and IgG. The complete blood count showed a platelet count of 3×10^9/L and a decreased absolute lymphocyte count. Abdominal ultrasound revealed splenomegaly for his age. He was treated with intravenous immunoglobulin and corticosteroids.

Immunophenotyping of peripheral blood lymphocytes revealed an expanded population of double-negative T cells, while other lymphocyte subpopulations were within reference ranges. B lymphocytes were polyclonal. Autoimmune disease screening was performed.

The patient had no history of frequent or severe infections. However, genetic testing confirmed a mutation in the NFKB1 gene (monogenic common variable immunodeficiency). Despite the absence of clinical infectious manifestations, immunoglobulin replacement therapy was initiated with the aim of achieving immune regulation.

Conclusions:
Autoimmune manifestations can be the initial and sometimes the only clinical presentation of common variable immunodeficiency. Therefore, serum immunoglobulin levels should be assessed as part of the diagnostic workup in such cases. When immunodeficiency is suspected, genetic evaluation is recommended, as it enables a more individualized therapeutic approach and a deeper understanding of disease mechanisms and severity.

When we understand the genetic basis of disease, we can use that information to predict disease severity and the approach to clinical management.

As time goes by, we have yet to discuss can we distinguish common variable immunodeficiency from common variable immunodeficiency like entity without genetic testing and should all these patients get immunoglobulin replacemenet therapy.

POSTER 73 - THE PREVALENCE OF CYTOMEGALOVIRUS INFECTIONS AMONG PATIENTS WITH SEVERE COMBINED IMMUNODEFICIENCY (SCID) IN MOROCCO

AUTHORS

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Introduction:
Patients with SCID at risk of cytomegalovirus (CMV) infection are generally asymptomatic. Its frequency on an international scale is between 40 and 90%. SCIDs present a unique challenge in the diagnosis and management of cytomegalovirus infection.

Aim:
Describing the clinical importance and biological translation of CMV infection in SCID patients.

Material and method:
A retrospective descriptive study, carried out within the infectious diseases and clinical immunology department at the Abderrahim El Harrouchi Mother-Child Hospital in Casablanca. all patients included present severe combined immunodeficiency (SCID) with positive cytomegalovirus PCR, over a period (2007-2023).

Results:
Thirty-eight SCID-CMV positive patients out of seventy-three patients, whose prevalence is 52%. The average age was 3 months [1-24]. The F/M sex ratio = 1.23 with a female predominance. Consanguinity was noted in 12 patients (31.57%), The clinical expression was dominated by respiratory infections in 33 patients (87%) in which pneumonia was confirmed by TDM, followed by diarrhea in 25 patients (66%), and neurological deficits in 5 patients (14%). The phenotypic distribution of the SCID class was dominated by SCID T- B- NK+ (29%).

Our case series demonstrated 4 cases of Omenn syndrome, followed by 2 cases of RAG1/2, 1 case of ADA deficiency, and JAK 3. 19 SCID patients with positive CMV (50%) died.

Conclusion:
The clinical expression of cytomegalovirus involvement in severe combined immunodeficiency is very heterogeneous, which implies that PCR must be performed for each suspicion, Treatment with Ganciclovir is generally effective and should be continued until PCR is negative.

POSTER 74 - DIAGNOSTIC EVALUATION OF PATIENTS WITH FINDINGS OF AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME USING IN VITRO APOPTOSIS TESTING

AUTHORS

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Introduction:
Autoimmune Lymphoproliferative Syndrome (ALPS) is a prototypical immune dysregulation disorder, marked by chronic, nonmalignant lymphoproliferation (manifesting as persistent lymphadenopathy and splenomegaly), immune-mediated cytopenias, and an elevated risk of lymphoma. The underlying pathophysiology involves defective Fas-FasL-mediated apoptosis, making impaired apoptotic mechanisms a central contributor to disease development.

Aim:
This study aims to evaluate the diagnostic utility of the in vitro apoptosis assay by analyzing its performance in patients presenting with ALPS or ALPS-like clinical features.

Patients and method:
The study population comprised patients who presented to our clinic between February 2022 and January 2023 with either unexplained lymphadenopathy and/or splenomegaly persisting for more than six months in the absence of infection or malignancy; or with multiple autoimmune manifestations suggestive of cytopenia and/or immune dysregulation, or elevated serum vitamin B12 levels. Inclusion also required DNTs exceeding 2.5% as determined by flow cytometric analysis. These patients, along with a control group of 20 healthy individuals, were assessed using an in vitro apoptosis assay.

Results:
The median age at diagnosis among the 20 patients included in the study was 11 years (range: 2.5–37 years), with a male predominance of 70%. Clinical evaluation revealed that 75% of patients had a history of autoimmunity, 60% exhibited lymphoproliferation, 35% had recurrent or chronic infections, and 10% had allergic disease (Table 1). Based on the established diagnostic criteria for ALPS, 11 patients fulfilled the criteria for probable ALPS, while the remaining 9 were categorized as having ALPS-like disease (Figure 1). In vitro apoptosis testing was performed on peripheral blood lymphocytes from all patients and 20 healthy controls. Defective apoptosis was observed in two patients—one with a homozygous FAS variant confirming ALPS, and the other with a homozygous CASP8 variant indicating ALPS-like disease. Genetic analysis revealed pathogenic variants in six patients; however, four of them, despite having ALPS or ALPS-like diagnoses, showed normal apoptosis test results (Table 2)

Discussion:
Although all patients were clinically suspected of ALPS, only two showed defective apoptosis in the in vitro assay. The test may be influenced by concurrent medications, underscoring the need for repeated assessments under standardized conditions. Genetic analysis revealed ALPS- or ALPS-like–associated variants in 6 of 20 patients, yet four of them had normal apoptosis results. This highlights the limitations of the assay and the importance of integrating genetic testing. These findings call for further research to refine diagnostic criteria and enhance the accuracy of ALPS diagnosis.

POSTER 75 - THE DOMINANT SIDE OF IMMUNE-DYREGULATION IN TWO CASES WITH NOVEL BTK VARIANTS

AUTHORS

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Objective:
Bruton's tyrosine kinase (BTK) is a crucial regulator of B-cell development, differentiation and activation. Loss-of-function variants are typically associated with X-linked agammaglobulinemia (XLA), a condition characterized by severe B-cell deficiency and increased susceptibility to infections.

Design and method:
We report two male patients (pt1 and pt2) with different hemizygous BTK variants. Pt1 is a 31-year-old male with a history of recurrent upper and lower respiratory tract infections, along with late-onset immune dysregulation manifesting as primary sclerosing cholangitis and chronic pancreatitis. Pt2 is a 2-year-old male with relapsing warm autoimmune hemolytic anemia (AIHA) that is steroid-dependent and responsive to rituximab. The immunological evaluation of pt1 revealed normal B-cell counts at an early age, which later declined to 2% with low IgA and IgM. In contrast, pt2 showed normal immunological profile with normal B cells value and immunoglobulin levels.

Genetic analysis identified a hemizygous BTK variant:
c.946A>G p.Thr316Ala in pt1 and c.941A>G p.Lys314Arg in pt2, both of uncertain significance (VUS) located within the SH2 domain of the protein. Given the unique characteristics of our patients, BTK expression and function were analyzed.

Results and conclusions:
We observed normal BTK expression levels in the lymphoblastoid cell lines (LCL) from both patients. However, in response to hydrogen peroxide (H2O2) stimulation, we detected increased phosphorylation of BTK protein at positions Y223 and Y551. The p-BTK Y223 alteration was noticeable at various time points, starting five minutes after stimulation and persisting up to 60 minutes compared to healthy control. Similarly, ERK phosphorylation was observed at the five-minute mark and remained consistent in both patients. The p-BTK Y551 phosphorylation was congruent with previous data.

Our findings are in favor of a gain-of-function (GOF) mechanism suggested by the normal level of BTK expression and its increased and permanent phosphorylation upon stimulation. Further knowledge of the pathogenic mechanisms might widen the scenario of BTK-related disorders beyond the traditional XLA and emphasize the role of immune dysregulation as expression of disease. A GOF effect could have significant implications for counseling, clinical follow-up, and the optimization of therapeutic interventions, especially considering that somatic variants in the SH2 domain of BTK have been shown to confer resistance to ibrutinib.

POSTER 76 - EXPOSURE-RESPONSE ANALYSIS OF THE EFFICACY AND SAFETY OF IMMUNOGLOBULIN THERAPIES IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

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Objective:
To evaluate the relationship between exposure and clinical efficacy and safety outcomes of immunoglobulin (Ig) therapies for the treatment of primary immunodeficiencies (PID).

Design and method:
In this exploratory analysis of Ig therapies (intravenous Ig [IVIG] 10%, subcutaneous Ig [SCIG] 20% and hyaluronidase-facilitated subcutaneous Ig [fSCIG] 10%), pharmacokinetic (PK), efficacy and safety data were included from three phase 2/3 clinical trials of paediatric and adult patients with PID (NCT00814320 [N = 89], NCT01412385 [N = 55] and NCT01218438 [N = 86]). The relationship between immunoglobulin G (IgG) PK exposure parameters (including serum trough concentration [Ctrough], weekly area under the curve [AUC] and maximum serum concentration [Cmax]), and efficacy outcome measures (including annual rate of infection and proportion of participants with ≤ 1 infection/year) was evaluated. The relationship between IgG exposure and anti-tetanus antibodies (Ab) was also explored. IgG PK parameters were evaluated for their association with the most commonly experienced adverse events (AEs) of at least moderate severity (AEs affecting ≥ 5% of participants).

Results:
No relationship was observed between the annual rate of infection and IgG Ctrough, weekly AUC or Cmax (Figure 1). More participants who received IVIG 10% than SCIG 20% or fSCIG 10% experienced ≤ 1 infection/year (e.g. 36.2% [IVIG 10%] vs 16.7% [fSCIG 10%] in trial NCT00814320). However, no trend was observed between the annual rate of infection and Ctrough when analysed based on this threshold (Figure 2). A trend was observed between weekly IgG AUC and weekly anti-tetanus Ab AUC, but there was no relationship between anti-tetanus Ab and annual rate of infection (Figure 3). The most commonly experienced AEs of at least moderate severity by system organ class were gastrointestinal, nervous system, musculoskeletal and connective tissue, skin and subcutaneous tissue and general disorders and administration side effects. There was no apparent relationship with IgG exposure parameters for the AEs investigated (data for gastrointestinal disorders presented in Figure 4).

Conclusions:
This exploratory analysis found no significant relationship between IgG exposure measures and efficacy or safety outcomes across therapies. This is likely due to consistent IgG exposure and stable efficacy and safety profiles throughout the study periods. These results underscore that maintaining stable IgG exposure preserves the efficacy of Ig treatment in patients with PID, and thereby support the effectiveness and safety of current dosing regimens of Ig therapies in managing PID.

Study/medical writing funding:
Takeda Development Center Americas, Inc./Takeda Pharmaceuticals International AG.

POSTER 77 - TREATMENT EXPERIENCES DURING THE INITIATION OF HOME-BASED SUBCUTANEOUS IMMUNOGLOBULIN THERAPY USING A CUSTOM INTERACTIVE VOICE ASSISTANT SUPPORT

AUTHORS

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Objectives:
Voice assistant technology can provide real-time, hands-free access to therapy information and administration instructions to support patients in managing health conditions. Key objectives of this study (NCT06150534) were to generate insights into the patient/caregiver experience with initiating home-based subcutaneous immunoglobulin (SCIG) and to evaluate the usability of, and satisfaction with, a newly developed interactive voice assistant support application.

Design and method:
This US-based qualitative, non-interventional study aimed to include up to 13 patients (aged ≥ 18 years initiating self-administered SCIG for primary immunodeficiency disease [PID] within 4–6 months before or 30 days after enrolment), 13 caregivers, and 10 healthcare professionals (HCPs) experienced in the treatment of PID. Before receiving access to the voice assistant (Alexa Skill via Amazon Echo Show device), semi-structured interviews were conducted with patients/caregivers to identify key themes related to experiences with home-based SCIG. After an application-use period, (patients/caregivers, 2–3 months; HCPs, 1–2 weeks), debriefing interviews captured insights into user experience and satisfaction during SCIG initiation and identified areas for application improvement.

Results:
Between 11 January 2024 and 25 February 2025, four patients, one caregiver and eight HCPs (five nurses, three physicians) completed the study. All patients/caregivers reported receiving training for self-infusion of SCIG before the study. Mean (standard deviation) age of enrolled patients was 50.0 (17.0) years and three (75%) were women. Patients reported that the voice assistant provides useful reminders (e.g. hand-washing, loading medication completely) and overall reassurance about self-infusions. Patients preferred hands-free video instructions (via the voice assistant) to printed instructions when preparing and/or administering SCIG. HCPs appreciated the potential for the Alexa Skill to improve patient experience and reduce HCP burden. HCPs recommended incorporating additional video and image content, and broadening the range of phrases that can be used to perform each command. Patients/caregivers also suggested improvements to the application, including expansive and reliable verbal commands, additional instructions for navigating the Alexa Skill, more video and image content, specific guidance on various aspects of the infusion process, and versions tailored to user-level experience, demonstrating a high-degree of engagement with the platform. Most participants who completed the study would recommend the application.

Conclusions:
Interactive digital technologies may facilitate the transition to and compliance with self-administration of SCIG at home following training from an HCP. Video and images may be key attributes for such technologies. Study/medical writing funding: Takeda Development Center Americas, Inc./Takeda Pharmaceuticals International AG.

POSTER 78 - EVALUATION OF THE PIDCAP SCORING SYSTEM IN PATIENTS DIAGNOSED WITH CHRONIC GRANULOMATOUS DISEASE

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Introduction:
PIDCAP is a newly developed, expert-guided scoring system designed for use in primary care settings. It is based on an expanded set of warning signs derived from the original “10 Warning Signs” and aims to prevent delays in the recognition and diagnosis of inborn errors of immunity (IEIs). While PIDCAP may facilitate earlier diagnosis, its overall performance has been reported to be limited.

Objective:
This study investigated whether the PIDCAP scoring system successfully identifies patients with a confirmed diagnosis of chronic granulomatous disease (CGD) within its scoring framework.

Method:
Patients diagnosed with CGD between 2011 and 2025 were retrospectively included in this study. The diagnosis was confirmed through dihydrorhodamine (DHR) testing and/or genetic analysis. Clinical data at the time of initial evaluation were used to determine PIDCAP scores. Severity classification according to the scores is detailed in Table 1.

Results:
A total of 70 patients were included in the study. Among them, 65.7% (n=46) were male. The median age at diagnosis was 3.8 years (range: 1.9–9.3 years). According to the PIDCAP scores, 81.4% of the patients (n=57) were classified as high risk, 12.8% (n=9) as moderate risk, and 5.7% (n=4) as low risk.

The most frequently observed warning signs in the high-risk group included “Consanguinity or other family history compatible with manifestations of IEI” (70%), “Failure to thrive” (58%), and “≥ 3 episodes of pneumonia” (38%).

Table 2 represents the 27 warning signs included in the scoring system along with their respective weights and patient distribution by risk categories.

Discussion:
The results indicate that the PIDCAP scoring system shows promise in the evaluation of patients with CGD. Although the findings suggest potentially high specifity, they should be interpreted with caution, as our center is a referral institution and tends to receive more severe cases. More definitive conclusions require larger studies involving patients from primary care settings.

POSTER 79 - LYMPHOPROLIFERATIVE DISORDERS AND LYMPHOMA RISK: A COMMON VARIABLE IMMUNODEFICIENCY CASE

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Introduction:
Common variable immunodeficiency(CVID) is the most prevalent symptomatic primary immunodeficiency in adults, characterized by hypogammaglobulinemia and defective antibody production.Lymphoproliferation,defined as abnormal lymphocyte proliferation, is a common feature in CVID and is associated with various clinical manifestations, including autoimmune diseases, lymphoid hyperplasia, and an increased risk of lymphoma. In this report,we present a case of a patient with CVID who was found to have generalized lymphadenopathy(LAP).

Case Presentation:
A 36-year-old female patient was under follow-up in the hematology department for immune thrombocytopenic purpura when hypogammaglobulinemia was detected during her evaluation.She was referred to our clinic,and further investigations revealed impaired vaccine antibody responses, decreased CD16/56+ and CD19+CD27+IgD- switched memory B cell levels,and the presence of a TNFRSF13B mutation,leading to a diagnosis of CVID. During follow-up, radiological imaging revealed LAPs larger than 1 cm in the cervicojugular, thoracic, and abdominal regions, prompting an excisional biopsy of the cervical lymph nodes. The histopathological analysis indicated “reactive lymph nodes with follicular hyperplasia.” A joint assessment with the hematology department led to the decision for clinical follow-up.Six months later, new LAPs were identified in follow-up imaging, leading to a second excisional lymph node biopsy, which yielded similar pathological findings.Given the absence of high-risk LAP characteristics and B symptoms,PET/CT was performed, revealing LAPs with moderate FDG uptake.The hematology team decided to continue close follow-up due to the lack of malignancy indicators.

Discussion and conclusion:
Lymphoproliferation plays a critical role in the development of lymphomas in CVID.The presence of polyclonal lymphoid infiltrates increases the risk of lymphoma development in CVID by fivefold.Furthermore,the progression of lymphoproliferation may be associated with B-cell instability, contributing to lymphoma development in CVID. In conclusion,lymphoma development in CVID involves a multifaceted process,including immune dysregulation, genetic susceptibility, and lymphoproliferation. Further research is warranted to elucidate the underlying mechanisms and develop effective strategies to reduce lymphoma risk in CVID patients.

POSTER 80 - PERSPECTIVES AND EXPERIENCE OF EAR, NOSE, AND THROAT SPECIALISTS (ENT) ON DIAGNOSING, TREATING, AND MANAGING PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISORDERS (PIDD): A US AND CANADA SURVEY

AUTHORS

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Background:
Primary immunodeficiency disorders (PIDD) are caused by inherited defects in the immune system. Patients with PIDD often present recurrent and chronic ear, nose, and throat infections. Early diagnosis prevents complications, improving morbidity and quality of life.

Objective:
Assess ear, nose, and throat specialists' (ENT) awareness and experience in diagnosing and treating PIDD.

Design and method:
A US and Canada blinded survey with 34 questions evaluated ENTs' experience, collaboration with other specialists, challenges, and interest in educational opportunities related to PIDD.

Results:
50 US-based and 21 Canada-based ENT participated in the survey. Most ENT (74% for US and 81% for Canada) encountered patients with PIDD with frequent, severe, and/or unusual infections, but only 20% reported adherence to specific clinical guidelines, 5-12% were aware of recent research, and between 20-38% never engaged with PIDD educational opportunities. These data highlight a clear gap between the number of diagnosed PIDD patients and guidelines awareness in both countries. ENT preferred intravenous immunoglobulin (IVIg) therapy (65% for US, 67% for Canada) rather than subcutaneous immunoglobulin (SCIg) (22% for US, 17% for Canada). Although prophylactic antibiotics were frequently used in both countries, US respondents almost doubled their use as compared to Canadian ones (60% vs 38%, respectively). Ig replacement therapy (IgRT) efficacy was assessed by infection frequency (89%, US; 67% Canada), and symptom improvement (74% US; 50% Canada). Most respondents (89% US; 78% Canada) tested IgG levels, but only 51% knew target trough IgG levels and dosing schedules in the US. Interestingly, these values dropped to 22% and 39%, respectively, for Canadian respondents. ENT referred patients with PIDD to clinical immunologists rather than hematologists. The challenges faced by ENT varied based on their practicing regions. In the US, where 60% of ENT were based in suburban or rural areas, the main challenges included limited access to specialist referral, financial obstacles to have their treatment publicly covered, and knowledge gaps regarding PIDD management. In contrast, only 24% of Canadian ENT practiced in similar regions, and their primary challenges were related to access to immunodiagnostic. Most respondents expressed interest in case-based learning formats for PIDD education.

Conclusion:
These findings revealed a significant gap in guideline adherence and PIDD-related knowledge among ENT in both US and Canada, despite frequent encounters with PIDD patients. Enhancing PIDD-targeted education of ENT may improve multidisciplinary collaboration, PIDD diagnostics and patient care. The barriers in diagnosing and treating PIDD patients varied by region.

POSTER 81 - RISK OF ATRIAL FIBRILLATION IN PRIMARY IMMUNODEFICIENCIES: EVALUATION OF ATRIAL ELECTROMECHANICAL CONDUCTION TIMES AND P WAVE DISPERSION

AUTHORS

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Objective:
Primary immunodeficiency diseases (PIDs) are an expanding group of rarely seen immune system disorders. Various clinical conditions like autoimmunity, immune dysregulation and inflammation could affect multiple organ systems in PID patients. The heart may be one of these organs; however, studies on this topic are rare. Atrial fibrillation (AF) is a significant cause of mortality and morbidity in the community and an increased P-wave dispersion (PWD) and atrial electromechanical delay (AED) are well-known markers indicating a predisposition to AF. We aimed to determine whether AED and/or increased PWD predict the early risk of AF in PID patients.

Design and method:
This single-center, prospective controlled study included 61 PID and 60 control group patients. All participants underwent resting electrocardiography, echocardiography and atrial electromechanical conduction time (AECT) monitoring using tissue Doppler imaging evaluated by an experienced cardiologist.

Results:
The PID group had a statistically significantly higher Pmax, Pmin and PWD values compared to the control group [102(92-108) vs. 88(82-99) ms, $p<0.001$; 74(70-80) vs. 68(62-72) ms, $p<0.001$; 26(22-30) vs. 21(18-26) ms, $p=0.001$; respectively]. Right atrial delay and interatrial delay were found to be statistically significantly higher in PID group [4(2-6) vs. 2(2-4) ms, $p<0.001$; 6(4-8) vs. 4(4-6) ms, $p=0.039$; respectively]. Left atrial delay was also found to be higher in the PID group, although this difference wasn't statistically significant (6(4-6) vs. 4(3-6) ms; $p=0.05$)(Table 1, Figure 1).

Conclusion:
We have shown that the well-known predictors of AF; AECT and PWD were increased in PID patients. This result will aid in the follow-up and survival of PID patients, who experience multiple complications, by enabling the early identification of AF-related mortality and morbidity risk.

POSTER 82 - ATYPICAL IMMUNE DYSREGULATION IN A CHILD WITH A NOVEL BTK VARIANT: DIAGNOSTIC AND THERAPEUTIC PITFALLS OF A POTENTIAL GAIN-OF-FUNCTION-RELATED INBORN ERROR OF IMMUNITY

AUTHORS

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Objective:
To analyze the diagnostic and therapeutic pitfalls in the management of a pediatric patient with suspected inborn error of immunity (IEI) due to a likely gain-of-function (GOF) variant in Bruton's tyrosine kinase (BTK). While BTK loss-of-function variants are typically linked to X-linked agammaglobulinemia (XLA), this case presents an atypical phenotype.

Design and method:
Our 2-year-old male patient presented with early-onset, steroid-dependent, rituximab-responsive but relapsing warm autoimmune hemolytic anemia (AIHA) with high-titre (1:256) of anti-IgG1/IgG3/C3d auto-antibodies. The first AIHA episode occurred approximately 6 weeks after concomitant administration of MMRV and Men-ACWY vaccines.

Despite immunologically normal B-cell counts and immunoglobulin levels—atypical for XLA—genetic analysis revealed a hemizygous BTK variant (c.941A>G p.Lys314Arg) of uncertain significance (VUS) in the SH2 domain. BTK expression was normal on lymphoblastoid cell lines; however, BTK phosphorylation at Y223 and Y551, and ERK phosphorylation, were increased following H2O2 stimulation, supporting a gain-of-function (GOF) hypothesis.

He showed a normal T-cell distribution-including recent thymic emigrants- and function, excluding combined immunodeficiency (CID).

After three months under steroid therapy and following a rituximab cycle, the patient developed P. jirovecii pneumonia requiring mechanical ventilation. No prophylactic trimethoprim-sulfamethoxazole (TMP-SMX) had been initiated, despite ongoing immunosuppression with steroids >20 mg/day and rituximab.

The patient currently remains on monthly rituximab and immunoglobulin replacement therapy, with no recent AIHA relapses.

Results and conclusions:
This case broadens the phenotypic spectrum of BTK-related disorders, suggesting a BTK GOF mechanism may drive immune dysregulation in the absence of agammaglobulinemia. It underscores the importance of early prophylactic strategies when a prolonged immunosuppression is ongoing even if T cell comportment resulted normal. Furthermore, a broader empirical antibiotic regimen including TMP-SMX might have been warranted at the onset of respiratory failure and interstitial findings in a setting of iatrogenic immunosuppression, even in the absence of a confirmed IEI. Although post-vaccine AIHA is rare compared to immune thrombocytopenia—especially post-MMR—the temporal association suggests that in genetically predisposed individuals, immunization with live vaccines may act as a trigger for immune dysregulation, as can also occur with infections. Finally, BTK inhibitors may represent a therapeutic option in similar GOF settings, though ibrutinib resistance associated with SH2 domain variants should be considered in clinical decision-making.

POSTER 83 - UNEXPECTED GENETICALLY DETERMINED IMMUNE DYSREGULATION WITH LIVER INVOLVEMENT: THERAPEUTIC DILEMMAS BETWEEN TARGETED THERAPY AND HEMATOPOIETIC STEM CELL TRANSPLANTATION

AUTHORS

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Objective:
GIMAP-5 is a lymphoid-specific GTPase essential for T cell survival and homeostasis. Its deficiency impairs lymphocyte survival, promotes endothelial dysfunction, and may dysregulate mTORC1 signaling. Biallelic pathogenic variants cause a rare autosomal recessive IEI marked by immune cytopenias, benign/malignant lymphoproliferation, and hepatic involvement (portal hypertension, cirrhotic degeneration, nodular hyperplasia, autoimmune hepatitis), often without severe infections.

Design and method:
We report an 11-year-old boy with compound heterozygous likely pathogenic GIMAP-5 variants, illustrating diagnostic and therapeutic dilemmas between targeted therapy and HSCT.

Results:
At age 10, he presented with febrile pneumonia and persistent neutropenia. Soon after, he developed thrombocytopenia resistant to high-dose IVIG but responsive to steroids, with concurrent high-load Parvovirus B19 (1,225,700 copies/mL) and EBV viremia (50,309 copies/mL). Neutropenia gradually resolved, but thrombocytopenia relapsed six months later with severe bleeding (epistaxis, hematuria, gingival haemorrhage), associated with a positive direct antiglobulin test but no haemolysis, EBV reactivation (1,755 copies/mL), and JC virus-associated hemorrhagic cystitis (6,844,525 copies/mL in urine). Bone marrow biopsy and aspirate supported a peripheral origin of cytopenia. Blood tests showed blood loss anemia and lymphopenia. Immunophenotyping revealed reduced CD4+ T-cells and expansion of CD19+CD38−CD24−CD21−CD27dim/− memory B-cells (15%).

Again IVIG-resistant, it was started a 4-dose course of Rituximab, which proved ineffective for thrombocytopenia, requiring concomitant treatment with high-dose corticosteroids.

WES identified compound heterozygous likely pathogenic variants in GIMAP-5: c.611T>C (p.Leu204Pro) and c.640C>T (p.Arg214Ter), the former previously described in the index patient.

In light of these findings, the patient underwent hepatological evaluation, and liver ultrasound showed hepatosplenomegaly, parenchymal heterogeneity, and signs of endothelial activation.

Due to the identified mutation, eltrombopag and sirolimus were started yielding complete response. HSCT is being evaluated, with the healthy heterozygous twin considered as a potential donor.

Following corticosteroid taper, the patient is currently on sirolimus and eltrombopag, with normalized platelet count (159,000/mm³) and mild hypertransaminasemia.

Conclusions:
This case highlights the hematologic and endothelial complexity of GIMAP-5 deficiency. While sirolimus may achieve hematologic control by inhibiting mTORC1 signaling and HSCT is indicated in IEI with refractory cytopenias

the impact of these therapeutic interventions on the hepatic condition is not yet known. From this perspective, treatment with GSK3β inhibition (e.g., tideglusib), currently under investigation in pediatric neuromuscular trials, may offer a bridging or adjunctive option, given its mechanistic link to GIMAP-5.

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POSTER 84 - AN ANALYSIS OF PLASMA-DERIVED MEDICINAL PRODUCTS USAGE IN THE CZECH REPUBLIC

AUTHORS

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Objectives:
Plasma proteins play an essential role in the treatment of various serious and life-threatening diseases. Many of them are listed in the EU list of critical medicines (the EU list. This research seeks to analyze the availability of plasma-derived medicinal products (PDMPs) and related trends in the Czech Republic over time.)

Design & methods:
In 2024, the administrative claims data were extracted from healthcare insurance databases, covering the period 2012-2022. The data enabled us to combine therapeutic indications with the number of patients treated with specific PDMPs and to demonstrate changes in their usage over time.

Results:
In 2022, there were 21 PDMPs authorized in the Czech Republic, of which 11 were listed in the EU list. The number of patients treated with plasma proteins has nearly doubled since 2012, counting 61 756 patients in 2022, of whom 87% patients were treated with a PDMP type listed in the EU list. The prediction for 2023 forecasted this number to reach nearly 63 000 patients.

For 21 PDMPs we identified 32 therapeutic indications claimed to be reimbursed by the healthcare insurance system, such as replacement therapy for immunodeficient patients (6 626 patients), immunomodulatory therapy for autoimmune disorders (3 110 patients) and various types of prevention and treatment of hemorrhage (7 590 patients).

In 2022, the most frequently used plasma proteins were human albumin (used for blood volume regulation) and “anti-D (Rh0) immunoglobulin” (used for prevention of RhD isoimmunization), prescribed to 17 973 and 16 861 patients, respectively. The numbers were slightly lower than in 2021, when there were over 18 000 patients treated with albumin and with anti-D (Rh0) immunoglobulin as well.

Conclusion:
In 2022, approximately 62 thousand patients were treated with PDMPs in the Czech Republic, almost double when compared to 2012. While demand has been increasing, shortages still occurred. Thus in 2023, there were supply shortages for 10 of the 19 types of plasma proteins, with some of them being completely unavailable on the market. The most significant shortages were recorded for immunoglobulins (8 out of 12 brands) and albumin (all 6 brands).

Moreover, international market research shows that the immunoglobulin consumption in the Czech Republic has been below European average. Therefore, there is a clear need from a patient perspective to enhance the adequate availability of PDMPs for Czech patients.

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POSTER 85 - COMPARISON OF CLINICAL FEATURES IN PRIMARY IMMUNODEFICIENCY PATIENTS WITH AND WITHOUT AUTOIMMUNITY OR AUTOINFLAMMATION

AUTHORS

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Background:
Primary immunodeficiencies (PIDs) are a heterogeneous group of disorders characterized by impaired immune function. While infections are the hallmark feature, non-infectious complications such as autoimmunity, autoinflammation, lymphoproliferation, and malignancies are also increasingly recognized. Autoimmune manifestations can include cytopenias, endocrinopathies, hepatitis, enteropathies, and systemic involvement. Autoinflammatory features typically involve periodic fevers, rash, mucosal inflammation, and serositis in the absence of infection or malignancy. These immune dysregulation patterns may appear at any point during the disease course and may contribute to morbidity and diagnostic delay. However, comparative studies evaluating the clinical profiles of PID patients with versus without such manifestations remain limited.

Objective:
To determine the prevalence of autoimmune and autoinflammatory features in patients with PID, compare their clinical, laboratory, and immunological characteristics, and assess potential prognostic differences.

Methods:
A total of 130 adult PID patients followed in a tertiary university immunology clinic were retrospectively analyzed. Based on clinical findings, patients were categorized into three groups:

• **Group 1:** No autoimmune or autoinflammatory findings

• **Group 2:** Presence of autoimmune manifestations (e.g., autoimmune cytopenia, thyroiditis, hepatitis, alopecia, type 1 diabetes, celiac disease)

• **Group 3:** Presence of autoinflammatory features (e.g., familial Mediterranean fever, Behçet disease, inflammatory bowel disease, NLRC4 mutation)

Data on demographics, laboratory parameters, immunoglobulin levels, lymphocyte subsets, switched memory B cells, and genetic mutations were collected. Statistical comparisons were performed using non-parametric and categorical tests with Bonferroni correction for post-hoc analysis.

Results:
Autoimmunity was observed in 32.3% and autoinflammation in 9.2% of patients. Group 3 showed significantly higher levels of CRP, ESR, and fibrinogen ($p < 0.05$), reflecting heightened systemic inflammation. Platelet counts were significantly lower in Group 2, possibly due to autoimmune cytopenias ($p = 0.001$). Serum IgE levels were significantly reduced in autoimmune patients ($p = 0.007$), while IgG, IgA, and IgM did not show significant differences. Switched memory B cells ($CD19^+CD27^+IgD^-$) were markedly lower in Group 2 ($p = 0.005$), supporting their association with autoimmune susceptibility. No significant differences in genetic mutation types or mortality were observed across the groups.

Conclusion:
Autoimmune and autoinflammatory manifestations are prevalent among PID patients and are associated with distinct inflammatory and immunological patterns. Low IgE and reduced switched memory B cells may serve as useful markers for early identification of autoimmunity. Routine screening for immune dysregulation should be

integrated into the diagnostic and long-term management strategies of PID.

Keywords:
Primary immunodeficiency, Autoimmunity, Autoinflammation

POSTER 86 - SAFE AND EFFECTIVE USE OF EMPAGLIFLOZIN IN A 16-MONTH-OLD PATIENT WITH SEVERE CONGENITAL NEUTROPENIA DUE TO A NOVEL G6PC3 VARIANT

AUTHORS

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Objective:
Glucose-6-phosphatase catalytic subunit 3 (G6PC3) deficiency is a rare form of severe congenital neutropenia (SCN4), often associated with syndromic features such as cardiac and urogenital malformations (e.g., cryptorchidism), prominent superficial venous pattern, anemia, and thrombocytopenia. Complications may include refractory inflammatory bowel disease, acute leukemia, and myelodysplastic syndrome.

The enzymatic defect leads to intracellular accumulation of 1,5-anhydroglucitol-6-phosphate (1,5-AG6P), impairing neutrophil survival and function. While granulocyte colony-stimulating factor (G-CSF) can improve neutrophil counts, it does not correct the underlying metabolic defect.

Recently, sodium-glucose co-transporter 2 (SGLT2) inhibitors, also known as gliflozins, have shown efficacy in glycogen storage disease type Ib and in rare cases of G6PC3 deficiency by lowering plasma levels of 1,5-anhydroglucitol (1,5-AG) through enhanced urinary excretion. Reported side effects include hypoglycemia and genitourinary infections.

We report the safe and effective use of empagliflozin in a toddler with G6PC3 deficiency carrying a novel missense variant.

Design and method:
A 16-month-old male with persistent severe neutropenia, reduced diihydrorhodamine (DHR) test, and partial clinical response to G-CSF (5 mcg/kg every other day) was evaluated. His clinical history included necrotizing pneumonia at 2 months of age and right-sided cryptorchidism, which was surgically corrected.

Trio-based next-generation sequencing revealed compound heterozygosity in G6PC3: a known pathogenic splice-site variant (c.535+1G>A, paternal) and a novel missense variant (c.449A>C, maternal).

To better assess the metabolic impact of the genetic defect, plasma 1,5-AG levels were measured and found to be markedly elevated (201 µmol/L; reference range 37–163).

Empagliflozin was initiated at a gradually titrated dose, reaching 0.2 mg/kg/day, with glycemic control monitored via continuous glucose monitoring (CGM) over a 30-day period.

Results:
No hypoglycemic episodes, urinary tract infections, or other adverse events were observed. The absolute neutrophil count (ANC) gradually increased, allowing discontinuation of G-CSF after 65 days. At day +105, the ANC was 3150/µL, the DHR result had completely normalized, and plasma 1,5-AG had decreased to 26 µmol/L, with a concomitant increase in urinary excretion (see figure). The patient remains under regular clinical and laboratory follow-up.

Conclusions:
Empagliflozin was safe and effective in this young patient with G6PC3 deficiency, resulting in significant hematological and metabolic improvement. Early intervention with SGLT2 inhibitors may represent a promising therapeutic strategy for patients with G6PC3 deficiency even in early infancy.

POSTER 88 - RARE GENETIC BCL10 DEFICIENCY PRESENTING WITH MYOCARDITIS: MATERNAL UNIPARENTAL ISODISOMY

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Introduction:
B-cell lymphoma/leukemia(BCL10) protein plays a critical role in activating the NF-κB pathway, which is important in both innate and adaptive immune responses, by forming a CARD11-BCL10-MALT1(CBM) complex with MALT1 protein and Caspase recruitment domain-containing protein(CARD) proteins. BCL10 deficiency presents dysfunction of both B and T lymphocytes which is associated with combined immunodeficiency(CID). The only curative treatment is hematopoietic stem cell transplantation(HSCT).

Case report:
3.5-months-old girl was born to non-consanguineous parents and referred to pediatric intensive care unit due to fever, decreased sucking, tachycardia and arrhythmias under oral antibiotic treatment for upper respiratory tract infection(URTI). In her medical history she had an URTI with influenza virus not requiring hospitalization when she was 1.5 months old. She was evaluated in detail after admission to hospital; electrocardiogram was found to be compatible with sinus tachycardia and oral propranolol was initiated, and a patent foramen ovale(PFO) was observed in the echocardiogram(ECHO). Intravenous(IV) antibiotic treatment and supplemental O2 support were started for bronchopneumonia. Upon the observation of panhypogammaglobulinemia and B cell deficiency(Table 1) in the immunological evaluation, 0.5 g/kg/dose immunoglobulin replacement treatment(IgRT), trimethoprim-sulfamethoxazole and fluconazole prophylaxis were initiated due to the suspicion of immunodeficiency, and whole exome sequencing(WES) analysis was performed. After clinical improvement she was discharged to be followed up with aforementioned treatments. After 4 weeks she was admitted for routine check-up and had symptoms of URTI that had been present for a week. Due to tachycardia in physical examination, ECHO was performed again, and left ventricular systolic dysfunction and dilatation were detected. Cardiac enzymes were high, and the patient was hospitalized with a diagnosis of acute myocarditis. Captopril, furosemide, carnitine, methylprednisolone and 2 g/kg IgRT and IV ganciclovir treatments were started due to CMV PCR; 743403 IU/ml. During the follow-up, foscarnet for CMV myocarditis and weekly CMV hyperimmunoglobulin treatments were added. Parental segregation analysis was performed after the detection of homozygous BCL10 mutation in WES. The mother was heterozygous while the father's results were normal, creating a suspicion of possible first chromosome uniparental disomy. Additional genetic tests confirmed maternal uniparental isodisomy 1. She underwent HSCT from a 9/10 HLA-matched unrelated donor with a myeloablative regimen, but the patient deceased due to post-transplant CMV reactivation, sepsis, and multiorgan failure.

Conclusions:
Atypical mechanisms outside of classical inheritance patterns in immunodeficiencies cause complex phenotypes and require additional evaluations in genetic diagnosis. This rare case will guide clinicians in the diagnosis of patients with unusual features.

POSTER 90 - HIDDEN BURDEN: ELEVATED RISK OF SARCOPENIA IN ADULTS WITH PRIMARY IMMUNODEFICIENCIES

AUTHORS

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Introduction and aim:
Primary Immunodeficiencies (PIDs) are rare hereditary disorders involving defects in the development and function of the immune system. This leads to an increased frequency and severity of infections. They are also frequently associated with autoimmune, autoinflammatory, allergic manifestations and malignancies. Although sarcopenia is commonly considered a disease affecting the geriatric population, numerous studies have demonstrated an increased prevalence in individuals with various chronic diseases. Several mechanisms underlying its pathogenesis have also been proposed. The aim of this study was to evaluate sarcopenia-related parameters and investigate the prevalence of sarcopenia in patients with IEIs.

Materials and methods:
The study included 19 adult patients diagnosed with PIDs and 38 healthy volunteers as controls. The following tests and assessments were performed: anthropometric measurements; handgrip strength, as assessed by dynamometry; the SARC-F questionnaire; bioelectrical impedance analysis (BIA); and the timed up-and-go (TUG) test.

Results:
The mean age was 45.74 ± 13.87 years in the PIDs group and 45.34 ± 13.15 years in the control group. The SARC-F scores indicated a statistically significantly higher probability of sarcopenia in the PIDs group compared to controls ($p < 0.001$). Sarcopenia was identified in 2 patients (10.53%) in the PIDs group and in 1 individual (2.63%) in the control group. Although skeletal muscle mass, handgrip strength, and lean body mass were lower in the PIDs group, and TUG test scores were higher, these differences did not reach statistical significance. Correlation analysis showed that skeletal muscle quality was positively correlated with albumin and creatinine levels, and negatively correlated with erythrocyte sedimentation rate (ESR) and TUG test scores.

Conclusion:
The findings suggest that sarcopenia may develop at an earlier age than expected in patients with PIDs. We believe that screening tests on these patients and taking precautions at an early stage would be beneficial.

Keywords:
Inflammation, Primary Immunodeficiencies, Sarcopenia

POSTER 91 - SENTINEL CMV INFECTION LEADING TO THE DIAGNOSIS OF LRBA DEFICIENCY IN A PEDIATRIC PATIENT WITH CEREBRAL ANEURYSM

AUTHORS

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Introduction:
LPS-responsive beige-like anchor protein (LRBA) deficiency is an inborn errors of immunity (IEIs) caused by biallelic mutations in the LRBA gene. It leads to regulatory T-cell dysfunction, immune dysregulation, and autoimmunity. Patients typically present with infections, hypogammaglobulinemia, autoimmune manifestations, and lymphoproliferation.

Case presentation:
We present a male infant, born from a non-consanguineous dichorionic diamniotic twin pregnancy, who was initially followed for respiratory distress and pneumonia during the neonatal period. At nine months of age, he developed generalized tonic-clonic seizures followed by left-sided hemiplegia. Neuroimaging showed intracranial hemorrhage and a giant saccular aneurysm (22 mm) in the distal basilar artery. His condition detoriorated, culminating in brain death.

At this stage, the family consented to organ donation. During the donor work-up, thoracic CT revealed pneumomediastinum and bilateral ground-glass opacities. The serological evaluation showed positive CMV IgM, high CMV IgG avidity, and a CMV PCR of 25,119 copies/mL, consistent with active CMV viremia. Based on these findings, the patient was referred to our department with a suspicion of IEIs. Immunologic evaluation showed low IgG and normal lymphocyte subsets except for reduced switched memory B cells and TEMRA subsets.

Whole exome sequencing identified compound heterozygous mutations in the LRBA gene. Despite intensive medical care, the patient died. Genetic counseling was provided to the family, and screening of family members was recommended.

Conclusion:
Neurological involvement occurs in up to 25% of LRBA deficiency cases, but association with cerebral aneurysm is unreported and likely coincidental. In this case, CMV viremia, a sentinel infection, prompted immunological evaluation and led to a rare primary immunodeficiency diagnosis. This case emphasizes the importance of considering underlying immune defects in sentinel infections, particularly when clinical findings are atypical or complex. Early recognition can guide diagnosis, management, and familial genetic counseling.

POSTER 92 - A HIGH-RISK FACTOR IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES: CMV INFECTION

AUTHORS

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Introduction:
Cytomegalovirus (CMV), a human herpesvirus, causes significant morbidity and mortality in patients with combined immunodeficiencies (CID), syndromic CID, and immune dysregulation disorders due to defective T lymphocyte number and function. Control of CMV infection depends on adequate T cell quantity and function despite antiviral therapy.

Methods:
We retrospectively reviewed 58 patients with inborn errors of immunity (IEI) and positive CMV PCR tests between 2000 and 2024.

Results:
Table 1 summarizes demographic data, diagnoses, and treatments. Among CMV-positive patients, 89.7% had combined immunodeficiency. Higher CMV viral loads correlated significantly with pneumonia, central nervous system (CNS) involvement, and hepatitis ($p<0.001$, $p=0.003$, $p=0.017$, respectively), but not with retinitis ($p=0.387$). Both patients with myocarditis had viral loads exceeding 100000 IU/mL. Hematopoietic stem cell transplantation (HSCT) was performed on 47 patients (81%), with 85.1% of them experiencing viremia post-transplant. During follow-up, 17 patients (29.3%) died; 58.9% of deaths were CMV-related. Mortality was significantly associated with CNS involvement, hepatitis, high viral load, and pneumonia ($p=0.001$, $p=0.002$, $p=0.024$, $p=0.043$, respectively).

Conclusion:
CMV viremia in primary immunodeficiency patients frequently leads to organ involvement and increased mortality. CNS involvement, hepatitis, high viral load, and pneumonia are associated with increased mortality risk. Early recognition of underlying immunodeficiencies and prompt curative treatment remain essential to prevent severe CMV complications.

POSTER 93 - TOLERABILITY OF IMMUNOGLOBULIN PRODUCTS AND IMMUNOGLOBULINS SWITCHING PATTERNS IN CLINICAL PRACTICE: A RETROSPECTIVE STUDY

AUTHORS

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Objective:
To investigate the frequency of adverse reactions (ARs) to immunoglobulin products and switching patterns in clinical practice.

Design and methods:
This was a retrospective, single-center study. We included all patients who were treated with immunoglobulin products during the period June 2017 to May 2025.

Results:
We included 51 patients with a median (IQR) age of 54 (40-63) years, predominantly male (n=36, 70.6%), and diagnosed with primary immunodeficiency (n=22, 43.1%), secondary immunodeficiency (n=20, 39.2%), and other diagnoses (n=6, 17.6%). Forty-three patients received intravenous (IV) immunoglobulins (IV Flebogamma [n=42] and IV Privigen® [n=1]), and 8 patients received subcutaneous (SC) immunoglobulins (SC Hyqvia® [n=7] and SC Hizentra® [n=1])(Figure). Of the 42 patients who received IV Flebogamma, 22 (42%) experienced ARs; the most frequent ARs were back pain (n=10), headache (n=7), erythema (n=4), chills (n=3), and malaise (n=3). Bivariate analysis showed that older age was associated with experiencing ARs with IV Flebogamma (Table). There were no ARs in a single patient who received IV Privigen®. Twelve (28.6%) patients who received IV Grifols experienced ARs leading to switching to another immunoglobulin product; the most common ARs were back pain (n=5), headache (n=3), and increased blood pressure (n=2). The immunoglobulin products after switching included IV Intratect (n=2), IV Privigen® (n=4), SC Xembify® (n=1), and SC Hyqvia® (n=5); after switching, no ARs were reported. Of the 7 patients who received SC Hyqvia®, 3 (42.9%) experienced ARs; the most frequent ARs were edema (n=2) and erythema (n=2). No ARs were observed in patients who initially received SC Hizentra®. Of the 3 patients who experienced ARs with SC Hyqvia®, 1 patient was switched to SC Hizentra without ARs after switching. Fourteen (27.5%) patients switched immunoglobulins because of ease of administration. There were two cases of deep necrotic skin ulcers after administration of SC Hyqvia®: a 33 years-old female without comorbidities treated initially with SC Hyqvia® and a 25 years-old female with history of idiopathic thrombocytopenic purpura who was switched from IV Flebogamma; the ulcers did not recur after switching the needle length from 9 to 6 mm.

Conclusions:
Adverse reactions in patients who received IV immunoglobulins are common, seem to be associated with older age, and lead to switch to another product in a high proportion of patients; switching to another product seems to be well-tolerated. The use of shorter needles could prevent the recurrence of necrotic skin ulcers described in this and other studies with SC immunoglobulins.

POSTER 94 - PHARMACOKINETICS OF A NEW INTRAVENOUS IMMUNOGLOBULIN 10% (KIG10) IN PRIMARY IMMUNODEFICIENCY PATIENTS

AUTHORS

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Objective:
Intravenous immunoglobulin (IVIg) therapy is commonly used in the treatment of primary immunodeficiency (PI) disorders.

This open-label, prospective, single-arm, multicenter phase III study in adult PI patients (KIG10_US3_PID01; NCT01581593) investigated efficacy, safety and pharmacokinetics (PK) of a new 10% IVIg product (KIg10), given 200 to 800 mg/kg every 21 or 28 days for 48 weeks.

Primary PK endpoints included total IgG levels, IgG subclasses levels, selected specific antibody levels and PK parameters of total and baseline-corrected IgG.

Design and methods:
PK assessments were performed in 23 adult patients and blood samples from them were taken for PK parameters' analysis before and after 5th infusion for the 28-day infusion schedule or 7th infusion 7 for the 21-day infusion schedule, and at protocol pre-specified time points.

Results:
The estimated mean serum half-life (T1/2) for uncorrected total IgG was 24.5 days (587 h) and 37.3 days (896 h) for patients on 21 and 28-day schedule, respectively. The total serum IgG PK profiles were comparable between the two dosing schedules, with a numerically higher exposure for the 21-day schedule. All the mean values of IgG subclasses were maintained within the reference ranges following IV infusion of KIg10. All anti-tetanus toxoid antibody levels, mean values of anti-pneumococcal capsular polysaccharide antibodies and mean levels of anti-Haemophilus Influenzae type b antibodies were maintained above protective levels.

Conclusion:
In study KIG10_US3_PID01 measured PK parameters for KIg10 in adult patients with PID were considered comparable to previously published data for other IVIg treatments.

POSTER 95 - PRIMARY IMMUNE REGULATORY DISORDERS: A DIAGNOSTIC CHALLENGE BEYOND CLASSICAL IMMUNODEFICIENCIES

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Primary immune regulatory disorders (PIRDs) represent a distinct category within the spectrum of inborn errors of immunity. They are marked by features such as lymphoproliferation, autoimmunity, increased susceptibility to infections, and malignancies. In contrast to classical primary immunodeficiencies, PIRDs often present initially with autoimmune symptoms—such as cytopenias or enteropathies—that are frequently resistant to standard therapies and may precede infectious complications by several years. Enhancing awareness of PIRDs among healthcare professionals and fostering a multidisciplinary approach are vital for timely diagnosis and intervention, potentially mitigating irreversible organ damage. Advances in genetic and immunological research have led to the identification of numerous PIRDs and a deeper understanding of their pathophysiological mechanisms. This has enabled the development of targeted therapies aimed at specific molecular pathways, often providing more effective disease management than conventional immunosuppressive treatments. Drawing on the latest research, this review highlights common PIRDs, their clinical features, and recent progress in therapeutic strategies.

POSTER 96 - AUTOIMMUNITY IN THE WAKE OF INFECTION: THE ROLE OF AUTOANTIBODIES IN COVID-19 AND BEYOND

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Autoantibodies are antibodies produced by the immune system that mistakenly target and attack the body's own cells and tissues. The COVID-19 pandemic has shed light on the role of autoantibodies in influencing the severity of infection and in triggering various autoimmune conditions following recovery. This review provides an overview of autoimmune diseases, focusing on the involvement of autoantibodies in COVID-19 and other infectious illnesses. It examines the diverse types of autoantibodies identified in these diseases and explores the potential mechanisms through which they may exacerbate disease severity. Furthermore, the review addresses the possible link between vaccine-induced autoantibodies and related adverse effects. It also explores therapeutic approaches targeting autoantibodies. By analyzing recent research, this article enhances our understanding of the complex relationship between autoantibodies and infectious diseases, particularly in the context of COVID-19.

POSTER 97 - ARTIFICIAL INTELLIGENCE IN AUTOIMMUNE DISEASE MANAGEMENT: A NEW ERA OF PRECISION MEDICINE

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The integration of artificial intelligence (AI) into medical practice has significantly advanced the management of autoimmune diseases, paving the way for more individualized therapeutic strategies. This review explores recent developments in AI-enabled treatments for autoimmune conditions, focusing on both established and emerging methodologies. Conventional treatments, including immunosuppressants and biologic agents, primarily aim to control symptoms but often fall short in delivering personalized care. Innovations such as precision medicine, powered by AI, are reshaping the field by leveraging extensive patient datasets to tailor therapies more effectively. AI offers promising capabilities in improving diagnostic precision, identifying novel biomarkers, accelerating drug discovery, and customizing treatment plans. Case studies involving rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis illustrate the tangible benefits of machine learning in enhancing clinical decision-making. Despite these advancements, challenges remain—ranging from data privacy concerns and algorithmic biases to the need for large, high-quality datasets and increased transparency in AI models. This study highlights the potential of AI in refining patient stratification and predictive analytics while acknowledging the ethical and practical issues that must be addressed to fully embed AI within routine clinical care.

POSTER 99 - CLINICAL AND IMMUNOLOGICAL SPECTRUM OF PRIMARY IMMUNODEFICIENCY DISEASES IN CHILDREN: A TERTIARY CARE EXPERIENCE IN DELHI, INDIA

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This study was conducted to identify and classify various types of primary immunodeficiency diseases (PIDs) diagnosed in the paediatric children at the National Institute of Tuberculosis and Respiratory Diseases in Delhi, India. The primary aim was to detail the clinical, immunological, and flow cytometry profiles of different PIDs. Secondary objectives included analyzing complete blood count (CBC) patterns across PIDs and reporting bone marrow findings where applicable, particularly in cases suggestive of bone marrow failure syndromes. A descriptive, cross-sectional study was carried out from February 2023 to August 2024. Children up to 14 years of age presenting with warning signs of PID at the pediatric outpatient department were enrolled. Clinical information was obtained from outpatient and inpatient records as well as patient interviews. Laboratory analyses were performed in the Department of Paediatric to assess hematological and immunological parameters. Data were analyzed using descriptive statistics. A total of 104 children were diagnosed with PID. The most frequent age of onset was between 1 to 5 months (41%). According to the International Union of Immunological Societies (IUIS) classification, combined immunodeficiency with syndromic features constituted the largest group (31%). Hyper IgE syndrome (HIES) was the most frequently identified individual disorder. The respiratory system was the most commonly affected (73%), followed by the skin (51%) and gastrointestinal tract (36%). Hematological, immunological, and flow cytometry findings were analyzed in each PID subtype. PIDs present with diverse clinical features, often mimicking common infections. Therefore, heightened clinical suspicion is essential, especially in cases of recurrent or atypical infections. A comprehensive diagnostic approach, including CBC, peripheral smear examination, flow cytometry, and immunoglobulin profiling, is crucial for the early and accurate diagnosis of PIDs.

poner 100

POSTER 100 - PRIMARY IMMUNODEFICIENCY CASE WITH ENDOBRONCHIAL EBV-RELATED SMOOTH MUSCLE TUMOR

AUTHORS

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Background and aims:
FCHO1 (F-BAR domain only protein 1) is a molecule responsible for the formation of clathrin-coated vesicles. In this way, it plays a role in endocytosis into the cell. Although it is not clear what clinical findings FCHO1 mutation will cause in humans, there are studies showing that it disrupts T cell receptor (TCR)-mediated T lymphocyte stimulation. In this way, T lymphocyte proliferation is impaired, resulting in combined immunodeficiency. It may predispose to EBV infections and related malignancies, especially lymphoma.

Methods:
A case report will be submitted.

Results:
In our case, which had a history of recurrent pneumonia and showed endobronchial dissemination during follow-up, we detected a homozygous mutation in the FCHO1 gene while investigating the immunodeficiencies that may predispose to this condition upon the development of EBER-positive, EBV-related smooth muscle tumor (Figure 1,2). Although EBV-related tumors have been reported in the literature in patients with FCHO1 mutation, no case of EBV-related smooth muscle tumor with endobronchial spread in the lung has been reported.

Conclusions:
EBV-related smooth muscle tumors and diffuse large B-cell lymphoma can be seen especially in congenital diseases of the immune system. While the initial diagnosis in these patients may be malignancy, this may also occur after other immunodeficiency findings. Even if there is no previous infection history, findings in favor of underlying immunodeficiency in EBV-related smooth muscle tumors and lymphomas should be investigated and genetic examination should be sent if necessary. In most of these cases, the use of biological agents for B cell depletion and hematopoietic stem cell transplantation is required.

POSTER 101 - SAFETY AND TOLERABILITY OF A NEW INTRAVENOUS IMMUNOGLOBULIN 10% (KIG10) IN PRIMARY IMMUNODEFICIENCY ADULT PATIENTS

AUTHORS

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Objective:
Intravenous immunoglobulin (IVIg) therapy is commonly used in the treatment of primary immunodeficiency (PI) disorders. This open-label, prospective, single-arm, multicenter phase III study in adult PI patients (KIG10_US3_PID01; NCT01581593) investigated efficacy, safety and pharmacokinetics (PK) of a new 10% IVIg product (KIg10), given 200 to 800 mg/kg every 21 or 28 days for 48 weeks.

Safety and tolerability endpoints from this study are reported here and included treatment-emergent adverse events (TEAEs) from Day 1 to Week 51/52.

Design and method:
Forty-seven patients received study treatment and were analyzed for safety and efficacy. As per protocol, the 1st infusion was administered at an initial rate of 1 mg/kg/min for 30 minutes. If well tolerated, the rate was progressively increased to a maximum of 8 mg/kg/min. The rate of administration of subsequent infusions progressively increased to a maximum of 8 mg/kg/min at 15-min intervals.

Results:
Among both dosing schedules, 22 (46.8%) subjects reported 75 TEAEs. Most frequently reported (≥5%) were headache (25.5%), infusion-related reaction (10.6%), nausea, fatigue, and positive Coombs direct test (8.5% each). The most frequently reported (≥5%) infusional adverse event (AE) (defined as occurring during or within 72 hours after an infusion) were headache (25.5%), fatigue (14.9%), infusion-related reaction (10.6%), nausea (10.6%), positive Coombs direct test (10.6%), diarrhea (6.4%), dizziness (6.4%), and sinusitis (6.4%). No hemolysis events were reported, and no laboratory findings were suggestive of hemolysis associated with positive Coombs tests. No safety signal or trend was observed. None of the reported TEAEs were serious; no significant or life-threatening TEAEs were reported. No AEs led to study discontinuation, and no subjects died during the study due to an AE.

Conclusion:
In study KIG10_US3_PID01, KIg10 showed a favorable safety profile and was well tolerated in adult patients with PI at the dosing schedules and infusion rates used.

POSTER 102 - DEVELOPMENT OF A PREDICTIVE MODEL FOR LOCAL ADVERSE REACTIONS TO SCIG THERAPY IN PATIENTS WITH PRIMARY AND SECONDARY IMMUNODEFICIENCIES: A NATIONWIDE MULTICENTER STUDY

AUTHORS

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Background:
Subcutaneous immunoglobulin (SCIg) therapy is a cornerstone in the treatment of patients with primary (PID) and secondary (SID) immunodeficiencies. However, local adverse reactions are common and may impair adherence. We aimed to identify predictive factors for local adverse effects and develop a multivariable model to estimate individual risk.

Methods:
We conducted a multicenter, retrospective study including 223 patients aged ≥14 years with PID or SID who had received SCIg for at least one month. Data were collected through the nursing GEIE Spanish Registry, including sociodemographic, clinical, immunological, psychosocial, and technical administration variables. Local and systemic adverse effects were recorded based on patient-reported outcomes and nurse-led assessments. Descriptive and comparative analyses were performed, and a multivariable logistic regression model was constructed to identify independent predictors of local adverse reactions.

Results:
Among the 223 included patients (61.4% female; mean age 47.1 ± 18.6 years), 163 (73.1%) experienced at least one local adverse effect. The most frequent reactions were swelling (70.5%), pruritus (65.5%), and rash (65.1%). Multivariable analysis identified four independent predictors of local adverse events: smaller abdominal perimeter (OR 0.955; 95% CI 0.930–0.980; $p < 0.001$), history of skin disease (OR 2.75; 95% CI 1.03–7.38; $p = 0.044$), longer distance to hospital (OR 1.01; 95% CI 1.00–1.02; $p = 0.050$), and absence of anxiety or depression as a protective factor (OR 0.089; 95% CI 0.020–0.390; $p = 0.001$). The model showed good discriminative performance with an AUC of 0.801 (95% CI 0.733–0.869).

Conclusions: Local adverse reactions to SCIg are frequent and influenced by a combination of dermatological, anatomical, psychological, and geographical factors. The proposed predictive model may support nursing teams in identifying high-risk patients and personalizing education, support, and infusion protocols. These findings underscore the importance of integrated, multidisciplinary strategies in optimizing the management and tolerability of immunoglobulin therapy.

POSTER 103 - HUMAN DEFICIENCY OF THE INDUCIBLE T COSTIMULATORY LIGAND: IMPLICATIONS OF REGULATORY T CELLS-MEDIATED VIRAL PERSISTENCY

AUTHORS

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Objective:
Deficiency of the Inducible T costimulatory ligand (ICOSL protein, encoded by the ICOSLG gene) is a recently described autosomal recessive, combined immunodeficiency syndrome (CID). It is marked clinically by recurrent respiratory tract infections, and recurrent/ refractory disease with DNA-viruses. The affected patients we have identified bear a homozygous missense mutation (p.N219K) that abrogates ICOSL surface expression in cellular models (e.g. patient-derived lymphoblastoid cells (LCLs)). ICOSL on antigen-presenting cells normally interacts with ICOS on activated T cells; this co-stimulation results in B cells developing into antibody-producing cells and in T cells to develop into T follicular helper (Tfh) cells (Figure 1). Disruption of this T-B cell costimulation underlies the patients' abnormal Tfh homeostasis and hypogammaglobulinemia, resulting in recurrent respiratory tract infections. However, the refractory disease with DNA-based viruses (i.e. HPV, CMV) remains incompletely understood. Paradoxically, histopathology of affected tissue shows an abundance of CD3+ T cells. We hypothesized that loss of ICOSL function leads to dysregulated PD-L1 (programmed death-ligand 1)/PD-1 signaling and abnormal T cell develop at lesion sites, therefore promoting local immune suppression and viral persistence.

Methodology:
To test this hypothesis and gain mechanistic insights, we leveraged patient-derived ICOSL-deficient LCL cells to establish an in vitro co-culture system with LCL and allogeneic T cells (Figure 2) and investigate the consequences of ICOSL deficiency on T cell development by flow cytometry (Figure 3).

Result:
ICOSL-deficient LCLs exhibit PD-L1 upregulation, indicating these cells exist in a dysregulated activation state. Our results revealed that ICOSL-deficient LCLs excessively skew T cell development to CD4 Treg across distinct activation conditions (Figure 4). We functionally characterized these induced Treg and show aberrant surface expression of key immunosuppressive markers (e.g. ICOS, PD-1) with dysregulated T cell cytokine expression (e.g. IL-10, TGF-β, IFN-γ).

Conclusion:
These results indicate that disruption of ICOSL-ICOS interactions leads to overproduction of Treg with generation of immunosuppressive properties. These findings support a model in which ICOSL deficiency fosters an immunosuppressive environment, impairing viral clearance. This study offers new insights into the complex role of ICOSL in maintaining immune balance through regulation of Tregs and checkpoint pathways.

POSTER 104 - RETROSPECTIVE EVALUATION OF PATIENTS RECEIVING IVIG REPLACEMENT THERAPY WITH IGG SUBCLASS DEFICIENCY

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Introduction:
mmunoglobulin G (IgG) subclass deficiencies are an important part of primary immunodeficiencies and may increase the susceptibility of individuals to infections. IgG consists of four main subclasses: IgG1, IgG2, IgG3, and IgG4. IgG subclass deficiencies are generally associated with increased susceptibility to certain types of infections. IgG2, IgG3, and IgG4 deficiencies may be seen with normal serum IgG levels. This may render individuals vulnerable to certain pathogens. Studies show that IgG subclass deficiencies play an important role, especially in patients with bronchiectasis and recurrent respiratory tract infections. In such patients, assessment of IgG subclass levels is recommended as a critical strategy in the management of recurrent infections.

Materials and methods:
104 patients who were followed up due to IgG subclass deficiency and started IVIG replacement therapy at Sakarya University Research and Education Hospital Pediatric Immunology and Allergy Clinic were retrospectively evaluated in terms of demographic characteristics, laboratory findings, and response to treatment.

Results:
58 of the patients were male and 46 were female. Intravenous immunoglobulin (IVIG) replacement therapy was started mostly due to IgA and IgG3 deficiency (25 patients) and isolated IgG3 deficiency (22 patients). While the treatment of 82 of the patients was ongoing, 15 patients were in the follow-up process after the treatment. In 6 of the patients, the decision was made to start the treatment again after the treatment was interrupted. The most common reason for the patient's complaints was observed to be recurrent bronchitis (26 patients). Allergy tests were performed in 89 of the patients and allergies were detected in 23 of these patients. The most common was isolated dust mite allergy (7 patients). 7 of our patients continue their treatment by taking SCIG.

Conclusion:
Management of IgG subclass deficiencies includes vaccinations, prophylactic antibiotics, and IVIG therapy when necessary. Other studies have shown that IVIG therapy reduces the risk of infection by more than 50% in patients with recurrent infections. However, individuals with IgG subclass deficiencies may respond to treatment to prevent infection. For example, some patients do not show sufficient improvement in IgG subclass levels despite IVIG therapy. This suggests that treatment strategies should be individualized.

POSTER 105 - A FULLY AUTOMATED MOBILE WORKFLOW FOR PID SCREENING: OCR-DRIVEN DATA CAPTURE AND MULTI-REFERENCE IMMUNOGLOBULIN ANALYSIS

AUTHORS

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Introduction and aim:
The diagnostic pathway for Primary Immunodeficiencies (PIDs) relies on the accurate interpretation of immunoglobulin (Ig) levels, a process complicated by manual data entry and complex, age-specific reference standards. These manual steps are not only time-consuming but also introduce a significant risk of human error, potentially delaying critical therapeutic decisions (Acedo et al., 2023). This study aimed to develop and validate a complete, end-to-end mobile solution that automates the entire workflow from paper-based laboratory reports to an immediate, validated clinical interpretation, thereby enhancing diagnostic efficiency and safety.

Materials and methods:
A cross-platform mobile application was developed integrating two core technologies. First, an Optical Character Recognition (OCR) module was implemented, enabling clinicians to use the device's camera to instantly capture and digitize patient data and Ig values directly from laboratory printouts. Second, the captured data is processed by an automated analysis engine that evaluates the Ig levels against five distinct, validated age-specific guidelines (3 Turkish, 2 US-based). The system architecture, built on React Native and a local SQLite database, ensures rapid performance. Validation was conducted in two stages: assessing the OCR's accuracy on a set of test reports and confirming the calculation engine's 100% concordance with manual expert evaluation for a 200-patient cohort.

Results:
The integrated OCR module demonstrated over 99% accuracy in correctly capturing numerical and date values from standard laboratory reports, reducing data entry time from minutes to mere seconds and eliminating transcription errors. Subsequent analysis by the calculation engine showed 100% concordance with manual evaluation across all 200 retrospective cases. The complete, end-to-end workflow—from camera capture to final result display ('low', 'normal', 'high')—is completed in under 5 seconds, providing a seamless point-of-care solution.

Conclusions:
This mobile application is more than a calculation tool; it is a fully automated clinical workflow solution that digitizes and error-proofs the initial screening process for PIDs. By leveraging OCR and automated analytics, our system directly addresses the dual challenges of inefficient data entry and complex interpretation, offering a disruptive technology to advance data-driven PID care (Felice et al., 2024). This tool significantly enhances a clinician's ability to make rapid, reliable, and evidence-based decisions, setting a new standard for efficiency in immunological practice.

POSTER 106 - RE-ENGINEERING THE CLINICAL WORKFLOW FOR IMMUNODEFICIENCY SCREENING: A MOBILE PLATFORM WITH OCR-DRIVEN DATA INTEGRATION AND LONGITUDINAL ANALYSIS CAPABILITIES

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Introduction and aim:
Effective management of PIDs and secondary hypogammaglobulinemia is critically dependent on the accurate, timely interpretation of immunoglobulin (Ig) levels. This is vital in diverse clinical contexts, from managing infection risks in conditions like bronchiectasis to monitoring patients post-transplant or during chemotherapy. However, the clinical workflow is persistently bottlenecked by error-prone manual data transcription and complex, multi-standard calculations. This study aimed to architect and deploys a robust mobile platform to completely re-engineer this workflow, integrating secure, instantaneous data capture with powerful analytical tools to accelerate clinical decision-making.

Materials and methods:
The system was architected as a secure, on-device clinical decision support platform. 1) The Data Acquisition Layer: A Tesseract-based Optical Character Recognition (OCR) engine, fine-tuned for common laboratory report layouts, enables high-fidelity data capture directly from paper reports. 2) The Analytical Engine: Captured data is processed against five validated, age-specific Ig reference standards. The platform, developed in React Native with an on-device SQLite database, ensures full offline functionality and data privacy, critical for hospital environments. The primary endpoint, technical accuracy of the analytical engine, was validated by assessing concordance against expert manual calculations across a 200-patient retrospective cohort.

Results:
The OCR engine demonstrated >99.5% character-level accuracy, effectively digitizing patient reports in under 3 seconds and eliminating transcription errors. The core analytical engine showed 100% concordance with expert calculations. This provides a seamless, standardized point-of-care solution that can directly address the challenge of practice variability and resource utilization discrepancies documented across different healthcare systems. Pilot feedback from clinicians highlighted the intuitive design and overwhelmingly requested the implementation of longitudinal data tracking to monitor Ig trends over time.

Conclusions:
This platform transcends being a simple calculator; it is a fundamental shift in PID management. By seamlessly integrating OCR with a powerful analytical engine, we provide a disruptive technology that advances data-driven care. Our results establish a robust foundation for the platform's next evolution: an intelligent system capable of creating dynamic, personalized patient profiles from longitudinal data. This approach moves toward the data-rich, observational models required for optimizing individualized therapies, ultimately transforming a static data point into an interactive clinical asset that directly answers clinician demands for smarter diagnostic tools.

POSTER 107 - RECURRENT INFECTIONS AND IMMUNODEFICIENCY IN A PATIENT WITH SANFILIPPO (MPS TYPE 3) SYNDROME: A CASE REPORT

AUTHORS

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Introduction:
Sanfilippo syndrome (mucopolysaccharidosis type 3; MPS 3) is a rare, inherited lysosomal storage disorder characterized by progressive neurodegeneration. Clinically, it usually manifests in early childhood with developmental delays, behavioral problems, and susceptibility to infections. Over time, systemic retention may lead to neurological deterioration, swallowing dysfunction, and frequent respiratory tract infections. This article presents a case report of a patient diagnosed with MPS type 3 who started intravenous immunoglobulin (IVIG) therapy due to immunodeficiency.

Case presentation:
18 year-old-female patient diagnosed with San Flippo Syndrome, epilepsy, and hypothyroidism. She was under observation in the pediatric metabolism, neurology, and chest diseases departments. The patient first came to our outpatient clinic complaining of postnasal drip and recurrent upper respiratory tract infections. The patient's medical history included frequent hospitalizations due to infections and intravenous antibiotic treatment. In particular, frequent diarrhea, throat infections, recurrent coughing, and frequent inhaler treatment over the past three years were noteworthy. The patient had a history of adenoidectomy and previous tests showed growth of Staphylococcus aureus and Streptococcus pneumoniae in sputum culture. On physical examination, the patient was quadriplegic with widespread joint contractures in the upper and lower extremities. sIgE levels of <0.10 for mold, grass, dust, mites, and tree pollen panels, and the inhaler panel skin prick test at the same time were negative. IgG: 651 mg/dl (N: 830–1820), IgM: 151 mg/dL (N: 75–198.5), IgA: 88 mg/dL (N: 46.5–221), IgG1: 415 mg/dL (N: 528–1384), IgG2: 234 mg/dL (N: 147-610), IgG3: 16 mg/dL (N: 21-152), IgG4: 10.7 mg/dL (N: 15-202), anti-CMV IgG: 68 (Positive), anti-Rubella IgG: 17.5 (Positive), anti-B: 1/32+ The patient's follow-up tests one month later showed IgG1: 340 mg/dl (528-1384), IgG2: 171 (147–610), IgG3: 17 mg/dl (21–152), IgG4: 8.9 mg/dl (15–202). Due to low IgG1, IgG3, and IgG4 levels in the patient's tests and severe clinical symptoms, IVIG treatment was initiated with a diagnosis of IgG subclass deficiency. The patient's frequent upper and lower respiratory tract infection symptoms following IVIG treatment have subsided. The patient has been receiving IVIG treatment for 10 months, and during this period, there has been a decrease in hospital admissions, infection frequency, and inhaler use.

Conclusion:
Immunological evaluation may be necessary in the management of multisystemic, rare, and hereditary diseases such as Sanfilippo syndrome. This case may contribute to the literature by drawing attention to the immunodeficiency accompanying Sanfilippo syndrome.

POSTER 108 - GRANULOMATOUS LYMPHOCYTIC INTERSTITIAL LUNG DISEASE IN COMMON VARIABLE IMMUNODEFICIENCY: A CASE REPORT

AUTHORS

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Background:
Granulomatous Lymphocytic Interstitial Lung Disease (GLILD) is a pulmonary complication of Common Variable Immunodeficiency (CVID), characterized by lymphocytic infiltrates and/or non-caseating granulomas affecting the lung parenchyma. It involves 10–20% of CVID patients and appears to contribute to reduced life expectancy. Patients may be asymptomatic or show nonspecific symptoms like cough and exertional dyspnea. High-resolution CT (HRCT) typically reveals nodules, consolidations, or ground-glass opacities. Diagnosis is confirmed by lung biopsy, while FDG-PET-CT helps detect active inflammation. Regular chest imaging and pulmonary function tests are essential for monitoring disease progression.

Case presentation:
We present the case of a 46-year-old woman with CVID complicated by GLILD, portal hypertension due to nodular regenerative hyperplasia, splenomegaly, antral gastropathy, hemolytic anemia, psoriatic arthritis and a history of hemophagocytosis. In 2020, she developed autoimmune hemolytic anemia, treated with Rituximab, and later hepatocellular carcinoma, which was successfully managed with thermal ablation. Following the onset of dyspnea, an HRCT scan revealed an ILD pattern with pseudonodularity. Lung biopsy demonstrated lymphocytic bronchiolitis, non-necrotizing giant cell granulomas, subpleural and paraseptal fibrosis, and lymphomonocytic infiltrates consistent with non-fibrosing GLILD. Owing to her oncological history and detection of low levels of CD19+ cells, Rituximab was not indicated and Mycophenolate mofetil (2 g/day) therapy was initiated but then discontinued due to the onset of fever. A subsequent bone marrow biopsy confirmed hemophagocytosis and therefore the patient has been treated with dexamethasone (12 mg/day), cyclosporine (150 mg/day) and immunoglobulins (20 g for 3 consecutive days) with a significant clinical and radiological improvement also of the GLILD. Follow-up was conducted through serial MRI scans approximately every six months.

Conclusion:
This case highlights the potential benefit of a therapeutic strategy combining cyclosporine and immunoglobulins for treating GLILD in CVID patients. It also underscores the importance of a multidisciplinary approach in the management of CVID, considering the presence of comorbidities and the elevated risk of systemic complications.

POSTER 109 - MORTALITY PATTERNS IN PATIENTS UNDERGOING IMMUNOGLOBULIN REPLACEMENT THERAPY: A FIVE-YEAR REVIEW AT A TERTIARY HOSPITAL (2019–2024)

AUTHORS

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Background:
Immunoglobulin replacement therapy (IgRT) is the cornerstone of managing hypogammaglobulinemia in both primary and secondary immunodeficiencies. However, current literature offers limited insight into mortality rates among individuals undergoing IgRT.

Objective:
This study aims to detail and examine mortality trends, demographic profiles, and clinical features of patients receiving IgRT at the Immunology Day Clinic of Hospital General Universitario Gregorio Marañón (HGUGM) across a five-year period.

Methods:
A retrospective, descriptive analysis was conducted utilizing data extracted from the electronic medical records of patients registered in the IgRT database between 2019 and 2024.

Results:
A total of 25 deaths were recorded in this patient group—16 males and 10 females. The overall crude mortality rate was 126 per 1,000 person-years, representing a 15-fold increase compared to the general population. The mean age at death was 79 years (ranging from 63 to 94 years).

Indications for IgRT primarily included lymphoproliferative syndromes (36%), with primary antibody deficiency as the next most common (20%).

Most fatalities were seen in individuals with hematologic malignancies. Unlike the general population, infection emerged as a leading cause of death within this cohort, rather than neoplasia. Males predominantly died in the 70–74 age group (27%), while female deaths peaked in the 85–89 range (30%). Among patients with primary immunodeficiencies (PID), 60% of deaths occurred after more than two decades of IgRT, with causes spanning infections, frailty, and neoplasms. Notably, 44% of infection-related deaths occurred in patients with inadequate IgG trough levels.

Conclusions:
Our findings indicate extended survival in IgRT recipients, regardless of the etiology of hypogammaglobulinemia. Still, mortality remains significantly higher compared to the general population, with infections representing a prominent risk. Early detection of infections, prompt management, and diligent monitoring of IgG levels are essential for improving patient outcomes. Enhanced surveillance is particularly critical for male patients in their early 70s and females in their late 80s.

POSTER 110 - IMMUNOLOGICAL EVALUATION OF TWO CASES WITH NEURODEVELOPMENTAL DISORDER AND BCL11B MUTATION: CASE PRESENTATION

AUTHORS

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Introduction:
The BCL11B protein, which is highly expressed during the development of T lymphocytes, is a transcriptional regulatory protein. It plays a role in the development of the nervous system and immunity. We present two patients referred to us for immunological evaluation, who were followed up at the pediatric neurology outpatient clinic due to speech disorders, autism, dysmorphism, and neurodevelopmental delay, and in whom BCL11B gene mutations were detected.

Case 1:
A 14-year-old female patient with cerebral palsy and epilepsy. Due to dysmorphic facial features, genetic testing revealed a heterozygous pathogenic mutation in the BCL11B gene, and the patient was referred to us for immunological evaluation. The patient's history revealed no history of frequent illnesses, severe infections, or hospitalizations. Immunological values are shown in Tables 1 and 2. The patient's tests revealed low CD19 and high IgE levels. The patient was also found to be sensitized to inhaled allergens and was placed under immunological follow-up.

Case 2:
A 5.5-year-old male patient with speech delay and autism. Genetic testing was performed due to accompanying dysmorphic facial features, and a heterozygous potentially pathogenic mutation was identified in the BCL11B gene. The patient was referred to us for immunological evaluation, and his history revealed that he had been frequently ill, although he had not experienced severe illness, and had suffered from recurrent upper respiratory tract infections, including during the summer months. Immunological evaluation revealed an inverted CD4/CD8 ratio and low IgG2 and IgG3 levels for his age (Table 1 and Table 2). The patient was placed under follow-up. Due to frequent infections and persistent low IgG2 and IgG3 levels, intravenous immunoglobulin therapy was initiated.

Conclusion:
The BCL11B mutation is predicted to cause mental development disorders in association with speech delay, dysmorphic facial features, and T cell abnormalities. It is classified within the category of combined immunodeficiencies with syndromic features (1). There are only a limited number of case series reported in the literature. In our patients, the absence of the same protein appears to result in different phenotypes, likely due to the different mechanisms by which the mutation arises. Further case series will clarify the effects of BCL11B protein on immunity.

POSTER 112 - CHALLENGES IN DIAGNOSING MSMD-LIKE PHENOTYPES: GENOMIC AND TRANSCRIPTOMIC INSIGHTS FROM SOUTH AFRICA

AUTHORS

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Objective:
Tuberculosis (TB) persists as a global health threat, with many exposed to Mycobacterium tuberculosis (M.tb) showing no immunodiagnostic signs. Despite high exposure, clinical TB develops in only a small percentage, notably in TB-endemic regions like South Africa. Some children, despite being in their “golden age,” suffer from severe, persistent, unusual, or recurrent TB, indicating potential genetic immune defects like Mendelian susceptibility to Mycobacterial Disease (MSMD). The prevalence and impact of MSMD in these regions remain understudied. This study aimed to reveal transcriptomic profiles linked to this condition, enhancing our understanding of MSMD pathobiology and facilitating targeted interventions.

Design and method:
Whole blood samples were collected from paediatric patients suspected of MSMD based on specific selection criteria, including outcomes of panel testing and whole genome sequencing. RNA was extracted and subjected to whole transcriptome sequencing, followed by differential gene expression (DEG) analysis using R and Bioconductor packages. Transcriptome sequencing was also performed on age-matched Tuberculosis meningitis (TBM) cases to serve as a control.

Results:
In comparing MSMD cases to age-matched TBM cases, 1240 genes were significantly differentially expressed ($p<0.001$) of which 497 were upregulated and 743 downregulated. Functional enrichment analysis revealed the downregulation of pathways involved in innate immune responses, including TLR signalling and T cell activation. The adaptive immune system was upregulated and implicated in controlling TB, with CD4+ and CD8+ T cells playing pivotal roles.

Conclusion:
A distinct transcriptomic profile associated with the suspected MSMD cohort, which includes 36 DEGs, was identified. The enriched genes were characterised to be involved in the upregulation of IgE- and zinc ion binding, as well as the downregulation of the positive regulation of the immune response. Overall, these candidates may serve as potential biomarkers in the molecular diagnosis of MSMD, ultimately aiding the clinical management of the disease.

POSTER 113 - DEVELOPMENT OF CYTOMEGALOVIRUS (CMV) RETINITIS FOLLOWING INFLIXIMAB THERAPY IN A PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY (CVID)

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Introduction:
Common variable immunodeficiency (CVID) is a heterogeneous primary immunodeficiency characterized by hypogammaglobulinemia, recurrent infections, autoimmunity, and increased susceptibility to malignancies. Gastrointestinal involvement occurs in 20–60% of CVID patients, with inflammatory bowel disease (IBD)-like presentations being among the most common manifestations.

Tumor necrosis factor-alpha (TNF-α) inhibitors, particularly infliximab, are frequently used in the management of IBD. However, anti-TNF therapy can lead to profound immunosuppression, predisposing patients to opportunistic infections. Here, we present a case of CMV retinitis that developed following infliximab therapy in a patient with CVID.

Case presentation:
A 28-year-old male patient was diagnosed with CVID in 2018 and initiated on regular intravenous immunoglobulin (IVIG) replacement therapy. In June 2024, he began experiencing frequent watery diarrhea with intermittent hematochezia (8–10 episodes per day). Colonoscopy and histopathological examination led to a diagnosis of Crohn's disease by the gastroenterology department. The patient was subsequently started on infliximab therapy.

Following the third dose of infliximab, the patient developed complaints of blurred vision. Laboratory testing revealed a peripheral blood CMV DNA load of 110,000 copies/mL. Ophthalmologic evaluation confirmed the diagnosis of CMV retinitis, supported by the detection of CMV in intraocular fluid (Figure 1).

The patient was treated with systemic intravenous ganciclovir (5 mg/kg) in combination with intravitreal ganciclovir injections. Marked clinical improvement in visual symptoms was observed following the antiviral therapy.

Discussion:
Immunosuppressive therapies in CVID, particularly biologic agents such as infliximab, may significantly increase the risk of opportunistic infections. TNF-α plays a key role in host defense by promoting T cell-mediated immunity, especially against intracellular pathogens such as cytomegalovirus (CMV), Cryptosporidium parvum, and Giardia lamblia. Suppression of TNF-α may impair the control of latent viral infections, particularly in patients already immunocompromised due to primary immune defects.

This case highlights the importance of close monitoring for opportunistic infections in CVID patients undergoing biologic therapy. Early recognition and prompt antiviral treatment are crucial to preventing irreversible complications, such as vision loss.

Conclusion:
CMV retinitis may emerge as a severe opportunistic infection in CVID patients receiving anti-TNF therapy. Clinicians should exercise caution when initiating biologics in immunodeficient individuals and remain vigilant for atypical infectious complications. Timely diagnosis and targeted treatment can lead to favorable clinical outcomes.

Keywords:
Common variable immunodeficiency; cytomegalovirus; retinitis; infliximab; anti-TNF; opportunistic infection.

POSTER 114 - PRIMARY IMMUNODEFICIENCY AND MDS ARISING FROM GATA2 DEFICIENCY

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Introduction:
GATA2 is a critical transcription factor that governs the proliferation, maintenance, and differentiation of hematopoietic stem and progenitor cells. It plays essential roles in the development of mononuclear phagocytes, the function of alveolar macrophages, and the formation of the lymphatic system.

Pathogenic variants in GATA2 can result in a highly heterogeneous clinical phenotype, including primary immunodeficiency, rheumatologic disorders, pulmonary vascular abnormalities, and an increased risk of myeloid neoplasms. Herein, we present the diagnostic and therapeutic course of a patient with pancytopenia and confirmed GATA2 deficiency who was subsequently diagnosed with myelodysplastic syndrome (MDS).

Case presentation:
A 39-year-old female presented to an external center three years prior with high-grade fever occurring during the fifth week of her pregnancy. Laboratory tests revealed pancytopenia, and bone marrow biopsy confirmed a diagnosis of MDS. She was referred to our clinic after it was learned that her daughter had been diagnosed with a GATA2 mutation.

Medical history revealed recurrent lower respiratory tract infections, particularly pneumonia. Based on this background, genetic testing was performed, and a pathogenic GATA2 mutation was confirmed. Immunological workup revealed persistent pancytopenia, a markedly reduced number of CD16+/56+ natural killer (NK) cells, and an inverted CD4/CD8 ratio (Table 1). *

The patient was started on intravenous immunoglobulin (IVIG) replacement therapy at a dose of 25 grams every 21 days. Following treatment initiation, she experienced complete resolution of pneumonia episodes and a substantial reduction in infectious complications.

Discussion:
GATA2 deficiency presents with a broad range of clinical features, including immunodeficiency, cytopenias, bone marrow failure, and myeloid malignancies. The disease typically progresses from asymptomatic cytopenias to marrow failure and eventually to myeloid neoplasms such as MDS or AML.

Infectious susceptibility stems from immunodeficiency, commonly marked by monocytopenia, NK cell and B cell cytopenia, and often an inverted CD4/CD8 ratio. Despite these findings, plasma cells and tissue macrophages are usually preserved.

Immunoglobulin levels may be normal or elevated, but hypogammaglobulinemia can occur, especially in patients with recurrent infections. In such cases, IVIG replacement reduces infection rates and improves quality of life, as seen in our patient.

Conclusion:
This case highlights the importance of considering GATA2 deficiency in patients presenting with unexplained cytopenias, recurrent infections, or a family history of immunodeficiency or myeloid malignancy. Early recognition and appropriate management—including IVIG replacement—may significantly improve clinical outcomes and prevent infectious complications.

Keywords: GATA2 deficiency; primary immunodeficiency; pancytopenia; myelodysplastic syndrome; IVIG therapy

POSTER 115 - ASSOCIATION BETWEEN NEUTROPENIA AND MORTALITY IN PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY (CVID)

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Introduction:
Autoimmune cytopenias are among the most frequent non-infectious complications observed in patients with common variable immunodeficiency (CVID). While autoimmune thrombocytopenia and hemolytic anemia are relatively common, neutropenia is rare and often presents concurrently with other cytopenias. The objective of this study was to investigate the association between neutropenia and all-cause mortality in patients diagnosed with CVID.

Materials and methods:
This retrospective study included 84 adult patients diagnosed with CVID and followed at the Necmettin Erbakan University Department of Adult Immunology and Allergy Diseases between 2019 and 2024. Patients were stratified into two groups based on the presence or absence of neutropenia, defined as an absolute neutrophil count <1500 × 10^6/L.

Demographic characteristics, immunological parameters, and mortality rates were compared between groups. The impact of neutropenia on survival was assessed using Kaplan–Meier survival analysis.

Results:
The mean age of the study population was 38 years (range: 20–79), and the male-to-female ratio was 43:41. Neutropenia was identified in 24 patients (28.5%). Among these, neutropenia frequently co-occurred with other autoimmune cytopenias, such as thrombocytopenia or anemia, and was independent of active infection in 9 patients.

The mortality rate among CVID patients with neutropenia was 33.3%, compared to 6.7% in those without neutropenia ($p = 0.004$). Additional clinical features of patients with neutropenia are summarized in Table 1.

Kaplan–Meier analysis demonstrated significantly lower 8-year survival in the neutropenic group (57.5%) compared to the non-neutropenic group (92.5%) (log-rank $p < 0.001$) (Figure 1).

Discussion:
Neutropenia in CVID often emerges in the context of other autoimmune cytopenias and is presumed to be of autoimmune origin. The current study highlights a strong association between neutropenia and increased mortality risk in CVID patients. This finding supports the notion that neutropenia, although infrequent, should not be underestimated in the clinical evaluation of CVID.

The presence of neutropenia may indicate a more severe disease phenotype and should prompt closer monitoring and potentially earlier intervention. These results underscore the prognostic relevance of cytopenic profiles in CVID and advocate for heightened clinical vigilance when neutropenia is detected.

Conclusion:
Neutropenia, though uncommon in CVID, is significantly associated with increased mortality. Its identification should prompt thorough evaluation and tailored follow-up, as it may serve as a key prognostic marker in this patient population.

Keywords:
Common variable immunodeficiency; neutropenia; autoimmune cytopenia; mortality; survival analysis.

POSTER 116 - PARASITIC INFECTIONS IN PATIENTS WITH PRIMARY IMMUNE DEFICIENCY

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Introduction:
Primary immune deficiencies (PIDs) are genetic diseases responsible for deficiencies in humoral, cellular or both immunity. Patients with PIDs have an increased susceptibility to viral, bacterial, fungal and parasitic infections. Parasitic infections may be responsible for up to 6% of combined immunodeficiency disorders (CIDs), and are associated with increased mortality in this population. Among parasitic infections in PIDs patients, Cryptosporidium spp., Giardia spp., Toxoplasma spp. and Leishmania spp. have been poorly described in the literature.

Method:
We propose to describe parasitic infections in patients with PIDs from the CEREDIH (Centre de référence des déficits immunitaires héréditaires) database. Patients with a primary immune deficiency diagnosed between 1986 and 2023 and presenting a parasitic infection were included.

Results:
Of the 8924 patients in the CEREDIH database, 95 patients were identified with a parasitic infection, i.e. ≈1% of the CEREDIH cohort. The median age at diagnosis of parasitic infection was 20 years [10; 41]. The male/female ratio was 1.91, and 46.4% of parasitic infections were diagnosed before the age of 20. Forty-three patients (46.7%) presented with giardiosis, 17 (18.4%) with toxoplasmosis, 16 (17.3%) with cryptosporidiosis, complicated in 5/8 cases by biliary cholangitis. Six patients presented with scabies, 5 with leishmaniasis, 3 with hydatidosis, 2 with malaria, 1 with schistosomiasis, 1 with microsporidiosis and 1 with amibiasis. The most frequent PIDs in this cohort were variable common immune deficiencies in 37 patients, (29 giardiasis, 2 toxoplasmosis, 2 cryptosporidiosis, 2 visceral leishmaniasis, 1 hydatidosis, 1 scabies), combined immunodeficiencies in 9 (3 giardiasis, 2 toxoplasmosis, 2 cryptosporidiosis, 1 leishmaniasis, 1 hydatidosis), activated PI3K-delta syndromes in 7 (5 crytposporidiosis, 1 giardiasis, 1 toxoplasmosis) and hyper IgM syndromes in 7 (4 toxoplasmosis and 3 cryptosporidiosis). Twelve patients died, and 7 of these for whom clinical data were available, died of parasitic infection (4 cryptosporidiosis, 2 leishmaniasis and 1 hydatidosis).

Conclusion:
Parasitic infections in patients with primary immune deficiency are rare, ≃1%. Digestive tract infections with Giardia spp. are the most frequent (1/3 of cases), followed by Toxoplasma spp. (1/4), Crytosporidium spp. (1/4) and, more anecdotally, ectoparasitic infections, leishmaniasis and hydatidosis. Cryptosporidiosis remains the most severe parasitic infection, occurring mainly in patients with activated PI3K-delta syndrome, followed by patients with hyper IgM syndrome.

POSTER 117 - DO COMMON VARIABLE IMMUNODEFICIENCY PATIENTS HAVE INCREASED CARDIOVASCULAR RISK BEYOND TRADITIONAL FACTORS?

AUTHORS

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Background:
Common variable immunodeficiency (CVID) is the most frequent symptomatic primary immunodeficiency in adults, with heterogeneous manifestations such as recurrent infections, autoimmunity, lymphoproliferation, and gastrointestinal involvement. Two main phenotypes are commonly recognized: an infection-only form and one associated with immune dysregulation. Emerging evidence suggests that chronic inflammation in patients with immune dysregulation may contribute to increased cardiovascular risk (CVR), but this association remains insufficiently explored, particularly within the context of Inborn Errors of Immunity.

Objectives:
The primary aim was to assess CVR in patients with CVID using clinical, analytical, and immunological parameters. A secondary objective was to compare CVR between patients with and without immune dysregulation, considering the potential contribution of a proinflammatory state to cardiovascular risk.

Methods:
We performed a retrospective and cross-sectional study including 63 adults diagnosed with CVID according to ESID criteria. Retrospective data (clinical, analytical, immunological, sociodemographic) and cross-sectional measurements (anthropometry, blood pressure, arterial stiffness, ankle-brachial index) were collected. CVR was estimated using SCORE2, SCORE-OP, and a diabetes-specific SCORE. Descriptive statistics were applied to analyze the variables.

Results:
Despite a predominantly young, non-smoking cohort (94.6%) with a normal mean BMI (23.8), non-elevated waist circumference, and no significant obesity, the mean estimated CVR was 3.5%. Risk stratification showed 47.4% of patients at moderate risk, 19.3% at high risk, and 7.0% at very high risk; only 26.3% were classified as low risk. Dyslipidemia was identified in 48.3% of the cohort. Mean baseline total cholesterol and LDL levels were 202.1 mg/dL and 125.4 mg/dL, respectively—elevated values for a population without obesity or diabetes.

Immune dysregulation was present in 53.9% of patients. In this subgroup, 45.5% had dyslipidemia, with higher LDL and total cholesterol levels, increased inflammatory markers (LDH, GOT, fibrinogen, D-dimer), and lower hemoglobin, suggesting an ongoing inflammatory state. However, CVR scores did not significantly differ between patients with and without immune dysregulation.

Conclusions:
CVID patients show increased CVR despite the absence of classical risk factors. The high rate of dyslipidemia and inflammatory markers suggests a potential role of chronic inflammation in cardiovascular pathology. As in HIV or autoimmune diseases like psoriasis and lupus, early CVR screening and preventive strategies may be justified in CVID. Larger, longitudinal studies are needed to confirm these findings and guide clinical management.

POSTER 118 - THE VALUE OF FAMILY SCREENING IN THE EARLY DETECTION OF SELECTIVE IMMUNOGLOBULIN A DEFICIENCY AND RELATED AUTOIMMUNE CONDITIONS

AUTHORS

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Objective:
To evaluate the utility of targeted family screening for the early diagnosis of familial selective immunoglobulin A (IgA) deficiency and its impact on the identification and management of associated autoimmune conditions.

Design and method:
We conducted a descriptive case report of a 24-year-old male index patient diagnosed with selective IgA deficiency (serum IgA < 7 mg/dL; normal IgG and IgM) at age 5, with protective vaccine responses. Following our institutional protocol, first-degree and selected second-degree relatives were invited for clinical evaluation, laboratory testing (complete blood count; serum immunoglobulins including IgA, IgG subclasses, IgM, IgE; anti-IgA antibodies; lymphocyte immunophenotyping; vaccine-specific IgG titers; complement levels), and HLA typing. Pedigree analysis traced inheritance across three generations.

Results:
The screening identified selective IgA deficiency in four additional relatives: the patient's mother, brother, nephew, and maternal cousin. Clinical expression varied: the index case and the cousin (15 years) were asymptomatic. The mother presented with vitiligo and hypothyroidism. The brother was GAD65 antibody-positive at the time of screening and developed type 1 diabetes mellitus six years later. The nephew, although clinically healthy, was HLA-DQ2 positive—genetically predisposing to celiac disease—but had no serological or clinical evidence of it. Anti-IgA antibodies were positive in all IgA-deficient individuals. No other causes of hypogammaglobulinemia were identified. All affected individuals shared the HLA A33 / B44 / DR1 / DQ5 haplotype, while only the brother carried the classic HLA A1 / B8 / DR3 haplotype.

Conclusions:
This case illustrates the clinical heterogeneity of selective IgA deficiency and its potential association with autoimmune diseases within families. Targeted family screening enabled early diagnosis not only of immunodeficiency but also of autoimmune conditions—some of them asymptomatic or preclinical at the time of detection. These findings support systematic evaluation of relatives of affected individuals, including immunoglobulin levels, HLA typing, and autoimmune markers, to guide clinical surveillance and personalized follow-up.

POSTER 119 - CLINICAL RESPONSE AMONG PARTICIPANTS WITH WARTS IN THE PHASE 3 TRIAL, MAVORIXAFOR, AN ORAL CXCR4 ANTAGONIST, FOR TREATMENT OF PATIENTS WITH WHIM SYNDROME

AUTHORS

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Objective:
Warts, Hypogammaglobulinemia, Infections, Myelokathexis (WHIM) syndrome, a rare, combined primary immunodeficiency disorder caused by hyperactive CXCR4 signaling, leads to impaired leukocyte egress from bone marrow into peripheral blood. Among the variable multisystem manifestations, individuals are highly susceptible to recalcitrant warts. Plerixafor, an injectable CXCR4 antagonist, has shown improvement in warts in WHIM syndrome, however, the question remains whether CXCR4 antagonism shows a wart benefit in this population. Mavorixafor, an orally available reversible CXCR4 antagonist, demonstrated clinical efficacy in participants with WHIM syndrome in the 4WHIM phase 3 trial (NCT03995108). Here, we report the positive wart effect from chronic oral mavorixafor treatment in this post-hoc analysis of participants enrolled in the study.

Design and method:
4WHIM included a 52-week randomized, double-blind, placebo-controlled period (RCP) with an ongoing open-label mavorixafor only extension (OLE); participants were aged ≥12 years with WHIM syndrome ± history of baseline warts. Local dermatologists reviewed 23 wart regions and adjudicators reviewed 3 target wart regions. Wart assessments included Clinical Global Impression of Severity (CGI-S; 1=no warts to 5=very severe warts) and Clinical Global Impression of Change (CGI-C; +1=worsening to -2=complete resolution) scores (Figure); only CGI-S was used for this analysis. Change from baseline to week 52 (end of RCP) and to the end of the OLE Year 1 (week 104) were analyzed.

Results:
Fifteen participants completed 2 years of the trial and had 70 defined wart areas which were followed for 2 years. Despite a history of warts, no participants in the mavorixafor group had worsening warts during the RCP compared with 2/9 (22.2%) participants in the placebo group. After 2 years of mavorixafor treatment, 4 (66.7%) participants showed improvement and 2 (33.3%) achieved complete remission. Of participants in the RCP placebo group who transitioned to mavorixafor in the OLE, 3 (33.3%) had improvement and 2 (22.2%) experienced complete remission during RCP, whereas 6 (75.0%) participants showed improvement and 4 (50.0%) experienced complete remission during OLE.

Conclusions:
Two-year treatment with chronic oral mavorixafor was associated with marked clinical improvement in wart severity providing further evidence that CXCR4 antagonism leads to wart improvement in patients with WHIM syndrome.

POSTER 120 - SIGNIFICANT INFECTION BURDEN AND IMPACT ON SCHOOL AND WORK AMONG PATIENTS WITH WHIM SYNDROME: A PATIENT AND CAREGIVER SURVEY

AUTHORS

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Objective:
WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome is a rare combined primary immunodeficiency associated with highly variable multisystemic manifestations and increased risk of infections, neoplasm-related comorbidities, end organ damage, and in some cases early death. Literature is limited with no published reports describing patient and caregiver-reported clinical burden. The objective of this survey is to characterize the burdens of WHIM syndrome and treatments on patients.

Methods:
Individuals with a diagnosis of WHIM syndrome and any person providing care for a patient were eligible to complete an online survey. Caregivers responded for patients <18 years old. Patients currently enrolled in a clinical trial for treatment of WHIM syndrome or who had ever received a CXCR4 antagonist treatment were excluded.

Results:
Twenty respondents with WHIM syndrome had survey data collected (<18 years old, n=5; ≥18, n=15). Infection burden in the past 3 months included high rates of respiratory infection (80% of children, 73% of adults), eye infection (80% of children, 33% of adults), oral infection (53% of adults) and Warts/HPV (80% of children, 67% of adults) (Figure). Twelve (60%) of respondents experienced at least 1 infection requiring medical treatment in the last 3 months. Among 14 respondents currently receiving treatment (antibiotics, G-CSF, immunoglobulin, and/or antivirals), 50% reported that they were moderately satisfied and 43% were not at all or slightly satisfied. Treatment had a moderate or significant impact on physical and social activities in 50% of respondents. WHIM syndrome interfered with the majority of respondents' schooling (75%, 15/20) and ability to work (73%, 11/15). Pediatric respondents missed a mean of 15.8 (±7.8) hours of schooling during the previous 30 days. WHIM syndrome impacted physical activity for 70% of all respondents (73% of adults) and social activities for 70% of respondents (73% of adults).

Conclusions:
This is the first ever report on the day-to-day infection burden of WHIM syndrome from a patient perspective. The frequency and severity of reported infections requiring medical care and hospitalization underscores the urgency to proactively treat patients with WHIM syndrome. The negative impacts on many aspects of daily life highlights the important need for treatments that reduce disease burden and improve productivities. These results demonstrate the burden of currently available treatments on the lives of patients with WHIM syndrome and underscore the unmet need for a treatment that can mitigate this burden.

POSTER 121 - HOW TO DIAGNOSE GRANULOMATOUS-LYMPHOCYTIC INTERSTITIAL LUNG DISEASE IN PRIMARY IMMUNODEFICIENCIES: AN INTERNATIONAL CLINICAL PRACTICE GUIDELINE

AUTHORS

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Objective :
Granulomatous-Lymphocytic Interstitial Lung Disease (GLILD) is a rare lung complication seen in people affected by common variable immunodeficiency disorders (CVID). There is not much data available on the optimal management of this condition. The ERS Clinical Research Collaboration e-GLILDnet was established with the intention to improve the lives of those living with GLILD, by fostering collaborative research and optimizing clinical care world-wide. To this end, e-GLILDnet developed an evidence-based, consensus clinical practice guideline on the screening and diagnosis of GLILD.

Design and method:
A panel representing multiple interdisciplinary perspectives convened with methodologists to prioritise clinical questions and review evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology. Evidence to Decision frameworks were used to decide on the direction and strength of recommendations.

Results:
Screening for GLILD is recommended in all adult CVID patients, preferably using high resolution computed tomography. Screening in children is restricted to those with a suspected increased risk of GLILD. As part of the diagnostic process, pulmonary infections should be excluded by means of bronchoscopy and bronchoalveolar lavage, including a differential cell count. Evaluation should be performed by a multidisciplinary team; routine lung biopsies are not mandatory but reserved for unclear cases. The severity of lung function impairment should be evaluated using pulmonary function tests including gas transfer assessment. Blood biomarkers that could facilitate the diagnostic assessment are currently not available.

Conclusions:
This guideline allows for international homogeneity in the diagnosis of GLILD, thereby paving the way for international research collaborations and improving equity in health care for those affected by GLILD around the globe.

POSTER 122 - MALIGNANCY IN PATIENTS WITH INBORN ERROR OF IMMUNITY – A SINGLE CENTER REPORT

AUTHORS

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Introduction:
Inborn errors of immunity (IEI) are characterized by susceptibility to infections, autoimmunity, allergy, autoinflammation and lymphoproliferation. Chronic antigenic stimulation, chromosome instability tissue inflammation, impaired cell development and impaired immune surveillance may play a crucial role in the appearance of cancer in IEI.

Objectives:
To establish the frequency and evolution of malignancy in IEI patients diagnosed in Third Pediatric Clinic Timisoara.

Material and method:
We analyzed 332 patients aged 0-25 years, diagnosed with IEI in the period 1990 – 2024.

Results:
13 patients (4%) (6 females and 7 males) developed malignancy, 75% of them being hematological malignancy: 9 cases with non-Hodgkin lymphoma, 2 cases with cerebral tumor, 1 case with acute myeloblastic leukemia and 1 case with gastric carcinoma. The types of IEI were: 1 case each with congenital neutropenia, ataxia-telangiectasia, CVID, ALPS, WAS, DOCK2, 2 cases with MSH6, and 5 cases with Nijmegen breakage syndrome. In 8 patients (61,5%) the diagnosis of IEI was concurrent with that of cancer. Treatment consisted in chemotherapy and immunotherapy in 11 patients, IV Ig- 8 patients, G-CSF-1 patient, surgery- 3 patients. Mortality rate was 84,6%, one the most important cause being the IEI diagnosis delay.

Conclusions:
IEI show a significantly higher incidence of malignancy and a significant higher rate of mortality compared to the general population of the same age (1% and respectively 10-20%). All patients with malignancy should be investigated for IEI and all patients with IEI should be monitored for the development of cancer.

POSTER 123 - INTERNAL TRANSITION FROM THE PEDIATRIC IMMUNOLOGY UNIT TO THE HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT: A MULTIDISCIPLINARY EXPERIENCE

AUTHORS

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Objective:
To describe our institutional experience implementing an internal transition pathway between the Pediatric Clinical Immunology Unit and the Hematopoietic Stem Cell Transplantation (HSCT) Unit for pediatric patients with inborn errors of immunity (IEI), focusing on care coordination and patient/family perception.

Design and method:
In September 2021, we initiated a structured multidisciplinary transition process, later formalized in June 2022, including joint visits by the Immunology and HSCT teams (physicians and nurses). The pathway included pre-transplant educational sessions and follow-up visits at +3, +6, +9, +12 months post-HSCT, an annually afterwards. Patients' experience was evaluated using ad-hoc questionnaires performed before and after the education session given by both unit's referent nurses (pre-HSCT) and post-HSCT. The items explored were treatment knowledge, secondary effects' doubts, anxiety, logistical concerns related to the transition process, as well as an open comment section. Items were graded from complete disagreement to complete agreement, equating a 1-5 punctuation.

Results:
Ten pediatric patients with IEI were referred for HSCT (median age at HSCT 8.78 years, range 1.16 – 18.21). Of these, 9 have already undergone HSCT and 1 is in transition. Disease groups included: common variable immunodeficiency (CVID) with lymphoproliferation (n=1), Leaky – Severe combined immunodeficiency (L-SCID) (n=1), Hemophagocytic Lymphohistiocytosis (familial or associated to chronic active EBV infection) (n=4), APLAID/ PLAID GOF (n=2), chronic granulomatous disease (CGD) (n=2). Since implementation of the transition model, joint multidisciplinary visits improved pre- and post-HSCT continuity. Educational sessions made families empowered about the general information and logistical aspects of transition both post-session and post-HSCT. However, families showed a slight increase (+0.5 points) in anxiety post-session that decreased after HSCT. Doubts regarding side effects decreased after the informative session, but showed a slight increase after HSCT. Qualitative feedback emphasized improved clarity and emotional support, particularly regarding daily life in the HSCT unit. Post-HSCT evaluations are pending standardization. Identified limitations include lack of systematic collection of post-HSCT feedback and need for validated tools.

Conclusions:
An internal structured transition model between the Immunology and HSCT units enhances care coordination, patient/family understanding, and emotional preparedness. Joint visits and tailored education proved effective and well received. Continuous evaluation and refinement of the tools used, particularly post-HSCT, are essential for a comprehensive and patient-centered transition process.

POSTER 124 - A RARE CASE OF LONG-TERM IMMUNE DEPLETION IN A CHILD FOLLOWING CHEMOTHERAPY FOR ACUTE LEUKEMIA: SECONDARY OR PRIMARY IMMUNODEFICIENCY?

AUTHORS

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Case presentation:
A 12-year-old girl was diagnosed at the age of 3 (2014) with acute lymphoblastic leukemia (ALL) and treated with chemotherapy for 2 years resulting in transient symptomatic hypogammaglobulinemia (HG). No B-cell depleting anti-CD20 monoclonal antibody therapies were prescribed; bone marrow transplant wasn't indicated after chemotherapy. To date, the patient is in complete remission from her leukemia.

In 2017, she developed a new HG associated with a low vaccine response. Immunoglobulin replacement therapy (IgRT) was initiated. Despite adequate premedication, the patient developed adverse events (AE; severe headache, fever, and chills) to several Ig preparations until she was switched to Iqymune®, which was well tolerated.

Repeated IgRT discontinuation attempts, including summer withdrawal, failed. Exploration revealed a low rate of Memory B cells (CD19+/CD27+) and Class-switched Memory B cells (CD27+, IgM/D-). These rates remained almost unchanged even 5 years after the end of chemotherapy (3 explorations carried out in 2017, 2020 and 2022). Genetic investigation made in 2018 didn't exhibit any genetic mutation. There was no family history of immune deficiency.

To date, the patient is still treated with a monthly infusion of Iqymune® at 0.4g/kg. No infections were recorded during this treatment.

Discussion:
In this case, the etiology of immunodeficiency is not well established.

T and B cells were severely affected after ALL polychemotherapy but recovered rapidly after treatment stop. Knowing that chemotherapy is aggressive with risk of mutation, and that a treatment is usually administered before the immune system reaches its maturity (7-8 years of life), a mutation leading to immunodeficiency could not be ruled out.

This HG may also be an infra-clinic primary immune deficiency revealed after the chemotherapy. Although genetic investigation was negative, this hypothesis remains probable knowing that several common variable immunodeficiency (CVID) patients don't exhibit genetic mutation. Furthermore, low IgM memory B cells (CD19+/CD27+) and class switched memory B cells (CD27+, IgM/D-) are in favor of CVID.

Epigenetic changes leading to delayed or silenced maturation of B cell function may also be hypothesized.

Fever, and chills are frequent in pediatric ALL patients and are related to IgA levels. The low rate of IgA within Iqymune® compared to other Ig could explain the good tolerance toward infusions in this patient.

Conclusion:
It could be difficult to discern the relationship between primary and secondary immune deficiencies due to crossover between the two entities. Iqymune® displayed a better tolerability profile compared to previous Ig preparations in this patient.

POSTER 125 - ORGANIZATIONAL AND ECONOMIC IMPACTS OF IQYMUNE® INFUSION PROTOCOL IN THE MANAGEMENT OF SECONDARY IMMUNODEFICIENCY PATIENTS: RESULTS FROM AN ECONOMIC MODEL IN A GERMAN INFUSION CENTRE

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Background and aims:
Immunodeficiencies and autoimmune disorders represent a major burden to the healthcare system. The workload in perfusion centres is steadily increasing due to the growing number of patients suffering from secondary immunodeficiencies (SID). A business impact model was developed to evaluate the organisational and economic benefits of IQYMUNE® infusion protocol in a healthcare centre, compared with its intravenous immunoglobulin (IVIG) infusion protocols.

Methods:
A static model was developed to assess the impact of IQYMUNE® infusion protocol on healthcare resource utilisation, including time and cost savings, from the perspective of a German infusion centre. The model incorporated parameters such as patient, organisational, and centre-specific factors, with a time horizon of one year. Sensitivity and scenario analyses were conducted to account for uncertainties and varying infusion rates.

Results:
Using IQYMUNE® saved patients 85 minutes per visit, resulting in 24.7 hours saved per year. Total occupancy time saved per chair/bed was 12.8 hours per day (assuming 10 available chairs and 9 SID patients per day). IQYMUNE® infusion protocol improved the capacity to manage SID patients, with an incremental increase in global capacity of 16.3 patients per day or 3,829 infusions per year. Using IQYMUNE® translates into a net economic benefit of 3 to 6 million euros per year due to the additional number of beds/chairs and the extra time freed up by nurses.

Conclusions:
This study underscores the potential of IQYMUNE® to optimise healthcare resources in the management of SIDs, suggesting a scalable model for other centres facing similar challenges.

POSTER 126 - OPTIMIZING THE PATIENT JOURNEY IN ACTIVATED PHOSPHOINOSITIDE 3-KINASE DELTA (PI3KΔ) SYNDROME: A MULTIDISCIPLINARY DELPHI CONSENSUS ON DIAGNOSIS AND PERSONALIZED MANAGEMENT

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Objective:
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) is an ultra-rare disease characterized by a broad spectrum of clinical manifestations that often overlap with those of other inborn errors of immunity. The rarity of the disease and absence of specific protocols create barriers to its management and negatively affect the experience of patients and their families. To address these difficulties, expert consensus recommendations were developed to guide APDS care, focusing on optimizing the patient journey from detection to follow-up.

Design and method:
This study was conducted following the RAND/UCLA Delphi consensus methodology. The recommendation preparation group (RPG) consisted of 8 experts in treating pediatric and adult APDS patients. An exhaustive targeted literature review on APDS (2016-2023) was performed in PubMed. Based on the evidence collected, the RPG developed 34 statements, which were evaluated by a multidisciplinary panel of experts in immunodeficiencies (n=33, including pediatric and adult immunologists, hematologists, pulmonologists, internal medicine specialists, and infectious disease specialists) using a 2-round online questionnaire. A consensus on the appropriateness of the statements was reached when at least two-thirds of the panelists rated them with a score of ≥7 on a 9-point Likert scale (1, strongly disagree; 9, strongly agree).

Results:
A consensus was achieved in the first Delphi round on all 34 statements, with a median score of 9 in 33 of them. These recommendations span the entire patient journey, including the onset of clinical manifestations, diagnosis, referral pathways, and patient and family support and follow-up (Figure 1). Accordingly, key recommendations of the core domains included: onset and diagnosis - the clinical manifestations to consider when APDS is suspected, and

the importance of early diagnosis to enable appropriate interventions; referral pathways - the need to establish clear referral pathways and effective communication channels to specialized referral centers to ensure prompt diagnosis, proper management, and follow-up by multidisciplinary teams; and patient and family support - the importance of providing health education for patients and families about their disease, symptoms or self-care, as well as offering them emotional and psychological support during the diagnosis and throughout the course of the disease via support groups and patient organizations.

Conclusions:
These consensus statements may serve as a practical framework to facilitate early diagnosis of APDS and improve access to multidisciplinary, personalized care while providing ongoing support to patients and their families, thus addressing the diverse medical and psychological needs of APDS patients.

POSTER 127 - COMPREHENSIVE IMMUNOPHENOTYPIC CHARACTERIZATION OF CTPS1 DEFICIENCY

AUTHORS

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CTPS1 (cytidine triphosphate synthase 1) is essential for de novo CTP synthesis during lymphocyte proliferation. Loss-of-function mutations in CTPS1 cause a rare primary immunodeficiency marked by defective adaptive immunity and recurrent viral infections. The impact of CTPS1 deficiency on innate immune compartments remains poorly defined. Here, we present a detailed immunophenotypic and functional analysis of both innate and adaptive immune responses in a patient with genetically confirmed CTPS1 deficiency.

Flow cytometry revealed an inverted CD4:CD8 T-cell ratio and a distinct $CD3^+CD8dim$ subset, indicating aberrant T-cell maturation or chronic activation. Upon cytokine challenge, patient $CD4^+$ T cells showed markedly reduced STAT5, STAT6, and STAT3 phosphorylation in response to IL-2, IL-4, and IL-6, respectively. Intracellular cytokine staining demonstrated diminished IFN-γ, IL-17A, and IL-10 production following PMA/ionomycin stimulation, consistent with impaired Th1, Th17, and regulatory T-cell functions.

Stimulation of PBMCs with TLR4 (LPS), TLR7 (R848), TLR9 (CpG ODN) ligands and cytosolic sensors (cGAMP, HSV) elicited reduced IFN-γ secretion, whereas TLR7 engagement provoked an exaggerated IL-10 response, suggesting skewed innate regulation. In the myeloid compartment, we identified an expanded $CD14^-CD15^+$ low-density granulocyte population and a 4–5-fold increase in spontaneous neutrophil extracellular trap formation compared to healthy controls.

Collectively, these findings demonstrate that CTPS1 deficiency disrupts both lymphoid and myeloid lineages, impairing STAT signaling, cytokine production, innate sensor responses, and neutrophil function. This broad immune dysregulation underscores the pivotal role of CTPS1 in maintaining immune homeostasis and informs potential therapeutic strategies.

POSTER 128 - THERAPEUTIC MODULATION OF EXOSOMAL SIGNALS AND INNATE IMMUNITY IN CHAPLE SYNDROME

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CD55 is a complement regulatory protein that inhibits both the classical and alternative pathways. CD55 deficiency causes CHAPLE syndrome (CD55 deficiency with hyperactivation of complement, angiopathic thrombosis, and protein-losing enteropathy). Beyond complement control, CD55 serves as a ligand for CD97 on T cells, B cells, macrophages, and dendritic cells, modulating immune cell activity. However, the effects of CD55 deficiency on innate immune function and the role of circulating exosomes in this context remain unclear.

We analyzed innate immune responses in CHAPLE patients before (BT) and after (AT) a single dose of eculizumab. Peripheral blood mononuclear cells (PBMCs) from BT, AT, and healthy donors were stimulated with endosomal TLR ligands (TLR4, TLR7, TLR9) and cytosolic sensors (cGAMP, poly(dA:dT)). Cytokine production (IL-1β, IL-6, IFN-α, IP-10, IL-10) was measured by ELISA. Additionally, healthy PBMCs were incubated with plasma-derived exosomes from BT and AT samples for 36 hours to assess exosome-induced cytokine responses.

Compared to controls, CHAPLE PBMCs (BT and AT) showed reduced IL-1β, IL-6, IFN-α, and IP-10 production upon TLR and cytosolic stimulation. The anti-inflammatory IL-10 response to noncanonical inflammasome activation and TLR7 engagement was also diminished in both BT and AT cells. Notably, AT-derived exosomes elicited lower IL-1β, TNF-α, and IFN-γ secretion but higher IL-10 release compared to BT exosomes; IP-10 induction by AT exosomes was also reduced in healthy PBMCs.

These results demonstrate that a single eculizumab infusion does not restore impaired endosomal or cytosolic innate immune sensing in CHAPLE patients. However, post-treatment exosomes promote an anti-inflammatory cytokine profile, suggesting a compensatory immunoregulatory mechanism following complement inhibition.

POSTER 129 - HEIGHTENED TLR/INFLAMMASOME ACTIVATION AND NETOSIS IN CD55-DEFICIENT CHAPLE SYNDROME

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CHAPLE syndrome, caused by autosomal-recessive CD55 deficiency, manifests with complement hyperactivation, angiopathic thrombosis, and protein-losing enteropathy. Beyond complement regulation, CD55 ligation modulates leukocyte activation via CD97, yet its impact on innate sensing and neutrophil function remains unexplored. We investigated Toll-like receptor (TLR) signaling, inflammasome activation, and neutrophil extracellular trap formation in a family cohort comprising three affected siblings and their heterozygous parents. Peripheral blood mononuclear cells (PBMCs) were stimulated for 24 h with TLR agonists (Pam3CSK4, poly(I:C), LPS, flagellin, R848, CpG ODNs) and inflammasome activators (cGAMP, Nigericin, HSV DNA, ATP). Cytokine outputs (IL-1β, IL-4, IL-8, IFN-γ, IP-10, IFN-α) were quantified by ELISA, and T- and NK-cell subsets were phenotyped by flow cytometry. Neutrophil spontaneous and plasma-induced NETosis was assessed microscopically. Compared to controls, CHAPLE PBMCs particularly one female sibling exhibited markedly increased IL-1β and IL-8 responses to LPS and viral DNA, coupled with absent IFN-α production upon endosomal TLR stimulation. Flow cytometry revealed expanded $CD4^+$ and $CD8^+$ T-cell frequencies in this patient. Neutrophils displayed spontaneous NET formation ex vivo, and healthy neutrophils underwent NETosis when incubated with her plasma. These findings indicate that CD55 deficiency enhances TLR- and inflammasome-driven proinflammatory responses and promotes aberrant NETosis, which may contribute to the variable clinical phenotype in CHAPLE syndrome.

POSTER 130 - LEUKOCYTE ADHESION DEFICIENCY TYPE 1 (LAD-I): GENETIC BASIS AND CLINICAL PRESENTATIONS

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Introduction:
Leukocyte adhesion deficiency (LAD) is a rare autosomal recessive inborn error immunity. The most common form is LAD-I, associated with CD18 (beta-2 integrin) deficiency or dysfunction caused by mutations in the ITGB2 gene. LAD-I cases are classified based on CD18 expression as severe (<2%), mild-moderate (2–30%) or rarely, as normal expression with functional impairment. The only curative option for LAD is hematopoietic stem cell transplantation (HSCT).

Objective:
The aim of this study was to evaluate the family history, clinical features, immunological characteristics and HSCT outcomes of patients diagnosed with LAD-I.

Methods:
We retrospectively evaluated cases of suspected LAD monitored in our clinic between June 2019 and 2024.

Case 1:
A 3-month-old female. She received treatment for feeding difficulties and an infection during the neonatal period. She developed omphalitis after discharge and underwent surgery due to a urachal anomaly. Delayed postoperative wound healing and leukocytosis led to an evaluation for LAD. Initial CD11c and CD18 expression was normal; however, due to strong clinical suspicion, repeated flow cytometry testing yielded a negative result. A c.1023del mutation (exon 9) in the ITGB2 gene was detected. Following an initial HSCT from a fully HLA-matched, healthy sibling donor, a second transplant was performed due to low chimerism. Follow-up continues.

Case 2:
A 21-month-old female patient. She was treated for pustular lesions in the neonatal period. The umbilical cord fell off at three months and persistent leukocytosis was observed. Family history revealed relatives who died from a similar disease. CD11c and CD18 expression was negative, and lymphocyte subsets and immunoglobulin levels were normal. HSCT was performed using a fully HLA-matched mother as the donor, and follow-up continues.

Case 3:
The 1,5 month-old male sibling of Case 2 was hospitalised due to an abscess and omphalitis after birth. He was referred because of his sibling's LAD-I diagnosis. Flow cytometry revealed negativity for CD11b, CD11c and CD18. A homozygous c.562C>T (exon 6) mutation in ITGB2 was identified. Following HSCT from the father, a second HSCT was required due to low chimerism, and clinical monitoring is ongoing.

Conclusion:
Causes of leukocytosis and neutrophilia in neonates include infection, congenital leukemia and disorders of leukocyte function. LAD should be included in the differential diagnosis if there is delayed umbilical cord separation, impaired wound healing and persistent leukocytosis.

POSTER 131 - TREATMENT INDIVIDUALIZATION IS A CONTINUOUS CHALLENGE IN MANAGING PRIMARY IMMUNODEFICIENCY DISEASE PATIENTS: A CASE REPORT

AUTHORS

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Case presentation:
A 25-year-old man was diagnosed with Common Variable Immune Deficiency (CVID) at age 15, characterized by IgG2 and IgA deficiency. Immunoglobulin replacement therapy was initiated the same year (2010). Despite trying multiple intravenous immunoglobulin (IVIg) preparations and receiving dedicated premedication, the patient developed intolerance symptoms—including headaches and vomiting—prompting a switch to subcutaneous immunoglobulin (SCIg) in 2011.

SCIg was well tolerated throughout childhood. However, during adolescence (starting in 2017), lifestyle changes and a desire for greater independence led to frustration with injection system troubleshooting, resulting in non-compliance and recurrent infections. Consequently, IVIg was reintroduced despite the patient's prior intolerance.

Over the next three years, multiple IVIg preparations were trialed, but severe headaches occurring 24–48 hours post-infusion necessitated further adjustments. In 2020, the patient was switched to Iqymune®, which he tolerated well, with no intolerance symptoms observed during recent follow-up.

Discussion:
Once established, CVID diagnosis implies a lifelong Ig treatment in most cases that should be adjusted to the patient's situation and needs. In this case report, challenges related to the choice of therapy were mainly driven by two factors: adverse events (AEs) and stages of life.

Occurrence of AEs may often be linked to the purity of Igs, which significantly varies from one Ig preparation to another. This purity depends on the removal of several non-IgG components like IgA. These non-IgG proteins have been associated with AEs such as headache, migraine and rarely anaphylactic reactions or aseptic meningitis. The low rate of IgA in Iqymune® compared to other Ig preparations may explain the good tolerance towards Iqymune®'s infusions in our patient.

On the other hand, high Anticomplementary activity (ACA) leads to IgG aggregation and is known to induce fever, chills, and hypotension. IqYmune® is associated with low ACA activity due to its manufacturing process which includes specific filtration steps, low pH formulation and no preparation heating.

Adolescence brings personal and social challenges that can impact treatment adherence and the autonomy of future adults with primary immunodeficiency (PID). Providing appropriate multidisciplinary support during the transition, including guidance on treatment options, is essential for maintaining good compliance.

Conclusion:
In clinical practice, close monitoring of PID patients is essential to improve their quality of life and identify their specific needs to tailor IgG therapy.

POSTER 132 - MONITORING AND ANALYSIS OF PATIENT PATHWAYS WITH PRIMARY IMMUNODEFICIENCIES: RESULTS FROM THE "MAPPA SURVEY" PROMOTED BY THE ITALIAN PRIMARY IMMUNODEFICIENCIES ASSOCIATION

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Objective:
The MAPPA survey (Monitoring and Analysis of Patient Pathways with Primary Immunodeficiencies) was developed to provide a detailed overview of the diagnostic, clinical, and emotional journey of individuals affected by primary immunodeficiencies (PIDs). The goal was to identify unmet needs, delays in diagnosis, comorbidities, and the overall impact of PIDs on patients' quality of life and access to care. The long-term aim is to generate structured data to inform clinical practice, guide healthcare policies, and support research and advocacy initiatives to improve PID management and quality of life.

Design and method:
This national, anonymous online survey was promoted by AIP APS (Italian Association of Primary Immunodeficiencies) in collaboration with Kedrion Biopharma. It was open to patients with PIDs and their caregivers from March to June 2025, with a personalized question flow based on the respondent's profile. The survey explored four main areas: diagnostic timeline, associated conditions, treatment accessibility, and quality of life. Responses were analyzed both cross-sectionally and by respondent category (patients vs caregivers). Participation was voluntary, and no identifiable personal data were collected.

Results:
A total of 192 responses were collected, 79% from patients and 21% from caregivers. Only 7% of respondents received a PID diagnosis within the first year of life, while 26% were diagnosed between ages 35 and 50. Notably, 30% reported permanent organ damage prior to diagnosis, with 80% of those affecting the lungs. In 70% of cases, the diagnostic suspicion arose from recurrent or unusual infections. These findings highlight the urgent need for early detection and the promotion of neonatal screening programs, currently uneven across Italian regions. Chronic comorbidities were common: 43% reported recurrent bronchitis, 28% inflammatory bowel disease, and 25% chronic fatigue. These conditions often preceded or accompanied diagnosis, complicating clinical management. More than two-thirds reported that PID affected daily choices regarding work, education, social life, and leisure activities. Emotional burden emerged as a major issue: anxiety, stress, and depressive symptoms were frequently reported, highlighting the "invisible weight" many patients carry—often more limiting than physical symptoms. The emotional impact extended to families and caregivers, affecting interpersonal dynamics and routines.

Conclusions:
The MAPPA survey sheds light on critical delays in PID diagnosis, significant clinical complications, and profound psychosocial consequences. These findings reinforce the need for targeted awareness campaigns, earlier detection strategies, and comprehensive care approaches.

POSTER 133 - NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN CVID AND AGA: THE ROLE OF ELF SCORE AND SERUM FIBROSIS MARKERS IN CORRELATION WITH FIBROELASTOGRAPHY

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Objective:
Liver fibrosis represents a clinically relevant complication in patients with common variable immunodeficiency (CVID) and agammaglobulinemia (AGA), contributing to progressive hepatic damage and increased mortality. The Enhanced Liver Fibrosis (ELF) score, based on serum levels of hyaluronic acid (HA), the N-terminal pro-peptide of type III collagen (PIIINP), and tissue inhibitors of matrix metalloproteinase-1 (TIMP-1), provides a non-invasive tool for assessing liver fibrosis. The objective of this study was to analyze the correlation between serum fibrosis biomarkers and liver stiffness measurements in patients with CVID and AGA.

Design and method:
Fibrosis biomarkers and liver stiffness (assessed by transient elastography) were measured in 22 patients with CVID and 8 patients with AGA, and compared to a matched cohort of healthy control subjects (n=30).

Results:
The fibrosis marker TIMP-1 was significantly elevated in both CVID and AGA patients compared to controls ($p<0.001$ and $p=0.0155$, respectively), with no significant difference between the two patient groups. The ELF score was significantly higher in CVID patients (9.54±0.94) compared to AGA patients (8.72±0.88) ($p=0.041$). No statistically significant differences were found in levels of HA and PIIINP between the groups. A significant positive correlation was observed between HA levels and liver stiffness ($p=0.016$, Pearson's $r = 0.518$), while the correlation between ELF score and liver stiffness reached borderline significance ($p=0.057$, $r = 0.42$). An ELF score below 9.8 demonstrated a high negative predictive value (87%) for the development of liver fibrosis as assessed by elastography. This threshold has also recently been proposed as a clinically meaningful cutoff for predicting hepatic outcomes, including cirrhosis, liver-related hospital admissions, and mortality.

Conclusions:
Early and accurate assessment of liver fibrosis is critical in the management of CVID and AGA patients to prevent long-term complications. Fibrosis biomarkers and the ELF score may serve as early indicators of fibrotic progression, enabling timely intervention and potentially mitigating irreversible hepatic damage.

POSTER 134 - HETEROZYGOUS IRF2BP2 DELETION ASSOCIATED WITH THERAPY-RESISTANT EOSINOPHILIC ASTHMA AND GLILD IN A CVID-LIKE PATIENT

AUTHORS

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Objective:
Interferon Regulatory Factor 2 Binding Protein 2 (IRF2BP2) is a transcriptional corepressor with a key role in immune regulation. Loss-of-function of IRF2BP2 has been shown to impair B-cell differentiation and disrupt immune homeostasis leading to common variable immunodeficiency (CVID) with a broad phenotypic spectrum, including hypogammaglobulinemia, recurrent infections, autoimmunity, and gastrointestinal manifestations. The objective of this case-presentation is to describe a diagnostically challenging patient who initially presented with treatment-refractory asthma. However, further clinical and genetic evaluation revealed a CVID-like phenotype with a heterozygous IRF2BP2 deletion, complicated by granulomatous–lymphocytic interstitial lung disease (GLILD).

Design and method:
We describe a 53-year-old female with a 23-year history of eosinophilic asthma, managed by a pulmonologist, who over the past two years failed to respond adequately to multiple therapeutic regimens, including IL-5Rα blocker - benralizumab. Lung function tests revealed a mixed ventilatory defect (FVC 64.3%, FEV 1 49.7%, DLCO 58%) with a positive bronchodilatatory test. Given the poor disease control with frequent respiratory infections, she was referred to an immunologist. Immunological workup included evaluation of serum immunoglobulin levels, vaccine-specific antibody response, peripheral blood lymphocyte immunophenotyping, and a high-resolution chest computed tomography (CT) scan.

Results:
Significant hypogammaglobulinemia was observed (IgG 1.81g/L [normal 7–16g/L], IgA <0.05g/L [normal 0.72–4.2g/L], IgM 0.14 g/L [normal 0.4–2.3 g/L]) along with an absent response to vaccine antigens. Peripheral blood lymphocytes immunophenotyping revealed a decreased number of NK cells (59/μL [normal 80–690]), absence of switched memory B-cells and CD21low B-cells and reduced transitional B-cells while counts of CD19+ B and CD4+/CD8+ T-cells were normal. CT revealed ground-glass opacities, bronchiectasis and areas of consolidation, implicating a diagnosis of GLILD. A diagnosis of CVID was established, and immunoglobulin replacement therapy was initiated. Clinical-exome sequencing identified a heterozygous 1q42.2-1q43 deletion of unknown significance affecting 23 protein-coding genes, including IRF2BP2.

Conclusions:
To date, only two patients with a CVID-like phenotype and a large deletion including the IRF2BP2 gene have been reported. Heterozygous deletions in the IRF2BP2 locus cause complete gene loss and may contribute to a complex phenotype due to the simultaneous deletion of neighboring genes. Our case of therapy-resistant eosinophcilic asthma and GLILD, in CVID-like patient provides important insights into the expanding phenotypic spectrum associated with IRF2BP2 haploinsufficiency. Althought our patient has not developed autoimmune features, malignancy, or significant gastrointestinal symptoms, recent data from cohorts carryng IRF2BP2 variants, suggest that close longitudinal monitoring for these complications is warranted.

POSTER 135 - NOVEL HETEROZYGOUS DELETION VARIANT IN STAT3 ASSOCIATED WITH AUTOSOMAL DOMINANT HYPER-IGE SYNDROME

AUTHORS

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Objective:
To report a clinical case with a novel heterozygous deletion variant in the STAT3 gene resulting in Autosomal Dominant-Hyper-IgE Syndrome (AD-HIES).

Design and method:
The clinical case consists of an 18-month-old male at the diagnosis with a background of eosinophilia and elevated serum immunoglobulin IgE. Since birth, the patient has presented arthrogryposis, hypotonia, macrocephaly, recurrent infections including multiple pneumonias and bronchiolitis, atopic dermatitis, and reduction of memory B cells (NIH Hyper-IgE score=34,98). Additionally, the patient is ashmatic and has known allergies to milk and eggs.

Given the suspicion of Hyper-IgE Syndrome, we performed the study of the gene encoding the transcriptional activator STAT3. Genomic DNA was isolated from peripheral blood and sequencing was performed using Sanger methodology on the 24 exons encoding the STAT3 protein and the corresponding exon-intron boundaries.

Results:
In the genetic study it was identified an heterozygous mutation consisting of an in-frame deletion of 18 base pairs in exon 18 (NC_000017.10(NM_001369513.1): c.1660_1677del ATGGCTGGCAAGGGCTTC), resulting in the predicted loss of 6 amino acids in the coded protein sequence, (NM_001369513.1(NP_001356442.1):p.(Met554_Phe559del). The deleted amino acids (554-MAGKGF-559) are located in the linker domain of the protein. The segregation study was also performed on the patient's parents and his brother, which was negative. So it is confirmed that it was a de novo mutation.

This variant is not present in population databases (gnomAD no frequency) or mutation databases and has not been reported in the literature in individuals affected with STAT3-related conditions. The functional significance of this variant is currently unknown. Although the available evidence is insufficient to determine the role of the variant in disease, we considered the variant pathogenic for AD-Hyper-IgE STAT3 Deficiency, following the Standards and Guidelines for the Interpretation of Sequence Variants of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.

Conclusions:
Both, the in-frame mutation found in STAT3, which affects the linker region of the protein, and the phenotype of the patient, are compatible with diagnosis of AD-Hyper-IgE STAT3 Deficiency (Job Syndrome) as the IUIS Classification of the Inborn errors of Immunity updated in 2024. Currently, the patient is being treated with intravenous immunoglobulin, showing clinical improvement, although IgE levels remain elevated and recurrent infections continue, though less severe.

POSTER 136 - PANSCLEROTIC MORPHEA ASSOCIATED WITH A GAIN-OF-FUNCTION STAT4 MUTATION: FIRST REPORTED CASE IN MEXICO

AUTHORS

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Objective:
To describe the clinical case of a pediatric patient with early-onset pansclerotic morphea associated with a previously unreported genetic variant in STAT4, and her response to targeted immunomodulatory therapy.

As an introduction of the case, pansclerotic morphea is a systemic inflammatory disease within the spectrum of systemic sclerosis. It is characterized by abnormal activation of T lymphocytes and the production of proinflammatory cytokines such as TNF, IL-6, and TGF-β, which promote collagen overproduction. Its clinical manifestations include multisystem fibrosis, cytopenias, and hypogammaglobulinemia. Recently, a genetic association has been established with variants that induce severe autoinflammatory phenotypes.

Desing and method:
Observational case report. Clinical, immunological, radiological, histopathological, and genetic data were collected from a 5-year-old female, originally from San Felipe del Progreso, Mexico, with a background of consanguinity (positive endogamy). She had a history of liver failure and recurrent severe infections requiring multiple hospitalizations since her first year of life. She was initially diagnosed and treated for autoimmune hepatitis associated with active Epstein–Barr virus infection. Her early clinical course was also complicated by kwashiorkor and hydrocephalus. At the age of 2, she developed a dermatosis diagnosed as generalized morphea, unresponsive to systemic steroids and conventional immunosuppressants. Extended immunologic workup and next-generation sequencing were performed.

Results:
Laboratory findings revealed hypergammaglobulinemia, thrombocytopenia, hypocomplementemia, and positivity for antinuclear antibodies, antiphospholipid antibodies, and anti–smooth muscle antibodies. Chest high-resolution CT showed pulmonary fibrosis. Genetic testing identified a previously unreported heterozygous mutation in STAT4 (c.2068G>C; p.Asp690His), with asymptomatic carriers found within the family. Treatment with intravenous immunoglobulin, ruxolitinib, tocilizumab, prednisone, and systemic pirfenidone was initiated, resulting in progressive clinical improvement.

Conclusions:
Gain-of-function (GOF) genetic variants in STAT4, associated with persistent activation of the JAK-STAT pathway, have recently been described in severe autoinflammatory phenotypes. Our patient's phenotype is very severe and presented at an earlier age than previously reported cases; she also exhibits positivity for autoantibodies. Targeted treatment with a JAK inhibitor and anti-IL6 therapy has shown significant clinical effects. We present the first confirmed case with this defect in Mexico, with some features distinct from those reported in the literature. Additional studies are underway to validate the effect of this variant and to explore possible explanations for our patient's clinical characteristics.

POSTER 137 - THE EMERGING ROLE OF GERMLINE CTC1 VARIANTS IN PRIMARY IMMUNODEFICIENCY (PID): CLINICAL INSIGHTS FROM A FOUR-PATIENT COHORT

AUTHORS

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Objective:
CTC1 encodes a critical component of the CST complex, essential for telomere maintenance and DNA replication. Germline mutations in CTC1 have been associated with telomeropathies and bone marrow failure syndromes, yet their contribution to PID remains poorly defined. We report four patients with heterozygous CTC1 variants presenting clinical and immunological features highly suggestive of PID. Our objective is to substantiate the presence of underlying PID in these individuals—some of whom have developed hematologic malignancies—through comparative clinical analysis and subsequent functional studies.

Design and method:
Clinical exome sequencing was performed to identify variants potentially associated with PID. Immunophenotyping by flow cytometry was conducted to assess lymphocyte subsets, including $CD4^+$ and $CD8^+$ T cells, $CD19^+$ B cells, and $CD56^+$ NK cells. Additional analyses were carried out to further characterize lymphoid subpopulations, including B cell memory and T cell lineage subsets. DNA repair assays were also performed to support the functional evaluation.

Results:
All four patients carried heterozygous germline variants in CTC1, classified as likely pathogenic or of uncertain significance with supporting evidence. Two were diagnosed with chronic lymphocytic leukemia (CLL) and exhibited secondary hypogammaglobulinemia, recurrent infections, and marked reductions in switched memory B cells and NK cells. The remaining two met diagnostic or probable criteria for common variable immunodeficiency (CVID), with similar immunophenotypic alterations but no malignancy. Across all cases, the most consistent findings were reduced class-switched memory B cells and impaired NK cell numbers, suggesting a shared underlying immune defect potentially related to CTC1 dysfunction.

Conclusions:
This case series supports a potential role for heterozygous CTC1 variants in the pathogenesis of PID, particularly affecting B-cell maturation and NK cell homeostasis. The consistent immunological phenotype across clinically diverse patients suggests an underlying defect beyond secondary immune dysfunction. Ongoing studies assessing telomere integrity and DNA repair mechanisms will help clarify the functional consequences of these variants and their relevance in the diagnosis and classification of inborn errors of immunity.

POSTER 138 - ACTIN-INTERACTING PROTEIN WD REPEAT– CONTAINING PROTEIN 1 (WRD1) DEFICIENCY: IMMUNODEFICIENCY, AUTOIMMUNITY AND NEUROLOGICAL DEFECTS

AUTHORS

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Introduction:
The actin-interacting protein WD repeat– containing protein 1 (WDR1) regulates cofilin-dependent actin filament turnover. WDR1 is expressed in most leucocytes and plays an important role in both innate and adaptive immunity. Few cases with WDR1 deficiency have been reported in literature. Herein we report on two patients with WDR1 deficiency presenting with various manifestations including bronchiectasis, skin rash, myopathy and very early-onset inflammatory bowel disease (VEO-IBD).

Patients:

Patient I: female patient, born to consanguineous parents, presented at age of 7 months with VEO-IBD, persistent oral moniliasis and superficial abscesses.

Patient II: male patient, born to consanguineous parents. Since the age of one year, the patient suffered repeated upper respiratory tract infections, pneumonia complicated with bronchiectasis, draining ears and superficial abscesses. The patient had a waddling gait. At the age of 11 years, the patient suffered progressive myopathy and was unable to stand or sit without support.

Lab workup:
Both patients were immunologically investigated. Peripheral blood lymphocytes were tested by FCM, and serum immunoglobulins levels were quantitated. Genetic testing was done for both patients by next generation sequencing.

Results:
Both patients had normal immunoglobulins level, marked lymphopenia. Patient II had thrombocytopenia and low B cell percent and count with low memory cells.

Two homozygous missense variants were detected in WRD1 gene in the 2 patients predicted to be pathogenic according to the ACMG guidelines (Gly354Glu & p.Arg575Trp) respectively.

Conclusion:
WRD1 deficiency can present with various symptoms including IBD, repeated superficial and deep infections, skin rashes, and neurological defects.

POSTER 139 - TOLERABILITY OF MANUAL PUSH ADMINISTRATION OF A 20% SUBCUTANEOUS IMMUNOGLOBULIN PREPARATION: A CASE SERIES

AUTHORS

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Objective:
To describe the experience with manual push administration of a 20% subcutaneous immunoglobulin preparation (IgPro20; Hizentra®)

Design and methods:
We report the key demographic, clinical and treatment information of 5 cases.

Results:
Case 1: a 44-year-old female, diagnosed of PID. The patient initiated treatment with IgPro20 20 mg/month and after one month initiated IgPro20 (March 2025) with manual push, 4 g/6 days. The frequency of infusion was 1-2/week with a volume of infusion of 20 mL per infusion, the mean duration of infusion was 10 minutes, and the number of injection sites was 1. No adverse events were reported. Case 2: a 42-years-old male diagnosed of SID. Treatment was initiated with manual push administration of IgPro20 (April 2025), at a dose of 8 g/week, infusion volume of 20 mL, mean duration of infusion of 20 minutes and 2 injection sites. The patient reported hyperalgesia 48 hours after administration. Case 3: a 62-years-old female with SID. The patient has been receiving IgPro20 7 g/week since 2024 and was initiated with manual push administration of IgPro20 on May 2025 at a dose of 7 g/week. The required volume of infusion was 20 and 15 mL at 2 injection sites and with a mean duration of 10 minutes per injection site (20 minutes in total). The patient exhibited mild erythema at the 20 mL injection site. Case 4: a 67 years-old female diagnosed with SID. She had been receiving treatment with intravenous Flebogamma DIF 100 mg/ml (30 g/month) since 2011. The patient was initiated with manual push administration of IgPro20 on May 2025 at a dose of 7 g/week, requiring a volume of infusion of 20 and 15 mL at 2 injection sites and with a mean duration of 10 minutes per injection site (20-25 minutes in total). The patient reported mild swelling, without pain, at the injection site. Case 5: a 72 year-old female, with a BMI of 16.5 kg/m2 was diagnosed with severe PID. Treatment was initiated with manual push administration of IgPro20, administered by her husband, at a dose of 3 g/week, a volume of infusion of 15 mL, mean duration of infusion of 10 minutes and 1 injection site. No adverse events were reported.

Conclusions:
The initial administration of manual push infusions of a 20% subcutaneous immunoglobulin preparation in a heterogenous group of patients and clinical conditions was associated with short time of infusion and was well tolerated.

POSTER 140 - EVALUATION OF CLINICAL, IMMUNOLOGICAL, AND GENETIC OUTCOMES IN PATIENTS WITH X-LINKED AGAMMAGLOBULINEMIA

AUTHORS

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Objective:
X-linked agammaglobulinemia (XLA) is an inborn error of immunity (IEI) caused by a maturation arrest in B cells, leading to recurrent sinopulmonary and gastrointestinal infections. This study aimed to evaluate the clinical features and natural course of patients with XLA and to assess the disease's impact on quality of life.

Design and method:
Data from 13 pediatric and 12 adult patients diagnosed with XLA were retrospectively collected from medical records, including demographic, clinical, immunological, and genetic findings. Quality of life was assessed cross-sectionally using the KINDL questionnaire (child/self and parent forms) for pediatric patients and the SF-36 questionnaire for adult patients.

Results:
The median age of the patients was 16 years (IQR: 7–27). The median age at symptom onset was 4 months (IQR: 2.5–9), median age at diagnosis was 18 months (IQR: 6–45), and the median diagnostic delay was 16 months (IQR: 2.5–27.5). Eight patients (32%) were diagnosed through screening of affected family members. Recurrent upper respiratory tract infections were observed in 23 patients (92%), lower respiratory tract infections in 19 (76%), and acute gastroenteritis in 15 (60%). Osteomyelitis and pneumococcal meningitis were reported in 2 (8%) and 1 (4%) patients, respectively. Common complications included failure to thrive (76%), neutropenia (8%), and bronchiectasis (40%).

Seventeen distinct BTK gene variants were identified in 19 unrelated families, including 5 nonsense, 5 splice-site, 4 frameshift, and 3 missense mutations. Clinical comparisons among mutation types disrupting protein structure did not reveal a significant genotype-phenotype correlation ($p>0.05$).

Median immunoglobulin levels at diagnosis were: IgG 75 mg/dL (IQR: 43–149), IgA 10 mg/dL (IQR: 6–23), IgM 18 mg/dL (IQR: 9–20), and IgE 1 IU/mL (IQR: 1–6). All patients had CD19+ B cell percentages below 2%. At the time of evaluation, 56% were receiving intravenous and 44% subcutaneous immunoglobulin replacement therapy. Only 28% (n=7) were on antibacterial prophylaxis.

The median follow-up duration was 137 months (IQR: 61–272), and no deaths were reported. Median total quality of life scores were 71% (IQR: 65–78.5) for children, 75% (IQR: 69.5–79) for the KINDL parent form (n=11), and 71% (IQR: 67–78) for adults assessed using the SF-36.

Conclusions:
Although significant advances have been made in the treatment of XLA, delayed diagnosis and infection-related organ damage remain major concerns. Early diagnosis is critical for preventing comorbidities and irreversible complications, ultimately improving patients' quality of life.

POSTER 141 - B-CELL SUBSET ALTERATIONS IN TUBERCULOSIS PATIENT WITH SUBOPTIMAL TREATMENT RESPONSE

AUTHORS

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Introduction:
Mycobacterium tuberculosis (Mtb), the causative agent of pulmonary tuberculosis, remains the leading infectious cause of cumulative mortality worldwide. IFN-γ–mediated immunity, particularly through memory CD4+ T cells, has classically been considered the cornerstone of host defense. However, increasing evidence highlights the role of B lymphocytes (B cells) in the immune response to Mtb, suggesting potential clinical relevance.

Objective:
To evaluate the usefulness of B-cell subpopulation analysis in a patient with tuberculosis and suboptimal clinical response to standard treatment, in the absence of microbial resistance or IFN-γ pathway defects.

Materials and methods:
Bone marrow and peripheral blood samples collected in lithium heparin tubes were analyzed by flow cytometry (BD FACSCanto), using specific monoclonal antibodies. Data analysis was performed with Infinicyt software (Cytognos).

Results:
The initial bone marrow analysis revealed marked B-cell lymphopenia (0.02% of total cellularity; 0.35% of the lymphoid series) and a significant reduction in plasma cells (0.02%).

Sequential peripheral blood studies showed:

• **First analysis:** no detectable circulating B cells or plasmablasts.

• **Second analysis (3 months later):** B cells = 0.13% of leukocytes (1.9% of lymphocytes; 15 cells/μL); memory B cells = 4.1% (<1 cell/μL); plasmablasts undetectable.

• **Third analysis (1 month later):** B cells = 1.5% of leukocytes (13% of lymphocytes; 105 cells/μL); memory B cells = 1.7% (2 cells/μL); plasmablasts absent.

T-cell populations remained within normal ranges in all studies.

Conclusions:

• In tuberculosis patients with poor clinical evolution, B-cell immunophenotyping may offer valuable insights, even in the absence of IFN-γ pathway defects or drug resistance.

• Flow cytometry is a sensitive tool for detecting subtle immunological abnormalities in the B-cell compartment.

• The role of the clinical immunologist is crucial in the evaluation of diseases with suspected immune dysregulation.

POSTER 142 - NURSING EXPERIENCE IN THE ADMINISTRATION OF SUBCUTANEOUS IMMUNOGLOBULIN IN A PEDIATRIC PATIENT WITH AUTISM SPECTRUM DISORDER AND SPECFIC ANTIBODY DEFICIENCY

AUTHORS

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Objective:
To describe the nursing experience in implementing subcutaneous immunoglobulin (SCIG) treatment in a pediatric patient with autism spectrum disorder (ASD) and primary immunodeficiency, highlighting the educational, care, and family support approach.

Method:
Clinical case of a 4-year-old boy with a history of recurrent respiratory infections and specific antibody deficiency, who began SCIG treatment at a dose of 4 g every three weeks. The nursing intervention included structured training for the parents in suitable environment (four face-to-face sessions), covering administration technique, safety measures, incident management, health education, and emotional support. Continuous coordination was maintained with the responsible immunologist.

Results:
After one year of treatment, the patient gained 4 kg, which required adjusting the dose to 7 g every two weeks. The clinical course was very favorable: infections disappeared, IgG levels increased to 1,100 mg/dL, specific antibodies increased, cognitive stability improved, and behavioral regressions decreased. The treatment was well tolerated and accepted by the family, who showed high adherence and autonomy in home administration.

Conclusions:
The specialized nursing intervention of advanced practice was key to the successful initiation of SCIG treatment, family education and support, and joint clinical follow-up. Continuous collaboration between the specialized nurse and the responsible physician allowed for comprehensive, safe, and patient-centered care. This case demonstrates that subcutaneous immunoglobulin treatment can be an effective alternative in pediatric patients with ASD when accompanied by a structured and personalized nursing approach.

POSTER 143 - CLINICAL BENEFIT OF TARGETED THERAPY WITH JAK INHIBITORS IN A PATIENT WITH HETEROZYGOUS PSMB8 VARIANT: A CASE REPORT OF PROTEASOME-ASSOCIATED AUTOINFLAMMATORY SYNDROME

AUTHORS

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Objective:
Proteasome-associated autoinflammatory syndromes (PRAAS) belong to the group of type I interferonopathies and are characterized by dysregulation of the ubiquitin-proteasome system. Mutations in genes encoding proteasome subunits lead to the accumulation of ubiquitinated proteins, which act as stress signals and activate inflammatory cascades mediated by cytokines, including type I interferons. PRAAS are usually caused by autosomal recessive loss-of-function (LOF) mutations, most frequently in the PSMB8 gene, which encodes proteasome subunit β5. Clinically, PRAAS presents with recurrent fevers, lipodystrophy, panniculitis, myositis, basal ganglia calcification, and characteristic skin rashes.

Design and methods:
We describe a clinical case of a female patient who presented since adolescence with recurrent inflammatory flares suggestive of an interferonopathy. A complex diagnostic process led to the identification of a genetic variant and initiation of targeted therapy.

Results:
A 36-year-old woman with a history of childhood asthma due to sensitization to multiple aeroallergens developed frequent infections in adolescence, including infectious mononucleosis requiring hospitalization with leukocytosis, splenomegaly, and lymphadenopathy. Over time, she experienced oral ulcers, mucocutaneous candidiasis, and inflammatory flares marked by periodic lymph node enlargement, low-grade fever, fatigue, arthralgia with arthritis, and nodular skin lesions; biopsy showed features consistent with perniosis. Additional clinical findings included acute pericarditis, cognitive difficulties with an attentional profile, and possible malacia in the left hemisphere on neuroimaging.

Genetic testing revealed a heterozygous pathogenic variant in PSMB8 (p.Thr75Met), previously associated with PRAAS. A segregation study identified the same variant in her father and one sister. The patient was treated with oral prednisone during flares, with only partial improvement. Due to persistent inflammatory activity, treatment with the JAK inhibitor Baricitinib was initiated at a dose of 4 mg/day, with significant clinical improvement and reduced frequency and severity of flares.

Conclusions:
PRAAS and other interferonopathies require a high index of suspicion and confirmation through genetic testing. This case highlights that targeted therapy with JAK inhibitors may provide clinical benefit even in patients with heterozygous pathogenic variants, improving disease control and quality of life. Early recognition and individualized treatment strategies are essential in rare autoinflammatory syndromes.

POSTER 144 - ENGAGING A DIAGNOSTIC CHALLENGE: LINKING IMMUNODEFICIENCY WITH AUTOINFLAMATION

AUTHORS

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Objective:
To report a rare case of coexisting Common Variable Immunodeficiency (CVID) and Familial Mediterranean Fever (FMF) in the same patient, emphasizing the diagnostic complexity.

To illustrate the role of genetic testing and integrated treatment in improving outcomes in patients with overlapping immunodeficiency and autoinflammatory features.

Design and method:
We present the clinical case of a patient in whom two distinct immune-mediated diseases converge, fulfilling diagnostic criteria for both Common Variable Immunodeficiency and Familial Mediterranean Fever. We describe the patient's clinical evolution and treatment strategy in an integrated and comprehensive manner.

Results:
A 63-year-old woman, with no history of parental consanguinity, had a personal history of autoimmune hypothyroidism (positive antithyroglobulin antibodies) and multiple cardiovascular risk factors. Since childhood and adolescence, she had experienced recurrent tonsillitis, sinusitis, oral herpes infections, upper respiratory tract infections, diarrhea, abdominal pain, periodic fevers, and arthritis affecting both large and small joints.

In 2021, following COVID-19 infection, she developed severe asthenia, cognitive difficulties (e.g., impaired concentration and short-term memory), and recurrent febrile episodes (38°C) lasting 48–72 hours and occurring every 15–20 days.

Complementary testing revealed moderate hypogammaglobulinemia (IgG and IgA) and specific antibody deficiency, with normal naïve and memory B and T cell subpopulations. A chest CT scan showed bronchiectasis, thus fulfilling the diagnostic criteria for CVID. Immunoglobulin replacement therapy was initiated.

Genetic testing identified a heterozygous variant in the MEFV gene (c.2082G>A; p.Met694Ile), classified as pathogenic for FMF. Based on the Livneh clinical criteria, and supported by this genetic finding, a diagnosis of FMF was established. Colchicine therapy was initiated.

Following treatment, the patient experienced a marked reduction in infectious episodes with immunoglobulin therapy, and complete resolution of febrile episodes and significant improvement in joint symptoms with colchicine.

Conclusions:
This case illustrates the importance of not limiting diagnostic efforts after identifying a primary condition when clinical features suggest the coexistence of additional pathologies. The simultaneous diagnosis of CVID and FMF highlights the need for a comprehensive clinical and immunogenetic assessment in complex patients. Moreover, it emphasizes the value of genetic testing in guiding diagnosis and individualized therapy, allowing clinicians to anticipate and prevent potential complications associated with autoinflammatory and immunodeficient states.

POSTER 145 - CLINICAL AND LABORATORY FEATURES OF HYPER IGE SYNDROMES: A SINGLE-CENTER EXPERIENCE

AUTHORS

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Introduction:
When common atopic manifestations in childhood are accompanied by recurrent infections, therapy-resistant eczema, elevated serum IgE levels, and eosinophilia, underlying "inborn errors of immunity" should be considered. One of the classic examples of such disorders is Hyper IgE Syndromes (HIES), classified under the category of "Combined immunodeficiencies with associated or syndromic features" in the 2025 IUIS classification. This study aims to evaluate the demographic, clinical, and laboratory characteristics of patients diagnosed with HIES at our center, highlighting the diversity of their genetic subtypes and clinical presentations.

Methods:
Demographic and clinical data of 16 patients diagnosed with HIES at the Pediatric Immunology Department, Ege University Faculty of Medicine, were retrospectively reviewed from patient records. Each case was evaluated for clinical history, laboratory findings, and genetic analysis results. Molecular diagnoses were established using Next Generation Sequencing (NGS), and positive findings were confirmed via Sanger sequencing.

Results:
In this cohort, DOCK8 deficiency was identified in 10 patients, STAT3 mutations in 5 patients, and a CARD11 mutation in 1 patient. The median age and age at symptom onset were 12 years (4-21) and 9 months (0-36), respectively, in the DOCK8 group, while these values were 17 years (9-26) and 35 months (3-120) in the STAT3 group. A history of parental consanguinity was observed exclusively in the DOCK8 group (n=6, 60%). Patients with DOCK8 mutations more frequently exhibited viral cutaneous infections, whereas recurrent infections and eczema were common in both groups. Laboratory analysis demonstrated significantly elevated eosinophil counts in the DOCK8 group (7504 ± 15327/mm³), while total serum IgE levels were markedly higher in the STAT3 group (18490 ± 10593 IU/mL). High-resolution chest CT (HRCT), performed in eight DOCK8 patients, revealed chronic pulmonary changes in all cases. All patients were initiated on antifungal and antibacterial prophylaxis; five additionally received antiviral therapy. Immunoglobulin replacement therapy was administered to 13 patients. Hematopoietic stem cell transplantation (HSCT) was performed in seven patients with DOCK8 deficiency, with three additional patients awaiting transplantation. Among those who underwent HSCT, three patients died.

Conclusion:
Hyper IgE Syndromes (HIES) represent a group of disorders that require meticulous evaluation due to their clinical and genetic heterogeneity. Differentiation of HIES subtypes through careful clinical assessment and confirmation via genetic analyses is essential to guide treatment planning and long-term follow-up strategies.

POSTER 146 - SAME GENETIC VARIATION, DIFFERENT CLINICAL PRESENTATIONS: TWO SIBLINGS AFFECTED BY XMEN DISEASE

AUTHORS

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Background:
Mutations in MAGT1 impair intracellular magnesium homeostasis and N-linked glycosylation, resulting in XMEN disease (X-linked immunodeficiency with magnesium defect, Epstein-Barr virus infection, and neoplasia). This rare inborn error of immunity is characterized by chronic EBV viremia, immune dysregulation, and lymphoproliferative complications, as well as more rarely, neurological involvement. We present two adult male siblings who carry the same pathogenic MAGT1 variant but exhibit different clinical outcomes: one with neurodegenerative symptoms, and the other with EBV-related lymphoma and autoimmune hemolytic anemia.

Case 1:
A 27-year-old male presented with neurological manifestations including dysarthria, unsteadiness, and tremor following a COVID-19 infection in 2022. Neurological examination revealed dysarthria, lower limb weakness, dysmetria, ataxic gait, and balance impairment. Brain MRI showed global cerebral and cerebellar atrophy, corpus callosum thinning, and enlarged lateral ventricles (Figure 1). Immunoglobulin levels were within normal range, but chronic EBV viremia was detected (Table 1). Abdominal ultrasound showed no organomegaly or lymphadenopathy. Genetic testing revealed a hemizygous pathogenic variant in MAGT1 (c.369_370insCC; p.Gly124fs), supporting the diagnosis of XMEN disease. Flow cytometric analysis demonstrated absent NKG2D (CD314) expression on both $CD8^+$ T cells and natural killer (NK) cells, supporting the pathogenicity of the MAGT1 variant (Figure 2). The patient is under clinical follow-up and receiving neurorehabilitation.

Case 2:
A 33-year-old brother had a history of immune thrombocytopenia (ITP) in childhood. In 2020, he was diagnosed with AIHA and nodular lymphocyte-predominant Hodgkin lymphoma. He received R-CHOP therapy and subsequently achieved clinical remission. In recent years, he experienced recurrent respiratory tract infections. Immunologic workup showed hypogammaglobulinemia and persistent EBV viremia (Table 1). Despite appropriate therapy, episodes of autoimmune hemolytic anemia (AIHA) persisted. The same MAGT1 variant was identified, supporting the diagnosis of XMEN. Flow cytometric analysis showed absent NKG2D expression on both $CD8^+$ T cells and NK cells (Figure 2). Due to ongoing immune dysregulation and recurrent infections, the patient was started on immunoglobulin replacement therapy.

Conclusion:
These cases demonstrate the clinical variability of XMEN disease. Even with the same MAGT1 variant, affected individuals may follow distinct disease courses—from isolated neurological impairment to EBV-driven lymphoproliferation and autoimmunity. This suggests a role for additional immune or environmental modifiers. Early genetic diagnosis and multidisciplinary management are essential for individualized care.

POSTER 148 - ATAXIA-TELANGIECTASIA: REPORT OF SEVEN CASES

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Objective:
Ataxia-telangiectasia (A-T) is a rare inherited syndrome that primarily presents as ataxia due to cerebellar involvement and dilated capillaries in the oculocutaneous region. But many more serious complications of the condition exist, due to which both the quality and length of life are severely affected. The objective of our study is to determine the clinical and immunological characteristics of patients with ataxia telangiectasia syndrome.

Design and methods:
This concerns 07 patients examined in our laboratory, consisting of 04 boys and 03 girls aged between 04 and 20 years. The immunological exploration includes:

- The measurement of serum immunoglobulins (IgG, IgA, IgM) by laser nephelometry.
- The immunophenotyping of T cells and B cells by flow cytometry.
- The measurement of alpha-fetoprotein by chemiluminescence.

Results:
Among the 7 patients, the average age was 9.35 years, consanguinity was present in 57%, and similar cases in the siblings were 70%.

Ataxia-telangiectasia syndrome was present in all patients (100%), 67% of the patients had pulmonary infections, and 33% of the patients had skin infections, gingivitis, and a weight growth delay

The dosage of immunoglobulins showed: Collapsed levels of IgA in 85% of patients. Collapsed levels of IgG in 28% of patients, and normal levels of IgM for all patients.

Lymphocyte immunophenotyping revealed T and B lymphopenia in 57% of patients with an inverted CD4/CD8 ratio in 28% of cases.

The value of alpha-fetoprotein was very high in all patients (100%).

Conclusion:
Ataxia-Telangiectasia remains a rare and severe condition whose prognosis is linked to complications due to immune deficiency, involved in the control of lymphocyte maturation (T and B), a decrease in CD4 and CD8 is observed, disorders of humoral immunity are explained by the inability of the B cell to perform somatic hypermutations for the transformation of IgM into IgG and/or IgA, and the risk of developing cancers, hence the necessity for early diagnosis in the presence of ataxia and telangiectasias, for better management.

POSTER 149 - HIGH MORTALITY AND MALIGNANCY RATES IN IEI PATIENTS WITH EBV VIREMIA AND LPDS: A 13-YEAR COHORT STUDY

AUTHORS

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Objective/Introduction:
Epstein-Barr virus (EBV) is a widespread herpesvirus that infects over 95% of adults and typically establishes lifelong latency. In patients with inborn errors of immunity (IEI), EBV may cause persistent viremia, lymphoproliferative disorders (LPDs), and malignancies due to impaired T-cell and natural killer cell function, as well as immune regulation. Clinical presentations in IEI patients often include recurrent infections, EBV viremia, chronic active infection, and LPDs. These manifestations are associated with significant morbidity and mortality and can serve as early indicators of underlying immune defects. Timely recognition is crucial for accurate diagnosis and effective treatment. This observational study investigates EBV-related clinical outcomes in patients with IEI.

Methods:
We retrospectively analyzed patients with PID from 2012 to 2025. Of 2,500 cases, 150 had at least one EBV PCR-positive blood sample. Patients with two EBV PCR-positive samples (>300 copies/mL) or EBV-positive tissue were included. The collected data included clinical features, immune profiles, and diagnoses of LPD or malignancy.

Results:
Seventy-three patients met the inclusion criteria. Median age was 14 years (IQR 9–21); 43 (58.9%) were male. Most presented with recurrent infections and LPD findings. Of these, 41 (56.2%) were diagnosed with LPD, and 25 (61%) of them had malignancy, most frequently diffuse large B-cell lymphoma and Hodgkin lymphoma. Chemotherapy was used for malignancies, and rituximab-based regimens for pre-malignant LPDs. Comparisons were made between combined immunodeficiency (CID) and non-CID groups, as well as between LPD-positive and LPD-negative patients. Most non-CID patients had immune dysregulation syndromes, and LPD and malignancy were more frequent in this group. Recurrent infections were significantly more common in CID patients ($p<0.001$), while autoimmunity was more frequent in non-CID patients ($p<0.001$). Overall survival was low (25%), and significantly lower in CID patients compared to those without CID ($p< 0.05$).

Conclusion:
EBV viremia and related complications significantly contribute to morbidity and mortality in IEI. Early identification of EBV-related manifestations is crucial for effective risk stratification and intervention.

Key words:
PID, EBV, malignancy, lymphoproliferation,

POSTER 150 - A FAMILIAL FORM OF ATYPICAL HEMOLYTIC UREMIC SYNDROME ASSOCIATED WITH CD46 DEFICIENCY

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Introduction/ Objective:
Atypical hemolytic uremic syndrome (aHUS) is a rare thrombotic microangiopathy defined by the association of mechanical hemolytic anemia, consumptive thrombocytopenia and acute renal failure secondary to dysregulation of the alternative complement pathway. Mutations in the genes of CFH, CFI and CD46 have been reported in 30, 15 and 10% respectively.

We report for the first time, a case of a familial form of aHUS associated with CD46 deficiency.

Methods:
An 11-year-old female with a personal and family history of aHUS, from a consanguineous marriage, was hospitalized in the nephrology department of Tizi Ouzou University Hospital for management of a fifth aHUS episode.

Results:
Analysis of the alternative complement pathway showed normal antigenic levels of C3, C4, FH, FB and FI, whereas there was an absence of CD46 expression on lymphocytes.

A family investigation was requested, and a homozygous CD46 deficiency was found in a 28-year-old sister with no previous history, as well as a heterozygous CD46 deficiency in both parents and another 27-year-old sister.

Conclusion:
In about 20% of cases, HUS affects several members of the same family, giving rise to a familial form of the disease. And its penetrance is 50%, so only half the family members carrying a mutation have the disease.

POSTER 151 - AI-ASSISTED EARLY DIAGNOSIS OF INBORN IMMUNITY ERRORS: A PILOT STRATEGY FOR MOROCCAN HEALTH CENTERS

AUTHORS

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Context:
Inborn immunity errors (IIEs), formerly known as primary immune deficiencies, affect approximately 1 in 10,000 to 5,000 people in Europe and the United States but remain largely underdiagnosed, especially in resource-limited countries. According to the ARAPID 2025 congress, only 4% of cases are diagnosed in Arab countries. These conditions cause significant morbidity and mortality, with severe complications, infections, and fatal outcomes without treatment.

Early diagnosis is crucial but difficult, as IIEs often present non-specific symptoms, and general practitioners often lack specific training. Moreover, knowledge about these diseases evolves rapidly, complicating recognition.

The International Patient Organisation for Primary Immunodeficiencies (IPOPI) highlights the importance of using AI to improve early diagnosis and management of IIEs globally, supporting pilot projects like ours.

Objective:
To design and pilot an AI-based tool to help general practitioners (GPs) identify and refer suspected IIEs cases early in Moroccan primary health centres.

Methods:
In collaboration with several IIEs experts and immunologists, we are developing an easy-to-use tool integrated into a mobile or web platform accessible to frontline doctors. By entering common clinical and biological data (recurrent infections, consanguinity, growth retardation, blood abnormalities, etc.), the system generates a risk score or alert suggesting suspected IIEs and recommending specialist consultation.

The tool will also provide personalised recommendations on:
- Additional tests to be performed before referral,
- Initial treatments or measures to be started in primary care,
- Criteria for urgent referral to a specialist.

The diagnostic algorithm is based on validated clinical patterns and the most recent classification (IUIS 2025), covering more than 500 immunological entities.

The pilot phase will include:
- An assessment of the needs of doctors in the field,
- The design of a prototype based on validated databases and algorithms,
- An initial usage test in health centers in the Casablanca-Settat region.

Expected results:
The project should improve general practitioners' ability to detect IIEs early, reduce diagnostic delays, optimise referral pathways, provide practical support for initial management, and raise awareness among healthcare professionals in underserved areas.

Conclusion:
Early diagnosis and management of IIEs save lives by preventing complications and long-term effects. This pilot illustrates the potential of AI to support frontline providers in diagnosing and treating rare diseases, aiming to improve access to care for immunodeficient children in Morocco. Broader validation and deployment will follow pilot feedback.

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POSTER 152 - RETICULAR DYSGENESIS: CLINICAL, IMMUNOLOGICAL, MOLECULAR CHARACTERIZATION AND OUTCOME OF HEMATOPOIETIC STEM CELL TRANSPLANTATION OF SIX CASES. A SINGLE CENTRE EXPERIENCE

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Background:
Reticular dysgenesis (RD) is a rare and severe form of severe combined immunodeficiency (SCID), characterized by a classical phenotype of $T^-B^-NK^-$ SCID, agranulocytosis, sensorineural hearing loss (SNHL), and skeletal anomalies. It typically presents in the early neonatal period with profound neutropenia that is unresponsive to conventional treatments. Hematopoietic stem cell transplantation (HSCT) remains the only curative and life-saving intervention.

Methods:
We conducted a retrospective analysis of six patients diagnosed with genetically confirmed RD at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. Clinical, immunological, and laboratory data were reviewed, including HSCT characteristics and post-transplant outcomes.

Results:
All six patients harbored a homozygous AK2 c.524G>C (p.R175P) mutation. All were born prematurely and diagnosed at a median age of 2 months. Common clinical features included persistent neutropenia, agranulocytosis, and SNHL. Erythropoietic abnormalities were observed in 50% of cases. Five patients underwent HSCT and are currently alive with complete donor chimerism (100% myeloid and lymphoid) and robust immune reconstitution. One patient succumbed prior to transplantation.

Conclusion:
This report represents one of the largest single-center case series on RD. Our findings reinforce that HSCT is a highly effective therapeutic option for RD, leading to excellent engraftment and favorable clinical outcomes.

POSTER 153 - ACUTE PRESENTATIONS OF DISORDERS OF PHAGOCYTOSIS AND NEUTROPHIL FUNCTION TO THE PEDIATRIC INTENSIVE CARE UNIT – A CASE SERIES

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Objective:
Many children with underlying undiagnosed inborn errors of immunity present to the intensive care unit. We present here three such cases with fulminant infection and life threatening condition.

Design, method and results:

Case 1: A 2mo old girl, came with rapid breathing, neck swelling for 1 month. There was history of delayed cord fall.

The infant was intubated in view of increased distress and stridor (impending upper airway obstruction). Incision and drainage of neck swelling, culture was sent. It came positive for MRSA. ET aspirate grew Acinetobacter baumanii, E.coli pneumonia.

CECT Neck showed a large insinuating collection (abscess) on right side upto superior mediastinum with large retropharyngeal/prevertebral component.

Clinical exome sequencing reported PID-68 which is caused by homozygous or compound heterozygous mutations in the MYD88 gene. (likely pathogenic variant)

Case 2: A 10-year-old male child,was admitted with cough and difficulty in breathing for 3 days. He was shifted to the PICU and started on NIV (BiPAP) support .

Past history was significant. He was hospitalized in 2023 with bone marrow suppression, scalp abscess in 2023.

Investigations showed positive Mycoplasma serology,throat swab was positive for Strenotrophomonas maltophila. Investigations revealed severe neutropenia - Showed persistent pancytopenia, with total leaucocyte count ranging between 2.8–6.7 $\times 10^9$/L, Hb- 5.4 g/dL, and platelet count- 4–32 $\times 10^9$/L in initial days, later improving to 90 $\times 10^9$/L. Immunoglobulin profile and lymphocyte subsets were normal. 2D Echocardiography - moderate pulmonary arterial hypertension.

Clinical exome sequencing report showed Dursun syndrome is caused by homozygous mutations in the G6PC3 gene.

Case 3: 1 month old girl, admitted with fever, rapid breathing, swelling on the left wrist, right supra clavicular swelling, ear discharge for 20 days. On admission child was tachypneic with audible stridor. Incision and drainage of supraclavicular swelling done,culture came positive for MRSA.

There was history delayed falling of cord, multiple abscesses, If profile IgE- 2688 mg/dl(1.4- 52.3), IgM 135.70 mg/dl (25-100), IgG 1620 mg/dl (200-700).

A CECT neck and thorax showed destruction of C3-C4 vertebrae involving posterior element of C2, C3 C4. Central area of liquefaction 14 mm*10 mm*15 mm in retropharyngeal location from C1-C7.

Neutrophil Oxidative Index Patient (%) Reference Range (%)
Unstimulated 64.2 50.1
Stimulated 448 9664
Neutrophil Oxidative Index 6.9 192.89
A diagnosis of chronic granulomatous disease was made and patient was advised genetic work up.

Conclusion:
Evaluation of children with severe sepsis presenting to the intensive care unit is warranted to screen for primary immunodeficiencies.

POSTER 154 - TEMPORAL TRENDS AND DISPARITIES IN SURVIVAL OF HIV-ASSOCIATED LYMPHOID MALIGNANCIES: A POPULATION-BASED STUDY

AUTHORS

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Objective:
To evaluate two-decade survival trends and identify racial/socioeconomic disparities among adults living with HIV diagnosed with HL, DLBCL or PBL, using SEER data spanning 2000–2020, in the context of evolving ART strategies.

Design and methods:
A retrospective cohort was assembled using SEER-18 data from 2000–2020, including adults (≥18 years) with HIV-associated Hodgkin lymphoma (HL), diffuse large B-cell lymphoma (DLBCL), or plasmablastic lymphoma (PBL). Diagnosis eras were categorized as Early ART (2000–2010) and Modern ART (2011–2020). We extracted demographics (age, sex, race/ethnicity), stage at diagnosis, treatment (chemotherapy; radiotherapy), and ZIP-code-level income as proxy for socioeconomic status (SES). Survival outcomes were assessed with Kaplan–Meier analysis, and multivariable Cox proportional hazards models quantified independent predictors of overall survival (OS), including era, race, SES, clinical stage, and treatment.

Results:
Of the 2,084 HIV-positive lymphoma cases, median age at diagnosis was 46 years; 78 % were male, and 58 % belonged to African American or Hispanic ethnicities. Five-year OS improved significantly between eras (Modern ART: 42.1 % vs Early ART: 28.4 %; p<0.001). After adjustment, Modern ART era (HR 0.68; 95 % CI: 0.59–0.78), chemotherapy receipt (HR 0.53; 95 % CI: 0.45–0.63), and early-stage disease (HR 0.47; 95 % CI: 0.39–0.57) were independently associated with better OS. However, African American race (HR 1.37; 95 % CI: 1.19–1.58) and lower-income ZIP code (HR 1.29; 95 % CI: 1.12–1.49) were linked to significantly worse outcomes. Plasmablastic lymphoma exhibited the poorest survival (median OS 13.2 months).

Conclusions:
While advances in ART and oncology have improved OS for HIV-associated lymphoid malignancies, significant racial and socioeconomic survival disparities persist. These findings underscore the need for equitable, integrated immuno-oncologic strategies targeting marginalized PLWH. Future efforts should focus on improving access to comprehensive HIV and cancer care, reducing SES-related barriers, and optimizing treatment for aggressive lymphoma subtypes such as PBL.

POSTER 155 - TRANSCATHETER ARTERIAL ANTIMICROBIAL AND STEROID THERAPY FOR REFRACTORY HEPATIC ABSCESSES IN CHRONIC GRANULOMATOUS DISEASE: A CASE SERIES

AUTHORS

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Background:
Hepatic abscesses are a severe complication of Chronic Granulomatous Disease (CGD), typically caused by catalase-positive bacteria and fungi. These infections often prove resistant to standard medical and surgical treatments, highlighting the need for innovative therapeutic strategies. We describe two cases of refractory hepatic abscesses in CGD patients successfully managed with a novel, minimally invasive approach: transcatheter intrahepatic arterial infusion of antibiotics and corticosteroids, combined with systemic antimicrobial and immunomodulatory therapy.

Cases Presentation:
Patient 1: a 14-year-old male with autosomal recessive CGD due to a p47-phox (NCF1) gene mutation, and a prior history of hepatic abscess resection at age 3, was admitted for persistent fever and multiple hepatic abscesses. Liver biopsy revealed Methicillin-Susceptible Staphylococcus aureus (MSSA) and positive panfungal PCR assay. Despite broad-spectrum systemic therapy—including antibiotics, antifungals, corticosteroids, and anti-IL-1 agents—the lesions progressed and were complicated by cutaneous fistulization. A novel interventional approach was initiated: through catheterization of the right hepatic artery, weekly infusions of meropenem and methylprednisolone were administered (14 infusions total), in combination with oral antibiotics. The patient's fever resolved, and follow-up abdominal CT demonstrated a reduction in abscess size, along with marked clinical improvement. He remained stable and is currently scheduled for hematopoietic stem cell transplantation (HSCT).

Patient 2: a 30-year-old male with X-linked CGD due to a gp91^phox (CYBB) gene deletion presented with persistent fever and productive cough. Chest imaging was unremarkable, while abdominal CT revealed disseminated hepatic lesions involving both liver lobes. MSSA was isolated from percutaneous drainage. Despite targeted intravenous antibiotic therapy, follow-up abdominal imaging (ultrasound, CT) showed a new increase in the size of previously drained abscesses in the left hepatic lobe and the patient developed hepatic failure and encephalopathy. A transcatheter intrahepatic arterial infusion approach was initiated, involving selective catheterization of both the right and left hepatic arteries. Meropenem and methylprednisolone were administered over 11 infusion sessions, in combination with systemic antibiotics—initially intravenous, then transitioned to oral. This strategy stabilized hepatic function and resulted in progressive clinical and radiological improvement (see Figure 1).

Conclusion:
Intra-arterial infusion therapy, tailored to clinical response and imaging, led to resolution or improvement of hepatic abscesses in both patients. This minimally invasive approach was first described by Kitano et al. (2018) in a single CGD patient, using a different antibiotic strategy. Our experience supports its potential as a safe, effective option for managing this severe complication. Further studies are needed to confirm its safety and long-term efficacy.

POSTER 158 - HETEROZYGOUS MUTATION IN NCF1 GENE IN A PATIENT WITH REFRACTORY INDETERMINATE COLITIS TREATED WITH JANUS KINASE INHIBITOR

AUTHORS

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Introduction:
NCF1 deficiency is an autosomal recessive disorder that leads to chronic granulomatous disease (CGD), characterized by a defect in the NADPH oxidase complex. Several studies linked heterozygous NCF1 variants to increased susceptibility to autoimmune disorder even in the absence of full-blown CGD. While CGD is clinically associated with colitis that mimics inflammatory bowel disease (IBD), the question of whether NCF1 deficiency independently causes IBD-like disease has been the subject of both clinical and experimental research. Herein, we describe a case of a patient who has indeterminate colitis, refractory to standard therapy along with other autoimmune features. Her genetic test revealed a heterozygous mutation in the NCF1 gene.

Case presentation:
A 20-year-old female who was diagnosed with type 1 diabetes mellitus (DM) age 2 years, crohn's disease at age 10 years, short stature, and primary amenorrhea. Initially her colitis was labelled as Crohn's disease, but upon repeated colonoscopy which showed severe inflammation from rectum to hepatic flexure, her diagnosis revised to ulcerative colitis. Her course was refractory to conventional therapy including infliximab and ustekinumab. Ultimately, she was reclassified as indeterminate colitis. There is no consanguinity between parents, however, her father died at age 40 with type 1 DM and chronic kidney disease. Whole exome sequencing was performed and revealed a heterozygous variant c.579G>A p.(Trp193*) in the NCF1 gene reported pathogenic.

JAK inhibitors, particularly upadacitinib, have demonstrated efficacy in the management of inflammatory bowel disease (IBD). While upadacitinib is approved for IBD, there are no reported cases of its use in monogenic forms of IBD, such as chronic granulomatous disease (CGD). Therefore, we initiated upadacitinib therapy for her refractory colitis. After one year of treatment, the patient remained flare-free, with normalization of inflammatory markers and marked improvement in both endoscopic and biochemical parameters.

Figure.1 Colon Histopathology before treatment with Upadacitinib: Mild edematous changes and chronic inflammation, including scattered eosinophils in lamina propria as well as a fragment of granulation tissue, in keeping with mucosal ulceration and moderate active inflammation.

Figure.2 Colon Histopathology after 1 year treatment with Upadacitinib: Intact crypt architecture and epithelium, few eosinophils and focally cryptitis is seen. Features favoring Focal colitis.

Conclusion:
The use of upadacitinib in this patient with NCF1 colitis is unprecedented, marking a novel therapeutic approach for this rare condition.

POSTER 159 - HYPER IGM SYNDROME: A SINGLE-CENTER EXPERIENCE FROM TURKEY

AUTHORS

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Immunoglobulin isotype recombination defects known as Hyper Immunoglobulin M syndromes (HIGM) are rare primary immunodeficiency disorders characterized by low or normal levels of serum IgG, IgA, and IgE, with normal or elevated serum IgM levels. Patients may present with various clinical manifestations, including recurrent infections, autoimmune diseases, lymphoproliferation, and malignancies.

The clinical and laboratory characteristics of patients diagnosed with HIGM at Ege University Pediatric Immunology Clinic were retrospectively evaluated.

Of the 16 patients from 10 unrelated families, 13 (81.3%) were male. Parental consanguinity was present in 7 patients (43.8%). The median age at symptom onset was 6.7 months (range: 3.8–18.0), while the median age at initial presentation was 6.1 years (range: 0.5–7.9). In 4 patients (25.0%), symptom onset occurred after the age of 5 years, with the latest presentation recorded at 11.9 years. The most common presenting features were recurrent infections and lymphoproliferative findings. Five patients (31.2%) exhibited atypical clinical features such as late-onset symptoms, autoimmunity, or chronic liver disease being the initial finding. Four patients (25.0%) had normal CD40/CD40LG expression on flow cytometry. The median IgM level was 124 mg/dL (range: 36–585), and in 8 patients (50.0%), IgM levels were within the age-appropriate normal range.

Genetic analysis identified mutations in CD40LG in 10 patients (62.5%), CD40 in 4 patients (25.0%), and AID in 2 patients (12.5%).

Hematopoietic stem cell transplantation (HSCT) was performed in 6 of 10 CD40L-deficient patients (37.5%), while 2 patients were followed-up with regular intravenous immunoglobulin (IVIG) therapy. During follow-up, 5 patients (4 with CD40L and 1 with CD40 deficiency) (31.2%) died, all before HSCT.

In conclusion, although HIGM symptoms typically begin in infancy and are often associated with infections and lymphoproliferation, clinicians should be aware of atypical presentations such as autoimmunity, chronic liver disease, and late-onset symptoms. Additionally, normal IgM levels and CD40/CD40LG expression by flow cytometry do not exclude the diagnosis. Genetic analysis is essential for definitive diagnosis.

POSTER 160 - DEVELOPMENT OF RENAL AMYLOIDOSIS IN A PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY

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Objective:
Common variable immunodeficiency (CVID) is a primary immunodeficiency disorder characterized by impaired immunoglobulin production due to defects in B cell differentiation into plasma cells. CVID can present at any age and exhibits a highly heterogeneous clinical spectrum. Although patients typically present with recurrent infections, autoimmune disorders, pulmonary and gastrointestinal complications, and lymphoproliferative diseases may also occur before or after diagnosis. Renal involvement in CVID is rarely reported but may have significant implications for morbidity and mortality. In this case report, we present a patient with CVID who developed renal amyloidosis.

Case presentation:
A 54-year-old male patient was diagnosed with autoimmune hemolytic anemia (AIHA) eight years ago in the hematology department. The disease was controlled with corticosteroid therapy. During follow-up without immunosuppressive treatment, thoracic and abdominal CT imaging revealed multiple lymphadenopathies. Lymphoma was ruled out through an excisional lymph node biopsy. Given the presence of both AIHA and generalized lymphadenopathy, immunodeficiency was suspected. Laboratory investigations revealed hypogammaglobulinemia, and the patient was referred to our clinic. Further immunological workup confirmed the diagnosis of CVID (Table 1), and intravenous immunoglobulin (IVIG) therapy was initiated.

At the time of diagnosis, urinalysis and abdominal ultrasonography showed no evidence of renal pathology. However, during the first year of follow-up, although serum renal function tests remained within normal limits, proteinuria was detected in the urinalysis. A 24-hour urine collection revealed 1635 mg/day of proteinuria. Abdominal ultrasonography remained unremarkable. Renal biopsy was performed in consultation with the nephrology department, and the diagnosis of amyloidosis was confirmed. Angiotensin-converting enzyme (ACE) inhibitor and colchicine therapy were added to the patient's treatment regimen. In the most recent 24-hour urine analysis, proteinuria decreased to 70 mg/day.

Conclusion:
Renal involvement in patients with CVID should be monitored as closely as other common complications. In the presence of signs such as acute kidney injury, proteinuria, or hematuria, further diagnostic evaluation is warranted. As demonstrated in this case, despite the absence of radiological or biochemical abnormalities, a simple urinalysis led to the early diagnosis of renal pathology, allowing timely treatment and disease control. In addition to the monitoring of recurrent infections (e.g., bronchiectasis), regular renal surveillance may significantly reduce morbidity and mortality in CVID patients.

POSTER 161 - AUTOIMMUNE LYMPHOPROLIFERATIVE DISORDERS: GENETIC HETEROGENICITY AND UNIVOCAL PHENOTYPE

AUTHORS

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Background and aims:
Autoimmune lymphoproliferative syndrome (ALPS) is an inherited lymphoproliferative non-malignant disorder characterized by heterozygous mutations within the first apoptosis signal receptor (FAS) signaling pathway. Leading to the accumulation of auto-reactive CD4- and CD8- T-cells, leading to splenomegaly, lymphadenopathy, autoimmune disorders, and increased risk of lymphoma.

Methods:
Four Egyptians were confirmed as ALPS patients. They were diagnosed and followed up at the PID Unit, Pediatric Department of Cairo University Children's Hospital, Egypt. Two genetic mutational analysis were done by next-generation sequencing (NGS) targeting customized genes panels, while two patients were diagnosed by whole-exome sequencing (WES). Immunophenotyping of peripheral blood lymphocytes' subsets including CD3, CD4, CD8, CD19, CD56/CD16, and DNT cells were performed by flow cytometry. Serum immunoglobulin levels were measured.

Results:
Three females and one male from four different families were diagnosed genetically. The consanguinity rate was 75%, and their mean age was 10.62 SD ±7.56 years. The median age of their presentation was 2 (1-155) months. Two families had a history of sib deaths with lymphoma.

Regarding the clinical presentation, two patients had lymphoproliferation as a first presentation, one with AIHA, and one presented with regional BCG-itis. The most common clinical presentation was lymphoproliferation and AIHA 4/4 (100%), thrombocytopenia 2/4 (50%), followed by Eosinophil colitis and vasculitis 25% each.

Genetic mutations were confirmed in FAS with homozygote mutation c.52delT; p.Leu18TyrfsTer10, FASL with homozygous c.343C>T;p. Arg115Ter, CASP8 homozygous mutation c.897C>A p.Asn299Lys genes, and CASP 10 heterozygous mutation c.1565A>G stoploss .

Two patients 50% had elevated DNT TCRαβ, two patients had low switched memory B-cells. Three patients 75% had high IgG level while one patient had low IgG and IgA levels, and all patients had normal IgM levels.

All patients received steroids, two patients are receiving Sirolimus, while one patient with low IgG levels is receiving IVIG monthly.

Regarding the outcome, two patients are living, while two patients lost their follow up.

Conclusion:
The number of recognized inborn errors of immunity (IEIs) is increasing at an accelerating pace, with different presentations of infections, Immunodysregulation and increasing the risk of malignancy. In this evolving landscape, Autoimmune Lymphoproliferative Syndrome (ALPS) serves as a prototypical example of a univocal phenotype arising from genetic heterogeneity

POSTER 162 - CLINICAL AND DIAGNOSTIC CHALLENGES OF CHRONIC GRANULOMATOUS DISEASE: A SINGLE-CENTER EXPERIENCE FROM KAZAKHSTAN

AUTHORS

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Chronic granulomatous disease (CGD) is a group of rare primary inborn errors of immunity, characterized by defective phagocyte function due to impaired NADPH oxidase complex activity, which consequently results in significant and potentially life-threatening infectious and inflammatory complications. Early diagnosis is crucial, but it is often delayed due to its heterogeneous clinical presentation.

Objective:
This study aims to present the case of CGD to describe clinical manifestations and the importance of early diagnostics and treatment.

Design and method:
We report the case of a 3-year-old boy with a history of recurrent infectious diseases, skin abscesses and pneumonia since early childhood. He was treated multiple times with antibiotics with a temporary positive effect. At age one, he presented with a diagnosis of measles with complications, followed by a consultation with an immunologist, where the CGD was confirmed.

Results:
Immunological evaluation revealed increased IgM for cytomegalovirus infection in blood 4.02 S/CO (0.00 - 0.90), normal lymphocyte subset. Genetic analysis confirmed a hemizygous pathogenic variant in the CYBB gene, consistent with X-linked CGD. Prophylactic treatment with trimethoprim-sulfamethoxazole, itraconazole, and antiviral therapy was initiated for cytomegalovirus infection and replacement therapy with immunoglobulin G. The patient responded well to therapy.

Conclusions:
CGD remains underdiagnosed and often identified after significant infectious disease. Awareness among pediatricians and infectious disease specialists, combined with access to functional and genetic testing, is essential for early diagnosis and improved outcomes.

POSTER 163 - CLINICAL AND IMMUNOLOGICAL PROGNOSTIC FACTORS WITH NOVEL VARIANTS IN A LARGE COHORT OF DIACYLGLYCEROL ACYLTRANSFERASE 1 DEFICIENCY

AUTHORS

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Background:
Biallelic variants in DGAT1 have been implicated in causing congenital diarrhea and protein-losing enteropathy (PLE). Insights into the immunopathological features of this ultra-rare disorder remain scarce, with only one cohort published to date.

Objective:
To delineate the clinical presentations, laboratory and immunological profiles, and therapeutic responses associated with DGAT1-deficiency and identify prognostic indicators that affect survival rates.

Methods:
In this multicenter retrospective analysis of a comprehensive cohort of nine patients carrying seven novel variants, each displaying distinct phenotypic features, we recorded clinical, immunological, and laboratory data of patients and evaluated the impact of various factors on prognosis.

Results:
67% of patients (n=6) exhibited symptoms during the first month of life, while one demonstrated symptom onset after six months. 78% of patients (n=7) presented with diarrhea, of whom all exhibited vomiting, failure to thrive, hypoalbuminemia, and hypogammaglobulinemia, as the advent of PLE. Patients with reduced CD4+ T-cell frequency (n=2) exhibited severe infections with unexpected bacteria during the follow-up. Despite administering immunoglobulin replacement therapy (IgRT), 45% of patients (n=4) passed away from infective complications. A decreased CD4+/CD8+ T-cell ratio was observed in all deceased patients who showed marked inflammation or apoptosis in colon biopsy samples. Early fat-restricted nutrition extended survival, whereas early symptom onset, recurrent severe infections, and reduced CD4+/CD8+ T-cell ratio were associated with less favorable outcomes.

Conclusions:
Our findings advocate early fat restriction as a critical therapeutic strategy. Given the heightened risk of severe infections, antibiotic prophylaxis can be recommended in addition to IgRT for DGAT1-deficient patients exhibiting lymphopenia or diminished CD4+ T cells.

POSTER 164 - CLINICAL UTILITY OF MANUAL AND AUTOMATED QUANTITATIVE ASSESSMENT OF STRUCTURAL LUNG ABNORMALITIES IN A DUTCH COHORT OF PATIENTS WITH CVID AND GRANULOMATOUS-LYMPHOCYTIC INTERSTITIAL LUNG DISEASE (GLILD)

AUTHORS

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Granulomatous-Lymphocytic Interstitial Lung Disease (GLILD) is a severe pulmonary complication of inborn errors of immunity (IEI), particularly common variable immune deficiency (CVID), leading to progressive lung damage and associated with poor prognosis. Radiological evaluation, especially CT imaging, plays a crucial role in detecting and monitoring GLILD-related lung abnormalities, yet standardized automated tools for quantifying these abnormalities are lacking. This retrospective study involved 20 patients diagnosed with CVID or CTLA4/LRBA deficiency and GLILD, all of whom underwent at least two high-resolution CT scans during follow-up. Two quantitative techniques were applied: the semi-automated Bronchiectasis Scoring Technique for CT (BEST-CT) and the fully automated LungQ algorithm. These methods assessed lung parenchymal abnormalities, bronchial widening, airway wall thickness, and mucus plugging, with correlations to lung function tests (TLCO and FEV1) analyzed. The study revealed significant variability in GLILD-related abnormalities over time, with key findings including atelectasis, ground-glass opacities (GGO), and bronchiectasis. CVID patients exhibited more extensive lung damage than those with CTLA4/LRBA deficiency. BEST-CT demonstrated excellent reliability and highlighted dynamic changes, such as reductions in GGO and atelectasis, though these trends were not statistically significant. LungQ detected bronchiectasis well but identified less mucus plugging. No significant correlations were found between imaging scores and lung function tests. This study illustrates the utility of BEST-CT and LungQ as systematic tools for assessing lung abnormalities in GLILD, providing valuable insights into disease progression that may complement traditional lung function tests in clinical monitoring and research.

POSTER 165 - EFFECTS OF LENIOLISIB TREATMENT IN A PATIENT WITH ACTIVATED PHOSPHOINOSITIDE 3-KINASE DELTA (PI3KΔ) SYNDROME (APDS) : FOCUS ON PSYCHOLOGICAL AND BEHAVIOURAL PROFILING

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Background:
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) is an ultra-rare Inborn Error of Immunity (IEI), characterised by immune deficiency and dysregulation. Moreover, patients with APDS may suffer from specific neurodevelopmental disorders. Although the PI3Kδ inhibitor Leniolisib was shown effective for the immunological phenotype, it is unknown whether treatment has effects on the neurological symptoms.

Objective:
To evaluate the effect of Leniolisib treatment on the immunological phenotype, reflexes, visuomotor coordination and psychological profile in a patient with APDS.

Case description and methods:
We present a 33-year-old male patient with a diagnosis of CVID since the age of 5 years for which he was treated with antibiotics and immunoglobulin replacement therapy. Following auto-immune complications at age 11, he was treated with azathioprine, prednisolone and Rituximab. At age 28, a genetic diagnosis of APDS was confirmed (heterozygous E1021K variant). At age 29, he underwent liver transplantation because of auto-immune hepatitis induced liver cirrhosis, and he is currently on prednisone (5 mg o.d.) and tacrolimus (4 mg o.d.). He started Leniolisib treatment at age 32 (because of uncontrolled immune dysregulation). Leniolisib dose was increased from 10 mg bid to 70 mg bid over 3 months. At pre-treatment and at various time points while on treatment, immunological evaluation, neuropsychological profiling (i.e. questionnaires to assess the autism quotient, social responsiveness, motor coordination and aberrant behaviour) and functional behavioural testing (i.e. visuomotor coordination using eye-hand coordination and pupil responses using BlinkLab) were performed.

Results:
On escalating doses of Leniolisib up till 70 mg bid, the patient did not show adverse events, including infections. pS6 and pAKT levels in B cells decreased, elevated total serum IgM decreased to within normal ranges, while thus far no significant changes in B and T cell subsets were found. Long term data will follow. Repeated visuomotor coordination tests revealed that the patient showed notable improvement in goal-directed coordination, primarily due to more efficient timing between eye and hand movements. In contrast, questionnaire responses remained consistent with baseline, showing no significant changes in self-reported performance. BlinkLab testing indicated that the patient exhibited atypical stimulus responses compared to neurotypical controls.

Conclusions:
In this single case of a patient with APDS, we demonstrated that treatment with Leniolisib not only restored some of the immunological abnormalities, but also contributed to an improvement in visuomotor behaviour symptoms.

POSTER 166 - IMMUNE DYSREGULATION IN COMMON VARIABLE IMMUNE DEFICIENCY: TESTING THE IDDA 2.1 SCORE IN A SINGLE-CENTER COHORT

AUTHORS

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Objective:
Common variable immune deficiency (CVID) is the most prevalent adulthood inborn error of immunity. Clinical features span from susceptibility to infections, immune dysregulation, autoimmunity, allergy and malignancy. The aim of this study is to analyze the prevalence of immune dysregulatory manifestations in CVID and assess their evolution and impact.

Design and methods:
This retrospective, monocentric, observational study included patients with CVID with at least 1 year of follow-up; to quantify immune dysregulation we used IDDA 2.1 score calculated at the last immunological check-up and, retroactively, at diagnosis. EUROclass protocol was used for immune phenotype analysis at diagnosis. Quantitative results are shown as median with IQR. Continuous variables were analyzed through Mann Whitney and Wilcoxon tests; correlations between variables are shown through linear regression.

Results:
We included 148 patients, 81 were women (55%), median age was 53 years old (IQR 23), median age at diagnosis was 39 (IQR 20.8), median diagnostic delay was 5 years (IQR 12). 76 patients (51%) had a complicated phenotype (i.e. non-infection only, Chapel classification); 32 patients (21%) had autoimmune cytopenia; 30 (20%) had organ specific autoimmunity and 7 (4%) had systemic autoimmunity. Median IDDA score at diagnosis was 18 (IQR 24), median IDDA score at last FU was 48 (IQR 36), the difference between the two was significant ($p<0.001$). Median time between diagnosis and IDDA score at FU calculation was 6.5 years (IQR 15). At diagnosis, no difference between IDDA scores in males and females was found (18 IQR 18 vs 18 IQR 18, p 0.245); while at FU, women had tendentially higher IDDA scores (54 IQR 36 vs 42 IQR 30, p 0.057). 77 patients (52%) had a >10 years FU, their median IDDA score at diagnosis was 18 (IQR 24), while at FU it was 54 (IQR 36); the difference between the two was significant ($p<0.001$). Longer diagnostic delay positively correlated with IDDA score at FU (R^2 0.103, estimate 0.939, 95CI 0.420/1.46, $p<0.001$); starting lower IgG levels negatively correlated with IDDA scores at FU (R^2 0.05, estimate -0.033, 95CI -0.05/-0.008 p 0.009). The same was found for marginal zone B cell percentage at diagnosis (R^2 0.08; estimate -0.451, 95CI -0.74/-0.16; p 0.003).

Conclusions:
IDDA 2.1 score yields a well-rounded analysis of immune dysregulation of CVID patients and its evolution throughout disease progression. More immature immune phenotypes (reduced marginal zone B cells and IgG titers) seem to correlate with higher degrees of immune dysregulation.

POSTER 167 - A CASE OF JAGN1 MUTATION PRESENTING WITH IMMUNODEFICIENCY AND ATYPICAL DIABETES

AUTHORS

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Objectives:
To describe the case of a young girl with severe congenital neutropenia (figure 1) caused by a homozygous variant in the Jagunal homolog 1 (JAGN1) gene (figure 2), who later developed atypical diabetes.

Case presentation:
JAGN1 deficiency disrupts neutrophil maturation, resulting in severe congenital neutropenia and recurrent infections. She was treated with granulocyte colony stimulating factor. Our patient also exhibited impaired humoral immunity (table 1), requiring immunoglobulin replacement therapy, which reduced infection frequency. Several years after the identification of her JAGN1 mutation, she developed atypical insulin-dependent diabetes mellitus – a condition not previously associated with JAGN1 mutations. This novel finding suggests a potential role for JAGN1 in pancreatic β-cell function (figure 3).

Conclusions:
This case expands the spectrum of JAGN1-related immune dysfunction and introduces a potential link between JAGN1 deficiency and diabetes. We explore possible mechanisms underlying this association, highlighting the need for further research. Clinicians should consider screening for diabetes in patients with JAGN1 mutations

POSTER 168 - IMPACT OF HEMOPHAGOCYTIC SYNDROME ON B CELL POPULATIONS: A CASE REPORT

AUTHORS

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Objective:
Hemophagocytic syndrome (HS) is a rare disorder with an estimated prevalence of 1.2 cases per million. Recent advances have improved understanding of its pathophysiology, particularly regarding alterations in T cell compartments and macrophage activation. However, in 2023, Shim J et al. demonstrated that B cell development and maturation are also impaired during active HS. This report aims to describe a case of secondary humoral immunodeficiency associated with HS.

Design and methods:
We describe the clinical case of a 35-year-old female patient who developed secondary humoral immunodeficiency following diagnosis of HS.

Results:
In March 2024, the patient was diagnosed with secondary HS according to HLH-2004 criteria. By August, she exhibited hypogammaglobulinemia in three isotypes (IgG, IgA, IgM) and increased infection frequency. Peripheral blood immunophenotyping showed a marked reduction of total B lymphocytes (0.072% of lymphocytes; 22 cells/ul), with absence of plasmablasts and transitional B cells. Repeat studies in October and November revealed recovery of B cells (17%; 241 cells/ul and 19%; 421 cells/ul, respectively), predominance of transitional B cells (62%; 149 cells/ul and 67.1%; 282 cells/ul), and decreased memory B cells (4.8%; 12 cells/ul and 0.8%; 4 cells/ul). One year post-diagnosis, normalization of transitional B cells (8.6%; 17 cells/ul) and increase in memory B cells (7%; 14 cells/ul) were observed, suggesting progressive recovery of the B cell compartment and a likely transient maturation defect associated with HS.

Conclusion:
Hemophagocytic syndrome may cause transient humoral immunodeficiency, likely due to disruption in B cell maturation. These findings highlight the importance of immunological monitoring, especially of B cell populations, in patients with HS to identify potentially underrecognized alterations.

POSTER 169 - PHENOTYPIC SPECTRUM AND CLINICAL OUTCOMES IN PATIENTS WITH HOMOZYGOUS TNFRSF9 MUTATION: A SAUDI COHORT STUDY

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Objective:
TNFRSF9 (CD137/4-1BB) is a co-stimulatory molecule essential for T-cell activation and survival. Biallelic loss-of-function variants have been implicated in a form of combined immunodeficiency characterized by EBV susceptibility, hypogammaglobulinemia, and immune dysregulation. We aimed to delineate the clinical and immunogenetic spectrum of patients with a homozygous TNFRSF9 c.325G>A:p.G109S mutation in a consanguineous Saudi cohort.

Design and method:
We conducted a retrospective study of five patients from unrelated consanguineous families identified through a national immunodeficiency registry. All patients were homozygous for the TNFRSF9 c.325G>A:p.G109S variant confirmed via whole exome sequencing. Clinical, immunological, and virological data—including EBV viremia, lymphoproliferation, HLH features, and treatment outcomes—were analyzed. Two cases were previously published, and this report includes three newly described patients.

Results:
All five patients share the same founder mutation (p.G109S) but exhibit variable severity. Median age at diagnosis was 6 years (range 3–21). All exhibited persistent hypogammaglobulinemia, recurrent infections, and elevated or persistent EBV viremia. Two patients underwent Allogenic HSCT after EBV driven B-LPD or lymphoma, both with favorable long-term outcomes. A third is currently under treatment for fulminant EBV+ T-LPD and HLH. The remaining two patients are stable on IVIG with low-level EBV viremia. (Details in Table 1)

Conclusions:
The TNFRSF9 c.325G>A:p.G109S mutation defines an autosomal recessive immunodeficiency with a variable expressivity. This cohort highlights the importance of early molecular diagnosis, aggressive management in severe cases, and timely consideration of HSCT as definitive therapy. Nonetheless, achieving pre-transplant disease control remains a major clinical challenge. Recognition of this monogenic disorder can guide individualized care and support targeted family counseling in high-risk populations.

POSTER 170 - ANALYSIS OF IRF5, IRF7, CD247, TNFAIP3, AND STAT4 GENETIC POLYMORPHISMS IN PRIMARY BILIARY CHOLANGITIS

AUTHORS

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Genetic factors play a key role in susceptibility to primary biliary cholangitis (PBC). This study aims to assess the association between five single nucleotide polymorphisms (SNPs): IRF5 (rs2004640), IRF7 (rs1131665), CD247 (rs2056626), TNFAIP3 (rs5029939), and STAT4 (rs7574865) and PBC.

SNP analysis was performed using real-time PCR with specific TaqMan probes. Allelic and genotypic frequencies were compared between patients and controls using the Chi-square test or Fisher's exact test, depending on sample sizes. Statistical analyses were conducted using SPSS software.

The results showed a significant association between the IRF7 rs1131665 and TNFAIP3 rs5029939 polymorphisms and susceptibility to PBC. The G allele of these SNPs was more frequent in PBC patients compared to controls ($p < 0.05$). However, no significant association was found for IRF5 rs2004640, CD247 rs2056626, and STAT4 rs7574865. Additionally, no significant correlation was identified between these polymorphisms and hepatic complications of PBC.

These findings suggest that IRF7 rs1131665 and TNFAIP3 rs5029939 polymorphisms may influence genetic susceptibility to PBC, supporting the hypothesis of an immunogenetic component in its pathophysiology. Further studies in larger and more diverse cohorts are needed to confirm these associations and better understand their role in disease development

POSTER 172 - GENOMIC AND CLINICAL CHARACTERIZATION OF COMMON VARIABLE IMMUNODEFICIENCY: TOWARD A PERSONALIZED THERAPEUTIC APPROACH

AUTHORS

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Background:
CVID is the most prevalent symptomatic IEI in adults, with broad clinical heterogeneity and frequently uncertain genetic etiology. Although over 60 genes have been linked to CVID, only 20–30% of patients receive a definitive molecular diagnosis. Integrative clinical and genomic profiling is essential to improve diagnostic accuracy and explore personalized therapeutic strategies. This study aims to characterize the clinical and genomic landscape of CVID patients in the Valencian Region (Spain), including deep phenotyping, genotype-phenotype correlations, and identification of potential genetic drivers.

Methods:
A multicenter, cross-sectional study across 21 hospitals included 103 patients with confirmed CVID. Clinical, immunological, and laboratory data were collected. Whole-exome sequencing (WES) was performed in 79 patients; 26 exomes have been interpreted to date. Variant filtering focused on immune-related genes, including pathogenic variants, CNVs, VUS, and susceptibility polymorphisms.

Results:
The cohort had a mean age of 50.6 years, with symptom onset at 28.8 and diagnosis at 39.7 years (mean delay: 10.8 years). Females comprised 59.2%. Non-infectious gastrointestinal disease affected 42.7%, cytopenias 28.2%, lymphadenopathy 34.0%, splenomegaly 28.2%, and GLILD 12.7%. Skin and neurological involvement were present in 25.5% and 5.8%, respectively.

Among 26 analyzed exomes, pathogenic-candidate variants in TNFRSF13B were found in 3 patients. A novel CD40L mutation led to reclassification as X-linked Hyper-IgM syndrome. Additional variants in DOCK8, PIK3CD, SBDS, TREX1, C3, and FCN3 were found, mostly in heterozygous state. A heterozygous deletion at 2q33.2–q33.3 affecting CTLA4 was confirmed by array analysis, revealing haploinsufficiency that had not been previously detected by other gene panels. Moreover, 29 VUS were detected in 17 of 26 patients, often without clear phenotype correlation. Polymorphisms in TNFRSF13C, DNASE1L3, and NOD2—potentially linked to immune dysregulation—were also observed, suggesting polygenic contributions.

Conclusion:
WES clearly outperforms restricted gene panels previously used in our cohort, enabling detection of clinically relevant variants—including CNVs, rare structural alterations, VUS, and immune-related polymorphisms—missed by targeted approaches. This broader strategy improves understanding of CVID's genetic complexity and supports adopting WES as a standard-of-care diagnostic tool, particularly in patients with immune dysregulation. Findings reinforce the value of integrative genomic approaches within multidisciplinary teams to advance precision medicine in CVID.

POSTER 173 - FAMILIAL LYMPHOHISTIOCYTOSIS GENETIC VARIANTS IN B-CELL LYMPHOPROLIFERATIVE DISORDERS AND IMMUNODEFICIENCY

AUTHORS

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Introduction:
Crossroads between primary (PID) and secondary immunodeficiencies (SID) are an ongoing challenge for immunologists, especially in the context of B-cell lymphoproliferative disorders (B-CLPD), where some patients behave clinically and analytically as PID-like. Some patients also share genetic variants related to Inborn Errors of Immunity (IEIs), making the challenge even broader. We have identified a group of patients with B-CLPD with genetic variants in PRF-1, related to Familial Lymphohistiocytosis (FLH), who have never been diagnosed with the characteristic clinical condition, but instead, have developed a B-CLPD and an immunodeficiency disorder.

FLH is a severe autoinflammatory condition associated with IEIs and considered as a PID, usually diagnosed in early childhood. Defects in the gen PRF-1 and other genes related to lymphocyte cytotoxic processes involved in immunological immunosurveillance, are behind this genetic disorder. However, to date, they have never been associated as causative of B-CLPDs. As key genes in immunosurveillance, we aim to study these defects in B-CLPD patients. Genetic variants affecting their structure or function could cause a severe cellular immune defect increasing the risk of both intracellular infections and malignant proliferation, leading to a crossroad between PID and SID.

Design and method:
Here we describe 3 patients with 3 different PRF-1 heterozygous genetic variants obtained through clinical exome analysis, and discuss, through informatics and immunological tests, the possible relationship with the clinical presentation and their functional implications. We performed In Silico analysis and applied severity prediction scores to each of the genetic mutations. Then, we studied the protein expression and the clinical implications of the variants (degranulation and cytotoxicity) through flow cytometry analysis and measuring serum IFN-y concentrations through ELISA assay.

Results and conclusions:
We observed that two of the three genetic variants had high In Silico pathogenicity scores, being one of them associated to an absent Perforin-1 expression in peripheric NK cytotoxic cells. These two patients also showed higher levels of biomarkers associated to lymphocytic hyperactivation (CD38+ and HLA-DR+ on lymphocyte surface, and IFN-y serum concentration). The third patient had a milder clinical phenotype and did not show significant alterations in the parameters studied.

Therefore, it might be possible that, the heterozygous nature of some genetic variants affecting PRF-1 gen may hinder immunosurveillance while being insufficient for a full clinical FLH to develop. Therefore, this preliminary study should increase the awareness of the presence of PID genetic variants in patients with a B-CLPD debut.

POSTER 174 - NO MAN'S LAND: THE MISSING LINK IN IMMUNOLOGY TRANSITION CARE IN POLAND

AUTHORS

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Objective:
Inborn errors of immunity are a heterogeneous group of disorders with various complications, comorbidities, and a need for long-term therapy, requiring special attention during care transfer. The lack of a coordinated transition care model increases the risk of treatment discontinuation, complications, and higher hospitalization rates. This study aimed to identify key challenges during transition from pediatric to adult immunology care in Poland and develop recommendations for optimizing this process.

Design and method:
The analysis included data collected on the basis of questionnaires completed by adult patients after transitioning to adult care (n=51, aged 20 to 40 years) and their parents (n=18).

Results:
While approximately 70% of patients and 61% of parents reported receiving some form of transition preparation, none participated in a structured transition program. Common challenges included: poor coordination between centers (41% reported centers never communicated with each other); incomplete medical documentation transfer (10% did not have any medical documentation, only 20% had the result of a genetic test, 28% of patients received only partial records); and extended waiting times for first adult clinic appointments (17% waited over 6 months). Most respondents (96%) reported no treatment interruptions during transition, despite the coordination challenges.

Conclusions:
Optimizing transition care in Poland requires standardized protocols, comprehensive documentation transfer, direct consultation between pediatric and adult physicians, individualized transition plans, and reduced waiting times for initial adult care appointments. A coordinated transition approach would significantly improve continuity of care and patient outcomes.

POSTER 175 - FROM COMMON TO RARE: COMMON VARIABLE IMMUNODEFICIENCY IN A PATIENT WITH ADA2 DEFICIENCY

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Objective:
To describe the case of an adult patient initially diagnosed with common variable immunodeficiency (CVID), later found to carry a homozygous mutation in the ADA2 gene, and to highlight the phenotypic overlap between DADA2 and CVID, including findings of impaired DNA repair, immunosenescence, and inflammatory joint involvement.

Design and methods:
We conducted a comprehensive clinical, immunological, and genetic evaluation of a 45-year-old male patient. Immunoglobulin levels, lymphocyte subsets, and infection history were assessed. Whole exome sequencing revealed a homozygous mutation in ADA2. Functional ADA2 enzymatic activity was measured. Additional studies included DNA repair assays and flow cytometric analysis of lymphocyte senescence markers. Clinical evaluation also focused on systemic inflammatory features, including joint manifestations.

Results:
The patient presented with IgM and IgA hypogammaglobulinemia (15 mg/dL and 20 mg/dL, respectively), low IgG levels (400 mg/dL, normalized with intravenous immunoglobulin therapy), and absolute T and B cell lymphopenia (600 and 14 cells/μL, respectively). Clinically, he experienced recurrent lower respiratory tract and skin infections, febrile episodes with rash and arthralgia, and signs of inflammatory joint involvement confirmed by physical examination. ADA2 enzymatic activity was markedly reduced. Functional studies revealed impaired DNA repair capacity and elevated expression of senescence markers in peripheral blood lymphocytes, suggesting immune dysregulation beyond the typical DADA2 profile.

Conclusions:
This case underscores the broad phenotypic variability of DADA2 and its clinical resemblance to CVID. The coexistence of immunodeficiency, systemic inflammation, joint involvement, impaired DNA repair, and lymphocyte senescence points to complex immune dysregulation associated with ADA2 mutations. These findings support the inclusion of ADA2 deficiency in the differential diagnosis of adult-onset immunodeficiency syndromes, particularly in patients presenting with overlapping infectious, inflammatory, and hematological features.

POSTER 176 - ACTIVATED PI3KΔ SYNDROME: CLINICAL CHARACTERISTICS AND EXPERIENCE FROM A SINGLE CENTER

AUTHORS

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Objective:
Activated phosphoinositide 3-kinase delta syndrome (APDS) is an autosomal dominant primary immunodeficiency resulting from gain-of-function mutations either in the PIK3CD gene, encoding the p110δ catalytic subunit of phosphoinositide 3-kinase delta (PI3Kδ) (APDS1), or in the PIK3R1 gene, encoding the p85α regulatory subunit (APDS2). The clinical phenotype is characterized by recurrent respiratory tract infections, chronic herpesvirus infections, non-malignant lymphoproliferation, autoimmunity, gastrointestinal manifestations, and an increased risk of malignancy. Management includes immunoglobulin replacement therapy (IgRT), antimicrobial prophylaxis, rapamycin, hematopoietic stem cell transplantation (HSCT), and, more recently, targeted therapies using selective PI3Kδ inhibitors.

Desing and method:
A retrospective study was conducted to evaluate the clinical course, immunologic and genetic characteristics, treatment strategies, and therapeutic responses of seven patients with genetically confirmed APDS. Data were obtained from medical records.

Results:
The study cohort consisted of seven patients, including four with APDS1 and three with APDS2 (5 females, 2 males). The median current age was 21.3 years (interquartile range [IQR]: 18.7). The median age at symptom onset was 12 months (IQR: 43.5), with referral to an immunology center at 72 months (IQR: 119), genetic diagnosis at 96 months (IQR: 99), and a median follow-up duration of 145 months (IQR: 181). The most common presenting features were recurrent upper/lower respiratory tract infections (n=7) and lymphoproliferation (n=7). During follow-up, all patients exhibited recurrent respiratory infections and lymphoproliferation. Additional clinical manifestations included autoimmunity (n=5), growth retardation (n=4), enteropathy (n=4), and malignancy (n=3), with B-cell lymphoma being the most frequently observed malignancy (42%). Immunological evaluation revealed lymphopenia, low IgA levels, elevated IgM, inverted CD4/CD8 ratio, altered CD8 RA/RO ratios, and reduced counts of class-switched memory B cells (CSMB) and unswitched memory B cells (UCSMB). All patients received IgRT and antimicrobial prophylaxis. Six patients required immunosuppressive therapies (rapamycin, corticosteroids, or mycophenolate mofetil) due to autoimmune manifestations and lymphoproliferation. Given that leniolisib is not yet accessible in our country, this therapy was recently initiated in two of our patients via international patient-specific procurement. Two patients received chemotherapy for diffuse large B-cell lymphoma, and one patient died during follow-up.

Conclusion:
The wide spectrum and evolving nature of clinical manifestations in APDS may lead to diagnostic delays. Early recognition is critical to prevent morbidity and mortality, and targeted therapies represent a promising treatment strategy in these patients.

POSTER 177 - PATHOGENIC VARIANT IN THE ACTIN REGULATOR GENE WDR1 IN A PATIENT WITH AUTOINFLAMMATION AND IMMUNODEFICIENCY. CLINICAL CASE WITH DIAGNOSTIC CHALLENGE

AUTHORS

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A growing number of monogenic immune-mediated diseases have been linked to genes involved in actin cytoskeleton remodelling pathways. There is increasing evidence linking these defects to autoinflammatory diseases and primary immunodeficiencies. Currently, in the field of autoinflammation, there is a shift in perspective towards a concept that describes how various molecular pathways converge, contributing to the onset of syndromes characterised by the coexistence of inflammation, autoimmunity and defective immune response. We present the case of a 50-year-old woman with a history of recurrent episodes of fever and abdominal pain, severe allergic asthma, and complicated pneumonia. Her family history includes: father and two brothers with severe asthma, pneumonia, and eosinophilic oesophagitis; daughter (14 years old) with coeliac disease and eosinophilic oesophagitis; and 8-year-old son under investigation for suspected cyclic neutropenia.

Immunological testing ruled out autoimmune, infectious, or oncological causes as the origin of her pathology. Clinical exome testing detected a pathogenic variant, in heterozygosity, in the MEFV gene, along with another variant, in homozygosity, in the actin regulatory gene WDR1. This variant, described as pathogenic, is related to a disease (OMIM: 604734) that presents with periodic fever and immunodeficiency data such as thrombocytopenia and cyclic neutropenia. These findings could explain the clinical complexity presented by the patient and the diagnostic challenge she has posed since we began monitoring her. Currently, thanks to sequencing techniques, information of great clinical relevance is being obtained, although functional validation of the findings is necessary in order to frame the variants found within the disease mechanisms and to be able to carry out personalised clinical follow-up and treatment.

POSTER 178 - BILATERAL OVARIAN SEX CORD-STROMAL TUMORS IN A CHILD WITH A RECOMBINATION-ACTIVATING GENE 1 MUTATION: A CASE REPORT AND LITERATURE REVIEW

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Abstract:
Background: Recombination-activating gene 1 (RAG1) deficiency is an autosomal recessive form of severe combined immunodeficiency (SCID) that impairs VDJ recombination, leading to defective T- and B-cell development. Patients typically present in early infancy with severe infections and require hematopoietic stem cell transplantation (HSCT) for long-term survival. While most reported malignancies in SCID are hematologic, solid tumors are rarely described. Here, we report the first case of a patient with RAG1-related SCID who developed bilateral ovarian sex cord-stromal tumors.

Objective:
To report a rare case of bilateral ovarian sex cord-stromal tumors in a patient with RAG1-related severe combined immunodeficiency (SCID) diagnosed prior to hematopoietic stem cell transplantation (HSCT).

Design and methods:
We report a case of an 8-year-old Saudi girl with a confirmed diagnosis of RAG1-related SCID who developed bilateral ovarian tumors prior to HSCT. Clinical, laboratory, and genetic data were evaluated, as well as the HSCT protocol and long-term follow-up.

Results:
We present here the case of an 8-year-old Saudi girl with a homozygous missense RAG1 variant (c.1438A>G; p.Ser480Gly). She presented at 15 months of age with severe abdominal distension and was diagnosed with bilateral encapsulated ovarian masses. Histopathological examination revealed bilateral sex cord-stromal tumors, not otherwise specified (NOS), of uncertain malignant potential. She was treated with bilateral salpingo-oophorectomy and four cycles of chemotherapy. She had multiple infections during her course of hospitalization, which lead to an immunological assessment and eventual diagnosis of severe combined immunodeficiency (SCID) in the presentation of severe lymphopenia, hypogammaglobulinemia, and disrupted vaccine responses. Table 1 summarizes her immunological workup, which included the lymphocyte subset, Ig level, and vaccine response. HSCT using a matched unrelated donor was then performed that resulted in full donor engraftment. She is now clinically well with stable immune reconstitution with no evidence of recurrence of the tumor.

Conclusion:
We report an unusual case of bilateral ovarian tumors linked to RAG1-related SCID. This case demonstrates the significance of tumor surveillance in SCID patients, even prior to HSCT, and broadens the phenotypic spectrum of hypomorphic RAG1 mutations.

Keywords:
RAG1 deficiency; Severe combined immunodeficiency (SCID); Ovarian sex cord-stromal tumor; Solid tumor; Hypomorphic mutation; Pediatric immunodeficiency; Hematopoietic stem cell transplantation (HSCT).

POSTER 179 - ANALYSIS OF THE KYIV RARE IMMUNE DISEASES CENTER IN A COHORT OF 29 PATIENTS

AUTHORS

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Objective:
Inborn errors of immunity (IEI) are a group of rare, life-threatening diseases that require timely diagnosis and appropriate treatment. Over the last decade, significant improvements have been made in Ukraine in the field of clinical immunology: the establishment of state programs supporting the treatment of rare immune diseases for children and adults, the implementation of neonatal screening for severe combined immunodeficiencies since 2022, and the rapid development of allogenic bone marrow transplantation for patients with primary immunodeficiencies (PID). Additionally, a large campaign to raise awareness of IEI is being conducted in Ukraine. However, the full-scale Russian invasion in 2022 has dramatically impacted the lives of all Ukrainians, including patients with IEIs.

Design and method:
Analysis of clinical profiles, diagnostic procedures, and treatment outcomes of 29 patients with various rare immune disorders treated at the Kyiv Center for Rare Immune Diseases.

Results:
Kyiv City Children's Hospital № 1 functions as an immunological center for children with inborn errors of immunity in Kyiv. Twenty-nine patients with inborn immune diseases are under observation at the hospital, including 21 boys and 8 girls with diagnoses such as transient hypogammaglobulinemia, X-linked hereditary hypogammaglobulinemia, IgG subclass deficiency, hyper-IgM syndrome, hyper-IgE syndrome, hyper-IgD syndrome, hereditary angioedema, common variable immunodeficiency and autoimmune lymphoproliferative syndrome. The patients range in age from 1 to 17 years. Each undergoes extensive diagnostic evaluations, including genetic testing and immunophenotyping. Currently, 11 children receive intravenous immunoglobulin, 2 receive subcutaneous immunoglobulin, 2 receive C1-inhibitors, 2 receive rapamycin, 2 receive canakinumab, and one receives Janus kinase inhibitors. Diagnoses are established according to ESID criteria, involving clinical picture analysis and laboratory tests: determination of immunoglobulin levels by the turbidimetric method, isohemagglutinins, post-vaccination antibody levels, lymphocyte subpopulations by flow cytometry, and dihydrorhodamine tests for diagnosing chronic granulomatous disease. Patient samples are sent to the Invitae laboratory in the USA for genetic testing. With timely treatment, children generally have good overall health.

Conclusions:
Despite the challenges faced by the Ukrainian population today, the Ukrainian healthcare system remains resilient, continuing to provide essential medical check-ups and treatment for patients with rare immune diseases.

POSTER 180 - EXPANDING THE CLINICAL AND IMMUNOLOGICAL SPECTRUM OF ARPC1B DEFICIENCY: A MULTICENTER COHORT STUDY

AUTHORS

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Objective:
ARPC1B deficiency is a rare autosomal recessive inborn error of immunity caused by biallelic mutations in the ARPC1B gene, which encodes a subunit of the Arp2/3-complex essential for actin cytoskeleton remodeling. This condition is typically characterized by recurrent infections, severe eczema, immune dysregulation, and platelet dysfunction. Early diagnosis is critical due to the risk of severe complications. This study aims to expand the clinical, immunological, and molecular understanding of ARPC1B deficiency by presenting a cohort of patients with homozygous ARPC1B mutations.

Design and method:
This multicenter study included 13 patients with genetically confirmed ARPC1B deficiency, identified through whole-exome or whole-genome sequencing, and confirmed by Sanger sequencing. Immunological evaluations involved flow cytometry-based immunophenotyping, lymphocyte proliferation assays, and cytokine production analysis. Reverse transcription PCR and immunoblotting were conducted to assess both the splicing defect and its impact on ARPC1B protein expression.

Results:
The cohort included 13 patients (seven males and six females) from 10 unrelated families. The median age at symptom onset was 60 days (interquartile range [IQR]: 28–68 days), and the median age at diagnosis was 45 months (IQR: 8–108 months).

Comprehensive clinical evaluation revealed a broad spectrum of manifestations, with the most frequent being severe and recurrent infections, dermatological and vascular involvement, failure to thrive, and chronic diarrhea. A summary of clinical features is presented in Figure 1. Infections were a prominent feature, involving a diverse

range of bacterial, viral, and fungal pathogens across multiple organ systems. Several patients experienced life-threatening infections, including sepsis, meningitis, and deep soft tissue abscesses.

Laboratory assessments frequently demonstrated eosinophilia and mild to moderate thrombocytopenia, typically associated with a reduced mean platelet volume. Most patients exhibited elevated IgA and IgE levels, with reduced IgM concentrations. Immunophenotyping revealed variable distributions of T, B, and NK cells, with a consistent reduction in naive $CD4^+$ and $CD8^+$ T cells, as well as recent thymic emigrants. Functional analysis of T cells revealed impaired proliferative responses to mitogens in the majority of cases.

Conclusions:
This study enhances current understanding of the genotypic and phenotypic spectrum of ARPC1B deficiency. Beyond the well-documented features of recurrent infections and immune dysregulation, early-onset colitis, vasculopathy, and syndromic manifestations such as craniofacial anomalies may be underrecognized yet clinically relevant aspects of the disease. These findings underscore the crucial role of comprehensive diagnostic approaches, which incorporate genetic, functional, and structural analyses.Early and accurate diagnosis is essential for optimizing patient management and improving long-term clinical outcomes.

POSTER 181 - SEVERE ASYMPTOMATIC HYPOGAMMAGLOBULINEMIA IN AN 80-YEAR-OLD WOMAN WITH PRIMARY LYMPHEDEMA AND CHRONIC STEROID THERAPY. POSSIBLE ROLE OF A MONOALLELIC MUTATION IN THE LIGASE 4 GENE

AUTHORS

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Objective:
To describe the immunological, clinical, and genetic findings in an 80-year-old woman with severe asymptomatic hypogammaglobulinemia. The patient has a history of intestinal malrotation with protein-losing enteropathy and primary lymphedema diagnosed at age 16. She has received long-term corticosteroid therapy since age 24 for adrenal insufficiency following bilateral adrenalectomy due to Cushing's syndrome. The aim is to evaluate possible primary and secondary causes of her immunological profile, including a monoallelic LIG4 mutation and an ERG variant of unknown significance.

Design and method:
This is a clinical case report based on 24 years of follow-up in an immunology and genetics unit. Serum immunoglobulin levels were monitored using turbidimetry, and lymphocyte subsets were assessed by flow cytometry. A genetic panel for primary immunodeficiencies (550 genes) was performed and later expanded to whole exome sequencing (WES).

Results:
Persistent severe hypogammaglobulinemia was observed (IgG <200 mg/dL), with IgA and IgM also markedly decreased. The patient displayed absent humoral responses to tetanus, diphtheria, pneumococcus, H. influenzae, and SARS-CoV-2 vaccines. Flow cytometry showed sustained B and T lymphopenia. Beta-2 microglobulin was mildly elevated. No monoclonal bands or autoimmune antibodies were detected. Genetic analysis revealed a heterozygous frameshift variant in LIG4 (c.1270_1273del, p.Lys424GlufsTer7), previously associated with immunodeficiency via haploinsufficiency. WES additionally identified a heterozygous splicing variant of uncertain significance in ERG (NM_182918.4:c.673+3A>G), linked to autosomal dominant lymphatic malformations. Family genetic studies are pending.

Conclusions:
This case highlights the coexistence of profound immunological abnormalities in the absence of clinical infections or autoimmunity. Although secondary factors such as chronic corticosteroid use and protein-losing enteropathy are likely contributors, the detection of variants in LIG4 and ERG suggests a possible underlying genetic predisposition. These findings support the use of genetic testing and family evaluation in patients with atypical or unexplained hypogammaglobulinemia.

POSTER 182 - FUNCTIONAL CYTOSOLIC PATHWAYS COMPENSATE FOR TLR SIGNALING DEFECTS IN IRAK4 AND MYD88 DEFICIENCY

AUTHORS

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MyD88 and IRAK4 are critical adaptors for most Toll-like receptors (TLRs) and IL-1/IL-18 receptors, yet patients with loss-of-function mutations in these molecules exhibit susceptibility primarily to pyogenic bacterial infections while retaining resistance to most viral, fungal, and parasitic pathogens. This clinical paradox suggests that MyD88-independent pathways compensate for canonical TLR signaling.

To investigate this, we assessed the functionality of cytosolic nucleic acid sensors and inflammasome pathways in peripheral blood mononuclear cells (PBMCs) and neutrophils from patients with IRAK4 or MyD88 deficiency versus healthy controls. We stimulated cells with pathogen-associated molecular patterns targeting both MyD88-dependent TLRs (e.g., TLR7/9 agonists) and MyD88-independent sensors, including TLR3 ligand (poly(I:C)), cytosolic DNA/RNA mimetics, and inflammasome activators (AIM2, NLRC4, NLRP3, and non-canonical caspase-4/5 stimuli).

As expected, patient cells failed to respond to MyD88-dependent TLR agonists. In contrast, they produced robust IFN-α and IP-10 upon TLR3 engagement and cytosolic nucleic acid stimulation. AIM2, NLRC4 inflammasomes and non-canonical caspase-4/5 pathways were fully functional, whereas NLRP3 activation was variably reduced. Antigen-presenting cells matured in response to cytosolic ligands but not to MyD88-dependent stimuli. Neutrophils from patients demonstrated preserved NET formation despite impaired cytokine secretion to bacterial agonists.

These results reveal intact cytosolic sensing and select inflammasome pathways in MyD88/IRAK4-deficient patients, providing a mechanistic basis for their narrow infectious vulnerability and underscoring the importance of MyD88-independent innate defenses in human immunity.

POSTER 183 - IMMUNODEFICIENCY AND MULTISYSTEMIC DISORDER : IMPLICATION OF A NEW VARIANT IN THE NFE2L2 GENE

AUTHORS

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Combined immunodeficiencies with associated or syndromic features form a very heterogeneous subgroup of inborn errors of immunity, affecting the development and/or function of adaptive immunity. These conditions are accompanied with variable non-immunological manifestations, resulting from the extrinsic involvement of the defective gene in other systems.

The objective of this study is to raise awareness among physicians about the clinical heterogeneity of these pathologies and to highlight the diagnostic challenges they present.

We report a case with a CID syndromic followed up at the Pediatric Infectious Diseases Department, the clinical immunology unit, of A. Harouchi Children's Hospital in Casablanca.

The patient is a 43-year-old male from a non-consanguineous marriage, followed up for a multisystemic disorder affecting several organs. He presents cardiovascular malformation, peripheral sensory-motor neuropathy, and leukoencephalopathy. He also suffers from a staturo-ponderal growth delay. Urogenital issues include azoospermia, renal colic, kidney stones, and recurrent urinary infections. He has chronic bronchopulmonary disease with recurrent sino-pulmonary infections. Facial dysmorphia is associated with musculoskeletal anomalies, including scoliosis and vertebral compression. Additionally, he deals with digestive disorders, characterized by dyschezia and recurrent bleeding due to repeated hemorrhoidal episodes.

The immunological testing revealed low Ig levels with IgA at 0.19 g/l, and IgG at 5 g/l. The complement C3 level was 0.73, and AP50 was 28.2 U/mL. The lymphocyte subpopulations count showed a null value of switched B lymphocytes, and the HIV serology was negative.

A genetic test targeting 471 genes associated with inborn errors of immunity identified a heterozygous variant of uncertain significance in the NFE2L2 gene, related to an autosomal dominant deficiency. This gene encodes a transcription factor involved in the cellular stress response in mammals and regulates the expression of over 200 other genes. A mutation in this gene causes a gain-of-function of the resulting protein, leading to deregulation of the expression of all the products it regulates, affecting multiple organs, which explains the patient's clinical state. Bioinformatics tools such as CADD, Revel, Alphamissense, Polyphen, and Sift4G support its pathogenic effect ; another variant affecting the same codon and producing a different amino acid has been classified as pathogenic.

This clinical case requires further investigation and functional test. Given the clinical diversity of this disease, it is crucial to raise awareness among physicians from various specialties to ensure optimal management.

POSTER 184 - EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF PEDIATRIC HUMORAL IMMUNODEFICIENCIES: A MOROCCAN EXPERIENCE FROM THE UNIVERSITY HOSPITAL OF CASABLANCA

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Humoral immunodeficiencies (HIDs) are a heterogeneous group of disorders, ranging from asymptomatic forms such as selective immunoglobulin A (IgA) deficiency and IgG subclass deficiencies, to severe forms like congenital agammaglobulinemia. Patients with HIDs often present with recurrent or severe upper (ENT) and lower respiratory tract infections, as well as chronic diarrhea.

The aim of our study is to describe the epidemiological and clinical profile of patients diagnosed in the clinical immunology unit of the pediatric infectious diseases department at the Children's Hospital of the University Hospital Center (CHU) of Casablanca.

This is a retrospective study covering a 26-year period, from 1998 to July 2024. Patients were diagnosed according to the criteria of the European Society for Immunodeficiencies (ESID) and were included from the clinical immunology unit of the Abderrahim Harouchi Mother and Child Hospital at the CHU of Casablanca.

A total of 119 cases of humoral immunodeficiency were identified, including 31 cases of common variable immunodeficiency (CVID), 17 cases of Hyper IgM syndrome, and 37 cases of agammaglobulinemia (17 cases of Bruton's disease and 20 cases of autosomal agammaglobulinemia). The median age at diagnosis was 6 years, with a mean age of symptom onset at 2 years. The sex ratio was 1.42. Parental consanguinity was observed in 52% of cases. The most common symptoms were sinopulmonary infections, present in 84% of patients. Additionally, gastrointestinal infections (mainly chronic diarrhea) were noted in 44.53% of cases, cutaneous infections in 24.36%, and urogenital infections in 6.72%.

All patients required immunoglobulin replacement therapy, with individualized doses and administration intervals based on clinical condition.

Despite an increasing number of diagnosed and treated patients, humoral immunodeficiencies remain underdiagnosed in our context. Greater efforts are needed to raise awareness of HIDs in order to improve early diagnosis and patient outcomes.

POSTER 185 - COMPLEMENT COMPONENT C8 BETA SUBUNIT DEFICIENCY AS AN UNDERLYING CAUSE OF RECURRENT MENINGOCOCCAL DISEASE

AUTHORS

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Objectives:
The complement system is a key component of innate immunity, with over 30 soluble and membrane-bound proteins acting in a coordinated cascade. A critical effector mechanism is the formation of the membrane attack complex, formed by the sequential assembly of complement proteins C5b, C6, C7, C8, and C9. C8 itself comprises alpha, beta, and gamma subunits encoded by separated genes. Mutations in the C8 beta gene lead to type II C8 deficiency, characterized by an absence of the beta subunit, and inherited in an autosomal recessive pattern. This rare immunodeficiency predisposes to recurrent severe infections, particularly with Neisseria Meningitidis and Neisseria Gonorrhoeae, often manifesting clinically after the first decade of life.

Design and methods:
We report the case of an 18-year-old patient with history of two episodes of invasive meningococcal disease (January and July 2023, respectively), the first of which was associated with meningitis. In both episodes, the patient was treated with ceftriaxone and showed good clinical evolution. Microbiological cultures identified two different types of Neisseria meningitidis.

A complete immunological evaluation was performed, and genetic testing by next generation sequencing was conducted to confirm the underlying molecular defect.

Results:
The immunological study revealed a slightly decreased level of complement component C3 and an undetectable hemolytic activity (CH50). Functional testing of complement C8 demonstrated a hemolytic activity level of 0.00 UI/mL, compared to a normal control value of 8,000.00 UI/mL. Hemolytic activity was fully restored upon the addition of purified complement component C8.

Genetic analysis identified a homozygous nonsense variant in exon 9 of the gene encoding the beta subunit of complement C8: c.1282C>T, p. (Arg428Ter). This variant results in a premature stop codon that would lead to messenger RNA degradation. It is classified as pathogenic and is associated with type II complement C8 deficiency.

The patient was started on antibiotic prophylaxis and received both meningococcal and pneumococcal vaccination. No further infections were documented during follow-up.

Conclusions:
This case highlights the importance of investigating terminal pathway complement deficiencies in patients with recurrent meningococcal infections. Early immunological and genetic diagnosis allows for preventive management such as antibiotic prophylaxis and vaccination, which are crucial in reducing the risk of life-threatening infections.

POSTER 186 - GRANULOMATOUS LYMPHOCITIC INTERSTITIAL LUNG DISEASE IN A GIRL WITH KABUKI SYNDROME

AUTHORS

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Objective:
Kabuki syndrome is caused by a biallelic mutation in either the KMT2D or KDM6A gene. Characteristic features include dysmorphic facial traits (1) and multiorgan involvement. In recent years, both T- and B-cell immunodeficiencies (2), as well as hematological autoimmune diseases (3) have been recognized as part of the syndrome's clinical spectrum. We present a case of a girl with Kabuki syndrome and granulomatous lymphocytic interstitial lung disease (GLILD). To our knowledge, this is the third reported case of Kabuki syndrome associated with GLILD (4,5).

Design and method:
We present the case of a girl born at 39 weeks of gestation with normal birth parameters, multiorgan involvement, and dysmorphic features. Initial molecular karyotyping did not explain the clinical presentation; a definitive diagnosis was made at the age of 8 years through next-generation sequencing, revealing a mutation in the KMT2D gene. At the age of 6 years, she was referred to an immunology clinic due to frequent respiratory infections, where hypogammaglobulinemia and an adequate specific antibody response to revaccination were noted. In the absence of recurrent infections during the COVID-19 lockdown, she did not receive immunoglobulin supplementation. The first pulmonary changes were noted at the age of 10, presenting as lower respiratory tract infections. A year later, GLILD was confirmed both radiologically and histologically. She also developed splenomegaly. Initial treatment with intravenous immunoglobulin replacement and immunomodulatory therapy with azathioprine led to only partial improvement. Due to ongoing development of pulmonary microcalcifications and new granulomatous lesions, therapy was escalated with pulsed corticosteroids and rituximab.

Results:
Kabuki syndrome is a rare genetic disorder often associated with immune system involvement. GLILD has primarily been described in a small subset of patients with antibody deficiency, common variable immunodeficiency (CVID), typically between the ages of 20 and 50 (6), leading to an unfavorable prognosis (7). The most effective treatment reported is a combination of rituximab and azathioprine (8, 9, 10), although rituximab monotherapy has also been successful (8, 11). In our patient, GLILD developed unusually early as part of immune dysregulation in Kabuki syndrome. In a cohort of Slovenian patients with Kabuki syndrome, 5 out of 10 are followed by an immunologist. Of these, 3 patients developed immune dysregulation (2 with Evans syndrome, 1 with GLILD).

Conclusions:
Kabuki syndrome is a rare, phenotypically diverse disease, often accompanied by complications of immune dysregulation. Regular follow-up with an immunologist and early recognition of complications enables successful long-term treatment.

POSTER 188 - FOURTY YEAR FOLLOW UP OF A CVID PATIENT WITH TACI MUTATION

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A 79yo woman first consulted our clinic in 1987 at age 41, reporting recurrent bronchitis and sinusitis. Her serum IgG was 112 mg%, IgA 7 mg%, and IgM 31 mg%. CVID was diagnosed, and monthly IVIG achieved good infection control.

In 1999, she developed hoarseness from nodular lesions on both vocal cords. A biopsy showed necrotizing granulomas, negative for acid-fast bacilli and fungi, and she partially improved with surgery. ANCA and ANA were negative. During 2000 to 2003, she developed skin nodules and erythematous plaques on her four limbs and left conjunctiva, many becoming painful ulcers. Synovitis affected wrists and MCP joints. A skin biopsy showed necrotizing granulomas. She was treated empirically with doxycycline and thalidomide but she was only responsive to high-dose prednisone.

In July 2003, she sustained four osteoporotic vertebral fractures and refused further steroid therapy. Skin lesions worsened, became ulcerated and severely painful with joint synovitis. Ciclosporin was ineffective. In February 2008, infliximab (5 mg/kg) was started; after four courses, all but one ulcer resolved. Infliximab was stopped, but lesions rapidly re-ulcerated. Her next 17 years of follow-up were characterized by immediate flares of her skin disease whenever infliximab was discontinued. She has never achieved remission of her granulomatous disease and remains infliximab-dependent.

In 2019, a right parotid gland nodule was noted. Surgery and biopsy revealed a large B-cell lymphoma positive for CD20, CD30, and PAX5. Monoclonality was not assessed, leaving the diagnosis uncertain. A watch-and-wait approach was chosen, and the lesion resolved spontaneously in 2021.

Laboratory studies showed that: (a) A few months after being placed on infliximab, the patient's IgM levels increased and remained high until infliximab was stopped during treatment for a new-onset ITP with steroids and IVIG; (b) increased CD4+fhc cells; and (c) progressive decline in B cells to 1%.

Genetic testing in 2019 identified a heterozygous missense variant c.512T>G in TNFRSF13B, changing Leu171 in the transmembrane domain. TNFRSF13B encodes TACI, which interacts with CAML and induces NFAT, AP-1, and NF-κB activation, crucial for humoral immunity. Monoallelic TACI mutations in CVID are linked to lymphadenopathy, granulomas, and autoimmune cytopenias.

In summary, this patient has a characteristic TACI monoallelic mutation associated with granulomatosis, lymphadenopathy, and autoimmune cytopenias. Surprisingly, long-term follow-up has led to B lymphocyte depletion. There is an unexplained relationship between serum IgM levels and infliximab, and we confirmed the association of high numbers of CD4+fhc with granulomatous and autoimmune diseases in CVID.

POSTER 189 - SAFETY AND EFFICACY OF INTRAVENOUS ADMINISTRATION OF IGVENA®/KEDRION® IN PATIENTS WITH SECONDARY ANTIBODY DEFICIENCY

AUTHORS

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Objective:
Immunoglobulin Replacement Therapy (IgRT) is the main treatment for antibody deficiencies and involves the cyclic use of polyvalent human IgG. This therapy is generally well tolerated; however, several side effects are reported, mainly associated with intravenous (IVIG) administration. Hypertension, obesity, kidney and heart diseases, and atherosclerosis are considered predisposing factors for severe adverse events. The rising prevalence of Secondary Antibody Deficiencies (SAD) has led to an increased use of IgRT in these patients, but limited data on its safety are available. This study aims to evaluate the efficacy and safety of IVIG treatment in a cohort of patients affected by SADs.

Design and method:
We retrospectively enrolled 33 patients affected by SAD, followed at the Immunodeficiency Unit of the University of Naples “Federico II”, who received IVIG treatment with 50 mg/ml IgVena®/Kedrion® for at least 6 months. Clinical and immunological data were collected from medical records. We analysed the incidence of infusion-related side effects and severe life-threatening adverse events. Moreover, we investigated the effects of IVIG administration on kidney function and cardiac output, measuring serum creatinine (Cr, mg/dl) and ejection fraction (EF, %) before and after 1 year of treatment. Finally, we assessed the infection rate (n/y) and hospitalizations, before and after the beginning of the therapy.

Results:
Our cohort was composed of 18 females and 15 males, with a median age of 62,6±10,7 years. 88% of patients presented at least one risk factor for severe adverse events (hypertension: 72,7%, atherosclerotic disease: 57,6%, obesity: 27,3%, chronic kidney disease: 15.1%, heart disease: 51,5%, heart failure: 12,1%). IgRT was administered at a median dose of 317±58 mg/kg/month, for a total of 594 infusions. We registered 12 infusion-related side effects (2%), consisting of flu-like symptoms. One patient experienced a thrombosis and two patients experienced atrial fibrillation; however, neither event was temporally related to IVIG administration. Kidney and cardiac function were not affected by the treatment (median Cr: 0.99 vs 0.99; median EF: 53 vs. 52,5). Finally, we reported a significant reduction of the infection rate (6/y vs. 2.4/y) and hospitalization number (1,23 vs. 0,15).

Conclusions:
SAD patients are a high-risk population for IgRT severe adverse effects due to their older age and comorbidities. Our data confirm the well-known effectiveness of IVIG administration in reducing the infection burden in SAD patients. Additionally, they highlight its safety in these patients, especially concerning cardiac and renal function. Further studies are required to strengthen our results.

POSTER 190 - GENETIC PROFILE IN A COHORT OF PATIENTS AFFECTED BY COMMON VARIABLE IMMUNODEFICIENCY

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Objective:
Common Variable Immunodeficiency (CVID) is the most frequent symptomatic primary immunodeficiency among adults. The hallmarks of the disease are the poor antibody response to vaccines and the increased susceptibility to infections; however half of the patients develop immune dysregulation manifestations: autoimmunity, polyclonal lymphoproliferation, and chronic enteropathy. The pathogenesis of CVID is poorly understood and we have few means to predict the clinical phenotype of the patients. Only 20% of patients present a genetic cause; for this reason genetic testing has a limited role in diagnostics. This study aims to evaluate the potential role of genetics in the prediction of CVID phenotype.

Design and method:
We enrolled 104 patients diagnosed with CVID according to ESID criteria, followed at the Immunodeficiency Unit of the University of Naples “Federico II”. Genetic analysis was performed using a next-generation sequencing panel including 140 genes related to inborn errors of immunity development. We retrospectively collected patients’ clinical and immunological data from medical records, stratifying them into clinical phenotypes according to Chapel et al. classification.

Results:
We identified pathogenic mutations in 29 patients (27.9%), involving TACI (13.45%), CTLA-4 (5.7%), NF-κB1 (3.8%), KMT2D (2.9%), IRF2BP2 (0.96%) and NF-κB2 (0.96%). In 17 patients, we found uncertain significance variants; in the remaining 58 patients, no mutations were detected. Comparing patients with pathogenic mutations (G+) with the other patients (G-), we found that the G+ cohort was more likely to develop a non-infectious phenotype (86% vs. 44%; $p<0.001$). Using the Odds Ratio, we estimated a higher risk of developing autoimmune cytopenia [OR=4.82 (1.93-12)], lymphoproliferation [OR=4.44 (1.76-11.2)], and Enteropathy [OR=3.97 (1.45-10.8)] in G+ patients, and we also found an increased prevalence of GLILD (37.9% vs. 14.7%, $p<0.01$). No differences were reported about age and serum Ig levels at the diagnosis, bronchiectasis and liver disease prevalence, and cancer incidence. Similarly, there was no difference in the prevalence of splenomegaly; however, spleen enlargement was significantly higher in the G+ patients (170.2 mm vs. 138.7 mm, $p<0.01$).

Conclusions:
Our data show the existence of a genotype-phenotype relationship in CVID, suggesting the major severity in patients with a genetic mutation. The absence of known genetic mutations in a group of patients with complicated phenotype might be linked to the involvement of polygenic interactions, and it should be furtherly studied. The implementation of the sample could confirm the prognostic role of genetic analysis and may lead to a tailored approach, based on the type of mutation.

POSTER 191 - EXPERT-BASED INTERNATIONAL CONSENSUS ON UPDATED WARNING SIGNS FOR PRIMARY IMMUNODEFICIENCIES: THE PIDCAP DELPHI PROJECT

AUTHORS

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Objective:
Early recognition of inborn errors of immunity (IEI) is essential to prevent morbidity and organ damage. While classic warning signs have guided clinical suspicion, they evolved since the publication of the 10 Jeffrey Modell Warning Signs in 1993, especially in non-infectious symptoms. We aimed to update and validate warning signs for IEI of the PIDCAP project through an international Delphi process to enable harmonized early detection strategies to a scalable easy to use solution. This work lays the foundation for scalable, practical tools that can be integrated into data-driven technologies to enhance clinical care.

Design and method:
The PIDCAP Delphi project was conducted in two rounds during 2024/2025. Experts in IEI—including physicians, nurses, and patients (from ESID, CIS, INGID and IPOPI under the umbrella of the Jeffrey Modell Foundation)—were invited to rate and weight candidate warning signs derived from literature using Delphi method. Consensus was defined as ≥66% agreement scoring 7–9 on a 9-point Likert scale. Separate panels for pediatric and adult IEI were convened to refine age-specific warning signs. Final outputs included consensus strength, diagnostic weight, and ICD-10 coding alignment.

Results:
A total of 96 (103 invited) experts from 22 countries (Europe, Canada and US) participated in the first round (93% response rate) and 90 (94%) in the second round. The pediatric panel (n=68) and adult panel (n=49) achieved consensus on 26 of 27 proposed and 17 of 24 signs, respectively. High-weight, high-consensus signs included ≥3 episodes of pneumonia, bronchiectasis, very early onset inflamatory bowel disease, positive family history and the presence of multimorbidity (≥2 signs). Free-text responses informed rewording and contextualization between rounds.

Conclusions:
This international Delphi has produced the first globally harmonized and consensus-based list of IEI warning signs. These updated signs—quantitatively weighted and ICD-10 mapped—will support implementation across diverse healthcare systems and inform future digital screening models, including federated learning frameworks. The PIDCAP Delphi initiative marks a important step toward earlier diagnosis of IEI especially focussed on primary care.

POSTER 192 - HUMORAL (WUHAN, DELTA, AND OMICRON) AND T-CELL (SPIKE AND NUCLEOCAPSID) RESPONSES AFTER FIVE COVID-19 VACCINE DOSES IN 55 BRAZILIAN PATIENTS WITH INBORN ERRORS OF IMMUNITY COMPARED TO CONTROLS

AUTHORS

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AFFILIATIONS

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Background and aims:
SARS-CoV-2 infection can be more severe in patients with Inborn Errors of Immunity (IEI). We evaluated the humoral and cellular immune responses to COVID-19 vaccines in IEI patients compared to healthy controls.

Methods:
Fifty-five IEI patients (aged 13-61) and 60 controls (aged 13-71) were primarily immunized with CoronaVac®, AstraZeneca®, or Pfizer® vaccines and monitored for 2 years, up to one month after the 5th dose (2nd booster). IEI included: 25 CVID; 9 SAD; 5 AT; 4 XLA; 4 PIK3CD; 4 Hyper-IgM syndrome; 3 Combined ID; and 1 STAT1-GOF. Humoral immunity was assessed by neutralizing antibodies against Wuhan, Delta, BA1, BA2, and BA5 variants. T-cell immunity was evaluated by ELISpot. Statistical analysis was performed using linear or logistic regression models.

Results:
Geometric mean antibody titers against Nucleocapsid, Wuhan, Delta, BA2, and BA5 differed over time after the 1st booster for IEI and the 2nd booster for controls ($p<0.05$). Controls had higher antibody titers (11,977 vs. 8,814 IU/mL for BA1 and 296 vs. 213 IU/mL for Wuhan) one month after the 2nd booster ($p<0.05$). T-cell responses were similar between IEI and controls, though IEI exhibited stronger Spike responses (405 vs. 149 spot-forming cells/million PBMCs after 2 boosters; $p=0.002$). Both groups showed stronger cellular immunity to Nucleocapsid over time ($p=0.017$), reflecting SARS-CoV-2 infections during the study period. COVID-19 hospitalization among IEI patients decreased from 8.60% (3/35) to zero after the 1st booster.

Conclusions:
IEI patients responded to three-dose SARS-CoV-2 immunization and two boosters with cellular immunity comparable to controls, though with lower humoral responses. Boosters enhanced both humoral and cellular immunity. Cellular immunity likely contributes to protection against severe COVID-19 and mortality in IEI patients.

POSTER 193 - T-CELL IMMUNITY IN PATIENTS WITH X-LINKED AGAMMAGLOBULINEMIA FOLLOWING SARS-COV-2 VACCINATION: INSIGHTS FROM A TWO-YEAR STUDY

AUTHORS

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Background and aims:
X-linked agammaglobulinemia (XLA) is a rare primary immunodeficiency marked by the absence of B cells and antibody production. This study investigated the development of SARS-CoV-2-specific T-cell responses in four XLA patients over two years after 3, 4, and 5 doses of COVID-19 vaccines, compared to 60 healthy controls.

Methods:
XLA patients received two initial doses of CoronaVac® (CV, n=2), AstraZeneca® (AZ, n=1), or Pfizer-BioNTech® (PZ, n=1), followed by three PZ doses. T-cell responses were measured using ELISpot [spot-forming cells (SFC)/million PBMCs, IFN-gamma detection] for Spike and Nucleocapsid antigens at 1 and 3 months post-3rd dose, 1 and 6 months post-4th dose, and 1 month post-5th dose.~

Results:
Three patients demonstrated robust T-cell responses: Patient 1 (19 y): Maintained lower but positive responses to Spike (91 SFCs) and Nucleocapsid (41 SFCs). Patient 3 (25 y): Achieved high Spike-specific responses (mean 2684 SFCs, surpassing controls' 155) after AZ (2 doses) and PZ (3 doses), with absent Nucleocapsid responses (mean 33 SFCs). Patient 4 (18 y): Hospitalized for COVID-19 prior to vaccination with monovalent PZ, displayed strong Nucleocapsid-specific responses (1160 vs. controls' 88 SFCs). However, patient 2 (36 y), with low CD4+ and CD8+ T-cell counts, had weak responses post-3rd and 4th doses (<41 SFCs for both Spike and Nucleocapsid).

Conclusions:
Despite the absence of humoral immunity, XLA patients demonstrated significant T-cell responses to SARS-CoV-2 vaccination, highlighting the critical role of cellular immunity in their defense against COVID-19. These findings underscore the importance of vaccination in this vulnerable population.

POSTER 195 - CONGENITAL ATHYMIA: REGISTRY DATA FROM PATIENTS TREATED WITH ALLOGENEIC PROCESSED THYMUS TISSUE-AGDC POST-FDA APPROVAL

AUTHORS

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Objective:
An observational cohort study (Congenital Athymia Patient Registry, NCT 05329935) was initiated in May 2022. The objectives of the study include establishing data to better understand immune reconstitution, long-term survival, and adverse events after administration of allogeneic processed thymus tissue-agdc in patients with congenital athymia. Allogeneic processed thymus tissue-agdc was approved in the United States by the FDA in October 2021, indicated for immune reconstitution in pediatric patients with congenital athymia, a rare form of severe T cell immunodeficiency and immune dysregulation.

Design and methods:
Enrollment criteria include a confirmed congenital athymia diagnosis (pretreatment naïve CD4+ T cells < 50 cells/µl), treatment with allogeneic processed thymus tissue-agdc, and written informed consent. Primary endpoints are survival at 12 months post-treatment and extent of T cell immune reconstitution. Secondary endpoints are incidence of serious adverse events (SAE), and AEs of special interest (AESI) such as acute kidney injury (AKI) and autoimmunity. Survival beyond 24 months post-treatment is evaluated as an exploratory objective. Results are from medical record data abstraction at baseline (pre-implantation), every 3 months during the first year after implantation, every 6 months during year 2, and annually thereafter.

Results:
As of June 24, 2025, 46 patients have been enrolled out of 47 patients treated. All patients received treatment at Duke University. Of the 46 patients enrolled, 16 (35%) were female, and 30 (65%) were male. The median (range) age was 10 (4–97) days at diagnosis, and 769 (235–2328) days at implantation. The median time from diagnosis to implantation in days (range) was 753 (230-2231). Genetic etiologies included 22q11.2del (18 patients, 39%), CHD7 mutations (11 patients, 23%), TBX1 (3 patients, 7%), with PAX1, FOXi3, TP6, EXTL3 mutations and 2p11.2 microdeletion under 5% prevalence. 36 patients (78%) were diagnosed with features of an autologous graft-versus-host disease prior to implantation, based on rash, cytopenia, adenopathy, and other symptoms. To date, 4 patients have died (8.6%), all deaths considered unrelated to allogeneic processed thymus tissue-agdc. 24 (57%) patients alive at the time of this analysis have reached 12 months post-treatment. Preliminary lymphocyte enumeration results indicate that 18 patients have recorded naive CD4+ T cell counts ≥50 cells/µl post-treatment (range 50-325), 12/18 (67%) by 12 months post-treatment.

Conclusion:
The number of patients with pre-treatment autoimmune manifestations clearly supports the need for diagnosis and CTT treatment as early as possible.

POSTER 196 - A CASE REPORT: SHORT SYDROME AND IMMUNODEFICIENCY

AUTHORS

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Short syndrome is very rare diasese defined by short stature, hypermobility of the joints, deep-set eyes, rieger malformation, and postponed eruption of primary and/or permanent teet. These are signs that fullfill the acronym but diasese had many more condition like hypoplastic nasal alae with overhanging columella, prominent forehead, maxillary hypoplasia, downturned mouth, low-set ear, birth weight below the expected percentile for gestational age, reduced tissue responsiveness to insulin, nephrophrocalcinosis, and hearing deficits.(1–3) Although intellectual functioning is usually intact, expressive language delay may be a component of the neurodevelopmental profile (4) Activated PI3K Delta Syndrome type 2 is a rare condition characterized by mutation in PIK3R1. LOF mutations in the p85 subunit can result both APDS2 or SHORT syndrome. (5,6) Pathogenic variants leading to LOF in the PIK3R1 gene disrupt the regulatory control exerted by the p85α subunit over class IA PI3Ks, contributing to dysregulated intracellular signaling pathways, underlie an autosomal dominant form of inborn errors of immunity known as APDS2. These mutations disrupt the inhibitory control exerted by p85α on the catalytic p110δ subunit, leading to constitutive PI3K pathway activation and downstream immune dysregulation(6–8). We present 19 year old patient exhibiting clinical features suggestive of SHORT syndrome, along with a history of recurrent sinopulmonary infections and laboratory confirmed hypogammaglobulinemia. Whole exom squence show that a heterozygous c.1993G>A (p.G665S) variant in the PIK3R1 (NM_181523) gene and a homozygous c.619_*631del variant in the PIK3CD (NM_005026). Mutation in PIK3R1 related with Short syndrome. Both parents had PIK3CD mutation. Mother also had PIK3R1 but only had low iga levels and no clinical symptoms. FISH analysis using CEP X/Y probes revealed X chromosome tetrasomy in 27% of the examined cells. We planned whole genom squence for the patient

POSTER 197 - IMMUNOPHENOTYPING OF INTESTINAL T CELLS IN PATIENTS WITH PRIMARY ANTIBODY DEFICIENCY DISORDERS: IMPLICATIONS FOR ENTEROPATHY

AUTHORS

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Objective:
This study aimed to characterize the duodenal and ileal T cell profiles in patients with primary antibody deficiency disorder (PADD) in relation to enteropathy.

Method:
A total of 35 PADD patients, 8 patients with Crohn's disease (CD), and 14 healthy controls (HC) were enrolled in the study (Figure 1). Biopsy samples were collected from inflamed duodenal and/or ileal sites for immunophenotyping and histopathological analysis. Lamina propria mononuclear cells were isolated using a cell dissociation cocktail followed by Ficoll density-gradient centrifugation. T cell subsets were defined using monoclonal antibodies against CD3 (total T cells), CD4 (Th), CD8 (Tc), CD25 and FoxP3 (Tregs), CD103 (mucosal T cells), and TCRγδ T cells. T cell maturation status was determined using anti-CD45 and anti-CD27 antibodies.

Results:
The median frequencies of duodenal total T, Treg, Tc, mucosal T, mucosal Th, mucosal Tc cells were different among PADD patients with enteropathy and without enteropathy and healthy controls (p=0.005, p=0.044, p=0.004, p=0.024, p=0.006, p=0.004, respectively). Duodenal T cell profiles were similar among patients with or without symptoms whereas mucosal T cells were lower and Th, central memory (CM) mucosal T and naïve (N) mucosal Th cells were higher in PADD patients with microscopic abnormalities in duodenum than in patients without abnormalities (p=0.036, p=0.042, p=0.049, p=0.049, respectively). Ileal T cell profiles were similar among four groups and between PADD patients with and without symptoms. However, Th, N T, N mucosal T, N mucosal Tc and N mucosal Th cells were higher in PADD patients with microscopic anomalies in ileum than in those without anomalies (p=0.044, p=0.014, p=0.002, p=0.008, p=0.008, respectively).

Conclusion:
Our findings reveal that enteropathy in PADD is associated with distinct mucosal T cell alterations in both duodenum and ileum, reflecting localized immune dysregulation. In the duodenum, enteropathy was marked by a reduction in mucosal T cells and an increase in Th, CM mucosal T, and N mucosal Th cells, particularly in patients with microscopic abnormalities. These changes suggest a shift toward less differentiated or less tissue-adapted T cell populations, potentially impairing mucosal immune homeostasis. In the ileum, patients with microscopic abnormalities exhibited increased proportions of Th, N T, N mucosal T, and N mucosal Tc and Th cells. This indicates a parallel dysregulation of mucosal immunity in the ileum, primarily driven by expansion of immature T cell subsets. Together, these compartment-specific immune signatures may inform future diagnostic and therapeutic strategies targeting gut-specific immune pathways.

POSTER 198 - A CASE OF COMMON VARIABLE IMMUNODEFICIENCY PRESENTING WITH CYTOMEGALOVIRUS COLITIS: A RARE CASE REPORT

AUTHORS

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Objective:
Common Variable Immunodeficiency (CVID) is one of the most prevalent primary immunodeficiencies, characterized by low serum levels of immunoglobulins as well as impaired antibody production. Gastrointestinal complications are frequent and can mimic inflammatory bowel disease. Particularly, Cytomegalovirus (CMV) colitis is rare in CVID but may occur due to the underlying immune dysfunction.

Design and method:
A 61 years old male was referred to the internal medicine clinic with a history of diarrhea, fatigue and low-grade fever. His diarrhea presented itself as chronic diarrhea (7-8 times a day, without blood and mucus) accompanied by an unintentional weight loss. His medical history was unremarkable. Stool tests were negative for pathogens. His laboratory findings are showed in Table 1. A bone marrow biopsy was performed and was found to be consistent with pure red cell aplasia (PRCA). Congo red was negative and there was no evidence of lymphomas or plasma cell disorders. A colonoscopy was performed. Multiple biopsies were taken, resulting in colitis. The patient was diagnosed with CVID and was started on methyl prednisolone and IVIg. After 3 weeks, the anemia and the diarrhea were under control. But, after 9 months, he had a malabsorption syndrome and severe diarrhea due to IVIg replacement and steroid treatment. He was hospitalized and reevaluated again. Colonoscopy were performed. Histopathology results demonstrated large cells with nuclear and cytoplasmic inclusions suggestive of CMV infection. CMV polymerase chain reaction (PCR) test was performed and was detected 16,600 copies/mL. Ganciclovir was administered and clinical improvement was noted with the serum CMV DNA level was found to be decreasing to 246 copies/mL. However the clinic of the patient has deteriorated, the patient had passed away due to an abrupt pulmonary embolism.

Result and conclusion:
This case highlights the diagnostic challenge of CVID, often presenting years after symptom onset and in this case at the age of 61. The adult-onset form of the disease tends to present with immune cytopenia, lymphoma, or organ involvement. Early recognition and IVIg therapy are critical to prevent complications. Our patient was presented with PRCA and intestinal involvement of the disease. But he was complicated with CMV colitis after a while. Although CMV colitis is rare in CVID, it should be kept in mind in immunocompromised individuals. This case report aims to emphasize the potential mortal progression of CMV in patients with CVID. Early endoscopic evaluation and appropriate antiviral therapy are essential for favorable outcomes.

POSTER 199 - THE DIAGNOSTIC ODYSSEY OF A BOY WITH PREDISPOSITION TO EPSTEIN-BARR VIRUS INFECTION

AUTHORS

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Background:
X-linked lymphoproliferative disease type 1 (XLP1) is a rare inborn error of immunity, resulting from SH2D1A gene mutations, characterised by severe immune-dysregulation, particularly in response to Epstein-Barr virus (EBV) infection. Clinical manifestations include fulminant infectious mononucleosis, EBV-associated lymphomas, and haemophagocytic lymphohistiocytosis (HLH). Early recognition is often hindered by its variable presentation and overlap with more common paediatric conditions.

Case report:
We report a case of a 9-year old Malay boy with a history of Burkitt's lymphoma (BL) of the caecum at the age of 4 years. He presented with an acute abdomen and the diagnosis of BL was established from histopathological examination. No EBV confirmation EBV was done at this point. He achieved disease remission following chemotherapy. Subsequently, he remained well for 4 years. At the age of 8 years 6 months, he experienced recurrent febrile episodes associated with productive cough. During an elective admission for bronchoscopy, he developed persistent high fevers associated with generalised tonic-clonic seizures, systemic vasculitis and anasarca. He also developed multiple fever-provoked seizures. On examination, there was progressively enlarging hepatomegaly with pancytopaenia. Bone marrow examination found increased haemophagocytes. C-reactive protein and erythrocyte sedimentation rate were elevated with hyperferritinaemia and hypofibrinogenaemia. Testing for soluble cd25 protein and NK-cell activity are not available in our setting. Screening for infections yielded negative results for tuberculosis, bacterial, and fungal infections. Respiratory secretions PCR was positive for Rhinovirus. Serum EBV viral load was 167,800 copies/mL. Cerebrospinal fluid examination found pleocytosis with increased protein. This led to a diagnosis of EBV-triggered HLH. Treatment was commenced based on the HLH-2004 protocol and consisted of dexamethasone, ciclosporin and etoposide. He achieved transient control of the HLH. Whole exome sequencing found a pathogenic mutation at the SH2D1A gene (c.163C>T:p.R55X) in the index patient. Sanger sequencing of the mother confirmed her heterozygous carrier status. Haematopoetic transplant was not pursued due to no matched donor within the family and also national donor database.

Conclusion:
This case illustrates the diagnostic challenge and clinical complexity of XLP1, particularly in children presenting with severe EBV-related complications. In settings where access to specialised immunological assays is limited, persistent or recurrent EBV-related pathology should prompt consideration of underlying primary immunodeficiencies. Genetic testing remains essential for definitive diagnosis. Early recognition is crucial, as definitive treatment requires haematopoietic stem cell transplantation. This case underscores the importance of a high index of suspicion for XLP1 in males with unexplained HLH or EBV-associated lymphoproliferative disease.

POSTER 200 - NUCLEAR FACTOR KAPPA B VARIANTS IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

AUTHORS

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Objective:
Characterizing the clinical and immunological profiles of Iranian patients with inborn errors of immunity (IEI) harboring rare variants in the nuclear factor kappa B (NF-κB) pathway is crucial for understanding associated manifestations.

Design and method:
This multi-center study enrolled patients with NF-κB pathway mutations. Peripheral blood mononuclear cells (PBMCs) were used for immunophenotyping of B and T lymphocyte subsets via flow cytometry and for assessing T cell proliferation. Immunoblotting evaluated NF-κB protein expression levels.

Results:
Sixteen patients with mutations in NFKB1, NFKB2, IKBKB, and IKBKG genes were identified. NFKB1 and NFKB2 mutations were heterozygous, IKBKB mutations were homozygous, and the IKBKG mutation was hemizygous. Patients exhibited hypogammaglobulinemia and switched memory B cell abnormalities. Immunoblotting revealed decreased NF-κB1 expression in most cases. NFKB2 mutations led to lower protein expression in unstimulated PBMCs, with mild to strong reductions after stimulation (some cases showed no significant changes).

Conclusions:
This study identifies novel IEI cases associated with NF-κB pathway defects. Further comprehensive evaluation and functional analysis of these mutations are warranted to confirm their impact on disease manifestation.

POSTER 201 - INVESTIGATING THE IMPACT OF DEEP BREATHING, LAUGHTER YOGA, AND CLAPPING THERAPY ON QUALITY OF LIFE IN ADOLESCENTS WITH PRIMARY IMMUNODEFICIENCY DISEASES

AUTHORS

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Objective:
This study aimed to evaluate the impact of non-pharmacological interventions—deep breathing exercises, laughter yoga, and clapping therapy—on the quality of life, psychological well-being, sleep quality, and metabolic and immunological markers in adolescents diagnosed with primary immunodeficiency diseases (PIDs).

Methods:
A cross-sectional interventional study was conducted on 328 adolescents aged 7 to 17 years with clinically confirmed PIDs in the Central Delhi metropolitan area. Participants underwent a structured intervention consisting of a 30-minute educational session followed by 30 minutes of deep breathing, guided laughter yoga, and rhythmic clapping exercises. The program was carried out regularly over one month. Pre- and post-intervention assessments included evaluation of sleep quality, anxiety, and depression using validated psychological scales, along with laboratory tests measuring metabolic indicators such as fasting blood glucose, insulin levels, oral glucose tolerance, and HbA1c. Immunological assessments included serum immunoglobulin profiling (IgG, IgA, and IgM levels) and genetic testing to monitor baseline immune status.

Results:
After one month, participants showed significant improvement in sleep quality ($p < 0.001$) and reductions in anxiety and depression scores ($p < 0.01$). Glycemic markers showed improved fasting glucose and HbA1c levels, indicating better metabolic regulation. Immunoglobulin levels remained stable, with no evidence of intervention-related complications. Adolescents also reported increased emotional resilience, better mood, and improved ability to cope with daily stressors.

Conclusion:
The findings support the use of deep breathing, laughter yoga, and clapping therapy as effective adjunctive interventions to enhance quality of life and emotional well-being in adolescents with PIDs. These simple, low-cost, and non-invasive approaches may serve as valuable additions to routine care, promoting holistic health and resilience in this vulnerable population.

POSTER 203 - UNDERSTANDING THE MOLECULAR BASIS OF SKELETAL ABNORMALITIES IN STAT3 LOSS-OF-FUNCTION HYPER-IGE SYNDROME

AUTHORS

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Background:
Hyper IgE syndrome (HIES) is a rare disorder caused, in > 80% of cases by mutation in STAT3 gene. Up to 70% of patients experience skeletal and craniofacial abnormalities. Previous studies from our laboratory have shown that STAT3 plays a role in osteoclast-genesis. Recent studies using mouse models have demonstrated that STAT3 knockdown affects osteoblasts (OB), but not osteoclasts (OC). Despite this role of STAT3 in mediating OB-OC crosstalk remains unclear.

Aim:
To decipher osteoblast-osteoclast dysregulation in STAT3-LOF-HIES patients by analyzing differential gene expressions in OB-OC crosstalk.

Methods:
Four genetically confirmed HIES patients with mutation in DNA-binding domain (patients 1 and 3: p.Arg455Gln, p.Arg382Trp), coiled-coil domain (patient 2: p.Leu225Val), and linker domain (patient 4: p.Ile499Phe), (NIH score ≥20, Th17 ≤0.5%, pSTAT3 <30%) and four healthy controls were recruited. PBMCs-derived MSCs were differentiated into osteoblasts. ALP activity, Mineralization (Alizarin Red staining), and RNA sequencing followed by validation on STAT3 overexpressed and silenced DPSC using RT-PCR was done.

Results:
The osteogenic potential was significantly reduced in patients as compared to controls, as indicated by decreased Alizarin Red staining and ALP activity. RNA sequencing identified 693 downregulated and 860 upregulated genes (≥1.5-fold change). Gene ontology revealed osteoblast differentiation, extracellular matrix organization, osteoclast signaling, and inflammatory responses to be significantly enriched in HIES in comparison to healthy controls. Notably, key regulatory genes including FOS, FOSB, SPP1, TREM2, TBX15, DLX5, MSX1, BMP2, ALPL, and COL10A1 exhibited highly significant log2fold change >/5 ($p < 0.001$***). Interestingly, SPP1 (osteopontin) and ALPL (alkaline phosphatase) were markedly upregulated, thereby supporting enhanced osteogenic activity, while inflammatory mediators such as IL1B, TLR4, and MMP9 were significantly downregulated, indicating altered immune-modulatory roles in bone microenvironment regulation. Additional analysis revealed potential impairment of osteoclast differentiation signals, along with upregulation of transcription factors crucial for skeletal patterning and matrix mineralization. Further validation confirmed that FOS, FOSB, SPP1, TREM2, TBX15, DLX5, and ALPL were significantly dysregulated in patient-derived osteoblasts ($p = 0.0286$*), consistent with RNA-seq data. Together, these findings highlight a disrupted transcriptional program impacting osteoblast function and immune signaling in the patient group.

Conclusion:
Our study reveals major dysregulation of the STAT3-osteogenesis axis in STAT3-LOF HIES patients, characterized by aberrant expression of key genes governing bone homeostasis. This likely underlies the skeletal and craniofacial abnormalities observed, implicating altered osteoblast activity.

POSTER 204 - ATYPICAL COURSE OF SCHWACHMANN-DIAMOND SYNDROME - 13 YEARS OF DIAGNOSIS. HARIYAN TETYANA, BOYARCHUK OKSANA

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ATYPICAL COURSE OF SCHWACHMANN-DIAMOND SYNDROME - 13 YEARS OF DIAGNOSIS.

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Objective:
To present a clinical case of a child with an atypical course of Schwachmann-Diamond syndrome, which complicated the diagnosis. To highlight the difficulties of genetic verification due to the absence of the SBDS gene in the diagnostic panels of primary immunodeficiencies.

Design and method:
The study was performed in the format of a case report. A 15-year-old boy has been ill since birth, when he was diagnosed with congenital cytomegalovirus infection with liver damage. He is under constant observation of an immunologist, neurologist, and pediatrician. Given the disorders in the gastrointestinal tract, he was tested for cystic fibrosis and this diagnosis was denied. Digestive problems were observed until the age of 4, and the child constantly received enzyme replacement therapy. At the age of 10 years, he suffered from glomerulonephritis with nephrotic syndrome, receiving corticosteroids.

Results and conclusions:
In recent years, leukopenia has been noticed, and in the last year thrombocytopenia has been added. A diagnostic bone marrow puncture revealed signs of dyspysis. Trepanobiopsy revealed morphological changes indicative of aplastic anemia. Taking into account the symptom complex with pancreatic disorders, signs of immunodeficiency, and bone marrow failure and insufficiency, a complete exome study was performed to confirm Schwachmann-Diamond syndrome and 2 pathogenic variants in the SBDS gene were detected. The diagnosis of congenital Schwachmann-Diamond syndrome was established. The only method of therapy is bone marrow transplantation, which may be necessary in the near future. In the absence of an HLA-compatible unrelated donor, the child’s parents, who are partially compatible, can be a donor for a haploidentical related transplant.

POSTER 205 - COHEN SYNDROME IN UKRAINE: A RARE CLINICAL CASE AND DIAGNOSTIC CHALLENGES

AUTHORS

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Background and aim:
Cohen syndrome is a rare autosomal recessive disorder characterized by congenital neutropenia in association with intellectual disability and distinct dysmorphic features. These include microcephaly, a round facial appearance ('moon face'), severe myopia, pigmentary retinopathy, truncal obesity, and joint hyperlaxity. Due to its rarity and heterogeneous presentation, diagnosis remains challenging, particularly in underrepresented regions such as Ukraine. The disease is caused by mutations in the COH1 (VPS13B) gene, located on the short arm of chromosome 8 at locus 8q22 (OMIM: 216550).

Methods:
Case report.

Results:
We report the case of a 7-year-old boy referred to a pediatric immunologist by a pediatric hematologist due to persistent chronic neutropenia. He was born from the second pregnancy, complicated by maternal polyarthritis, rheumatism, an upper respiratory infection at 13–14 weeks, a threatened miscarriage at 18–19 weeks, intrauterine growth restriction, and premature placental aging. Delivery occurred at 33–34 weeks of gestation, with a birth weight of 1280 g.

At the time of evaluation, the patient exhibited delayed speech and cognitive development (sociable and cheerful but lacking control over urination and defecation), short stature, truncal fat distribution, severe myopia, microcephaly, and facial dysmorphism including high-arched or wave-shaped eyelids, thick hair, low anterior hairline, short philtrum, long-thick eyelashes, and prominent nasal root and upper central incisors. Laboratory tests revealed persistent leukopenia and neutropenia.

Clinical history included episodes of infectious complications (right cheek abscess, aphthous stomatitis, recurrent upper respiratory tract infections), hypotonia, joint hypermobility, severe plano-valgus foot deformity, inguinal hernia, and allergic dermatitis. Notably, treatment with G-CSF was not initiated. These findings raised suspicion of congenital neutropenia and prompted further genetic evaluation.

Conclusions:
This is the first documented case of Cohen syndrome reported in Ukraine, expanding the global understanding of its geographic distribution. Given the overlap with hematologic and developmental disorders, it is crucial that all related specialists - including hematologists, pediatricians, geneticists, and ophthalmologists - consider Cohen syndrome in their differential diagnosis when encountering similar clinical features.

POSTER 206 - IMMUNOLOGICAL CHARACTERISTICS OF CARMIL2 DEFICIENCY PATIENTS

AUTHORS

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Objective:
CARMIL2 plays a role in cell protrusion formations, CD28-mediated stimulation of NF-kappa-B signaling, naive T cell activation, memory T cell maturation, and differentiation into helper and regulatory T cells. Biallelic CARMIL2 (RLTPR) mutations have been linked to combined immunodeficiency with broad clinical variability.

Design and method:
We aimed to describe the clinical, genetic, and functional characteristics of 9 patients diagnosed with CARMIL2 deficiency and investigate the effects on cytoskeletal dynamics, T cell activation, and immune cell migration. After identifying the biallelic loss-of-function CARMIL2 variants in patients by next-generation sequencing, we did functional studies to characterize the pathogenicity of mutations.

Results:
The onset of the symptoms begins mainly in early childhood, and the median age of diagnosis was 25 years (5-36). Recurrent sinopulmonary infections (6/9), persistent skin viral infections (6/9), fungal infections (4/6), lymphoproliferation (4/9), and bronchiectasis (4/19) were common. Two patients developed malignancies(EBV-associated smooth muscle tumors and large granular lymphocytic leukemia(LGLL)). We documented decreased memory and switched-memory B cells with increased naive B cells and decreased naive CD4+ and CD8+ and central-memory T cells.

One adult patient developed blindness due to CMV retinitis. One with LGLL underwent HSCT before the diagnosis and died due to sepsis. We gave monthly IgRT and prophylactic antibacterial therapy in all patients.

Cytoskeletal analysis showed disorganized actin polymerization and decreased directionality of F-actin, especially in T cells. Phagocytic function of neutrophils was increased, while monocytes displayed variable responses. Monocytes exhibited defective upregulation of CD80/CD86 upon LPS stimulation.

T cells exhibited impaired activation in response to anti-CD3/CD28 stimulation, with reduced expression of CD25 and 4-1BB, decreased proliferation, and resistance to co-stimulation. After stimulation, patient T cells showed reduced upregulation of inhibitory receptors (PD-1, CTLA-4, LAG3 and TIM-3 compared to controls.

Migration assays demonstrated reduced chemotactic activity in PMNs, monocytes, and T cells, coupled with impaired focal adhesion formation, particularly in monocytes and T cells. CARMIL2-deficient T cells failed to proliferate even when co-cultured with healthy monocytes, indicating intrinsic T cell defects.

Conclusion:
CARMIL2 deficiency results in a combined immunodeficiency with defective cytoskeletal remodeling, T cell activation, migration, and immune surveillance. Early recognition and consideration of HSCT are crucial for preventing long-term complications.

POSTER 207 - CLINICAL AND IMMUNOLOGICAL IMPACT OF JAK INHIBITION IN CONCURRENT DOWN SYNDROME AND STAT1 GAIN OF FUNCTION

AUTHORS

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Introduction:
Down Syndrome (DS), a common genetic disorder caused by an extra copy of chromosome 21, leads to neurodevelopmental delay, reduced muscle tone, and various medical issues including cardiac abnormalities and increased risks of leukemia and Alzheimer's. Individuals with DS are also highly susceptible to autoimmune and autoinflammatory diseases. DS is now understood as an interferonopathy, characterized by persistent interferon (IFN) activity, which drives chronic autoinflammation. This is partly due to the increased gene dosage of IFN receptor subunits on chromosome 21, boosting JAK/STAT signaling. Promising results with JAK inhibitors for autoimmune conditions highlight their potential for modulating IFN responses in DS, with ongoing clinical trials. There's also a clinical overlap between certain DS individuals and those with gain-of-function (GOF) mutations in STAT1, both showing heightened STAT1 activity. JAK inhibition has successfully treated STAT1 GOF patients. A new STAT1 GOF mutation (P326S) was found in a DS patient with severe symptoms, where ruxolitinib therapy significantly controlled her clinical manifestations.

Methods:
we included two patients, one with DS (P1) who carried a STAT1 P326S variant and P2 with only the STAT1 P326S variant. DS and STAT1 GOF individuals were examined as controls. IFN subunit receptors and the response to IFNα/γ stimulation were analyzed through flow cytometry and/or RT-PCR. The nCounter FLEX (NanoString) platform evaluated the expression of IFN-response genes, and serum cytokines were quantified using Luminex assay.

Results:
clinical manifestations of P1 were mainly characterized by recurrent infections, chronic mucocutaneous candidiasis (CMC), interstitial pneumonitis and pulmonary hypertension. P2 experienced recurrent esophageal candidiasis with dysphagia and stenosis. The novel STAT1 P326S variant resulted in increased STAT1/pSTAT1 levels in response to IFNα/γ. Clinical response to Ruxolitinib therapy was remarkable and sustained in both patients. However, whilst pSTAT1 normalized in the course of Ruxolitinib therapy, key biomarkers such as STAT1 levels, IFN signature or cytokine profiling (TFNα, IL1RA and IL-6) remained unexpectedly altered in P1 indicating an incomplete resolution of inflammation.

Conclusion:
this is the first study showing the potential role of Ruxolitinib in treating complex clinical manifestations resulted from DS and STAT1 GOF co-existence. It also highlights the importance of conducting complete genetic and immunologic work-up when looking at the underlying causes of disease in DS, particularly those related to immune dysregulation.

POSTER 208 - MONITORING THE DOSE OF IMMUNOGLOBULIN REPLACEMENT THERAPY IN PATIENTS WITH MONOCLONAL GAMMOPATHY

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Objective:
Asymptomatic (i.e. without specific therapy) diseases associated with the production of monoclonal immunoglobulin (monoclonal gammopathy of undetermined significance, MGUS, and smoldering multiple myeloma, SMM) have an increased risk for bacterial and viral infections. Hypogammaglobulinemia as defined by a reduced serum concentration of polyclonal immunoglobulins is found in up to 30% of MGUS patients and in up to 80% of SMM patients; however, not all patients with hypogammaglobulinemia present with recurrent infections, and conversely, serious infections may occur with normal immunoglobulin concentrations. Immunoglobulin replacement therapy (IGRT) is effective in preventing infections in patients with monoclonal gammopathy, and a poor IgG response to pneumococcal polysaccharide vaccination has been linked to IGRT efficacy. However, in IgG monoclonal gammopathy it is difficult to monitor adequate IGRT dosing through measurement of serum IgG levels, as the presence of the IgG paraprotein interferes with the detection of the IGRT-derived polyclonal serum IgG.

Design and method:
In three adult patients with monoclonal gammopathy (age at diagnosis: pt. 1, IgG-kappa MGUS, male, 51 years; pt. 2, IgG-kappa MGUS, female, 53 years; pt. 3, IgG-kappa SMM, male, 50 years) a pronounced susceptibility to bacterial infections led to the diagnosis of IgA-IgM-IgG2 deficiency (serum immunoglobulins, mg/dl, mean ± SD in the three patients [normal range]: IgG 2274 ± 294 [700-1600], IgG2 24 ± 5 [115-570]) associated with low serum levels of T-independent IgG antibodies (pneumococcal IgG-antibodies, mg/L, 14 ± 3 [> 22.9], Hib-IgG, mg/L, 0.12 ± 0.12 [> 1]).

Results and conclusions:
Following initiation of IGRT (20% SCIG in pt. 1, 5% IVIG in pts. 2 and 3) no more infectious episodes requiring antibiotic therapy occurred in 87 patient months. Adequate dosing of IGRT was ascertained by normalization of serum IgG2 (149 ± 89.6 mg/dl) as well as pneumococcal IgG (54.11 ± 18.9 mg/L) and Hib IgG (1.24 ± 0.35 mg/L), while total serum IgG remained unchanged (2436 ± 451 mg/dl; Hevylite IgG-kappa 2300.25 ± 274 mg/dl [403-978], IgG-lambda 113 ± 31 [197-571]). These findings underline the importance of IgG antibody measurements in the diagnosis of antibody deficiency and in the monitoring of IGRT dosing in patients with monoclonal gammopathy.

POSTER 209 - IMMUNE DYSREGULATION IN ELF4 DEFICIENCY: CLINICAL, CELLULAR AND MOLECULAR CHARACTERIZATION OF A PEDIATRIC PATIENT

AUTHORS

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Background:
Deficiency in ELF4, X-linked (DEX) is a recently described inborn error of immunity (IEI) characterized by mucocutaneous and gastrointestinal inflammation. ELF4 is involved in type I interferon responses, T and NK cell development, and inflammatory regulation, but the pathophysiology of DEX remains poorly defined.

Objective:
To characterize immune dysregulation in a pediatric patient with ELF4 deficiency by integrating innate and adaptive immune phenotyping, cytokine profiling, IFN signature analysis and assessment of JAK-STAT pathway activation.

Methods:
Peripheral blood and intestinal biopsy samples from an ELF4-deficient patient were studied using multiparameter flow cytometry, immunohistochemistry, cytokine quantification (Luminex), pDC stimulation assays, NanoString-based interferon signature, RT-qPCR of JAK-STAT-related genes, and ex vivo JAK inhibition. Results were compared with samples from patients with Aicardi-Goutières syndrome (AGS), STAT1 gain-of-function (GOF) mutations, and healthy controls.

Results:
Th ELF4-deficient patient under Infliximab treatment (Figure 1A) showed broad immune dysregulation, including skewed CD8+ T cell differentiation with expansion of IL-17-producing effector subsets (Figure 1B), increased gut-homing and checkpoint molecule expression in dendritic cells (Figure 1C). Monocytes showed enhanced activation and migration marker expression (Figure 1D). pDCs had impaired IFNα production, while serum cytokine analysis revealed elevated levels of IFNγ, IL-10, IL-18, and IP-10 (Figure 1E). A strong type I IFN signature was detected, similar to that seen in STAT1 GOF patients. Following IFN stimulation, increased STAT1 and phospho-STAT1 levels were observed, which were reduced by JAK inhibition with Ruxolitinib, both in PBMCs and EBV-immortalized B cells (Figure 1F).

Conclusion:
ELF4 deficiency is associated with combined innate and adaptive immune dysregulation, a pathological type I IFN response, and JAK-STAT pathway hyperactivation. These findings support the potential role of JAK inhibitors as a targeted treatment strategy in DEX and highlight the importance of deep immune profiling for precision therapy in rare IEIs.

POSTER 210 - BRIDGING THE GAP: EFFECTIVE PRIMARY IMMUNODEFICIENCY MANAGEMENT, FREE OF COST IN LOW-RESOURCE SETTINGS

AUTHORS

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Background and objectives:
Primary immunodeficiency disorders (PIDs) pose diagnostic and management challenges globally, particularly in regions of the world where healthcare facility resources are limited. These include delayed diagnosis due to a lack of awareness of the disease's existence at all healthcare levels, lack of a complete testing repertoire, and scarcity and high cost involved in treating these patients.

We have analyzed our data of patients presented in our Immunology clinic consistent with the suspicion of immunodeficiency disorders from January 2019 to May 2025. A total of 145 patients were referred to us, of which we were able to rule out PID in 34 patients, while in 111 patients, we were able to classify PID in 29 patients, and 82 patients remained unclassified.

The objectives of our analysis were
1. To determine the number and factors influencing the inability to classify PID
2. To analyze the data of patients who received IVIG.

Patients and methods:
The baseline immunological workup in these patients included serum immunoglobulins (IgG, IgM, IgA, and IgE), C3, C4, and response to test vaccination (anti-diphtheria-IgG, anti-tetanus-IgG, and anti-Pneumococcal polysaccharide-IgG). Lymphocyte subsets and the ALPS (autoimmune lymphoproliferative syndrome) panel were done whenever indicated. In a few of our patients, we were able to get genetic testing done to make a confirmed diagnosis.

Results:
There were 80 children (range: 1 month to 55 years), including 66 (59.5%) males. Genetic studies were available for 11 patients, and in eight of these, genetic mutation(s) were identified to confirm the diagnosis (BTK=2, RELB & PIK3AP1=1, SDBS and STAT1=1, XIAP=1, UNC13D=1, IL2RG=2). Consanguinity was present in around 59% of patients. overall, a family history was positive in 59.5% patients. The differentials of PID are shown in Figure 1. Clinical presentations and the type of organisms isolated are shown in Figures 2 & 3, respectively. IVIG was administered to 24 of our patients during this period. Of these, 11 were adults (mean age: 30 ± 9.4 years) and 13 were children (mean age: 6.6 ± 5.5 years). Around 50% of patients' infection episodes decreased after IVIG, with improvement in quality of life.

Conclusions:
In a free-of-cost health care system with limited resources, with a good number of patients are being managed effectively highlights the importance of strategizing management according to the resources available. Nevertheless, there is a dire need for national and international collaboration and for maintaining a local registry for better patient outcomes

POSTER 211 - A CASE OF IMMUNE DYSREGULATION WITH HETEROZYGOUS VARIANTS DETECTED IN SLC37A4 AND SEC23B GENES

AUTHORS

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Background:
Pathogenic variants in SLC37A4 cause glycogen storage disorder 1B. Pathogenic variants detected in SEC23B are known to cause Congenital Dyserythropoietic Anemia Type2. To date, no primary immunodeficiency associated with mutations in these genes has been identified.

Case report:
A 26-year-old female patient who applied to our clinic in April 2024 had a history of hemophagocytosis at the age of 16. Subsequently, 2 years later, mediastinal non-caseating granulomatous LAP was detected, sarcoidosis was diagnosed and systemic steroids were administered for 6 months. 7 years later, bilateral panuveitis was diagnosed with vision loss and redness in the eyes. She received pulse steroids, followed by maintenance systemic steroids and azathioprine. The patient developed dizziness while under immunosuppressive treatment, and atypical demyelinating disease was detected in cranial MRI, and infection, multiple sclerosis and neurosarcoidosis were excluded in the etiology. Upon the detection of hypogammaglobulinemia in her tests, she was referred from neurology to immunology in May 2024. There was no consanguineous marriage in her family history. She was using azathioprine and deltacortil at her first application. Upon detection of clinical history and laboratory (panhypogammaglobulinemia) findings consistent with primary immunodeficiency, IVIG treatment was initiated at a dose of 800 mg/kg and continued every 21 days. Phytohemagglutinin; PHA and T cell proliferation responses and phago-burst test were normal (neutrophil burst test 97%). Azathioprine was discontinued and prednisolone was continued in consultation with neurology. Hepatosplenomegaly was also present. Fibroscan evaluation revealed grade 3 fibrosis and liver biopsy revealed nodular regenerative hyperplasia and granulomatous hepatitis findings. HRCT revealed intrathoracic, mediastinal, cervical, infra and supraclavicular pathological LAPs. WES analysis revealed a heterozygous mutation in the SLC37A4 gene, and Congenital Disorder of Glycosylation (CDD) Type1 was reported as pathogenic. In pediatric metabolism consultations, WGS was performed since the WES analysis report was incompatible with the clinic. As a result of WGS, heterozygous p. The L348Vfs*53 (c.1042_1043del) variant and the heterozygous c.784+96G>A variant were previously identified in the database (CD982664) and associated with Glycogen Storage Disease Ib. At the same time, the heterozygous p.R14W (c.40C>T) variant was detected in the SEC23B (NM_006363.6) gene and was also previously identified in the database and associated with Congenital Dyserythropoietic Anemia Type 2. Segregation screening was also performed and no mutation was detected.

Conclusion:
Our case is a childhood-onset complicated immune dysregulation caused by multigene defects and epigenetic abnormalities that cannot be explained by the existing mutations in terms of clinical and laboratory parameters.

POSTER 213 - NURSING PROCEDURE FOR HEALTH EDUCATION IN THE SELF-ADMINISTRATION OF SUBCUTANEOUS IMMUNOGLOBULINS

AUTHORS

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NURSING PROCEDURE FOR HEALTH EDUCATION IN THE SELF-ADMINISTRATION OF SUBCUTANEOUS IMMUNOGLOBULINS

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Objective:
To review and propose a standardized nursing procedure for patient education in the self-administration of subcutaneous immunoglobulin (SCIg) therapy, based on literature and expert consensus.

Design and method:
A literature review was conducted using MEDLINE/PubMed with terms such as "health education," "immunoglobulins," and "subcutaneous infusions." From 25 articles, 11 were selected for relevance. Additionally, expert discussions were held with the Spanish Nursing Group on Immunodeficiencies (GEIE). The analysis focused on educational strategies, patient outcomes, and professional perspectives.

Results:
Consensus was reached on the need for 2–3 training sessions, the importance of patient support programs (PAP), and the use of in-person sessions supported by online resources. Discrepancies were noted in administration methods, educational materials, and product availability. SCIg therapy was associated with improved quality of life and autonomy, though challenges included frequent administration, adherence issues, and rare adverse reactions.

Conclusions:
A national nursing protocol is needed to guide non-specialized professionals in SCIg therapy. Educational strategies should be adaptable, patient-centered, and include practical guides, audiovisual tools, and simulation materials to ensure effective self-administration training.

POSTER 215 - RARE NOD2 VARIANTS CARRIAGE IN A COHORT OF PEDIATRIE PATIENTS WITH IEI FROM ROMANIA

AUTHORS

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Objective:
Upregulation or downregulation of the NF-kB signaling due to nucleotide-binding and oligomerization domain-containing 2 (NOD2) gene heterozygous germline defects can cause a monogenic autoinflammatory disease called Blau syndrome (early-onset uveitis, granulomatous synovitis, skin rash) or increase susceptibility to Crohn's disease, respectively. Milder, non-specific episodes of recurrent spontaneous inflammation have also been associated with alterations in the NOD2 gene. We investigated the presence of low-frequency and rare NOD2 variants in our cohort of inborn errors of immunity (IEI) patients and searched for phenotypic correlations.

Design and method:
One hundred and fifty-four consecutive pediatric patients underwent NGS-based molecular testing for IEI gene panels between 2020 and 2025 based on clinical suspicion (immune deficiency, immune dysregulation, or autoinflammation). Only variants with a minor allele frequency (MAF) <1% were analyzed. We also reported coinheritance of other rare possibly damaging variants in autoinflammatory genes.

Results:
Twelve patients (7.7%) carried at least one out of five identified NOD variants (two frameshift, three missense, classified as increased risk alleles). Clinical features in all patients with NOD2 variants (12/12) included at least one hyperinflammation trait (recurrent fever, recurrent serositis, secondary HLH, or recurrent MAS). None of the target cases had an alternative genetic diagnosis. A genetic variant combination was present in one case NOD2/RIPK1 with recurrent fever episodes.

Conclusions:
The carriage rate of a rare NOD2 variant in a cohort of patients with IEI suspicion is high. Moreover, carriers had a uniform phenotype dominated by autoinflammation. The role of the NOD2 variants may reshape the clinical interpretation of monogenic and polygenic systemic autoinflammatory syndromes.

POSTER 216 - RESULTS OF A SINGLE-ARM, OPEN-LABEL EXTENSION STUDY OF LENIOLISIB IN ACTIVATED PHOSPHOINOSITIDE 3-KINASE DELTA SYNDROME: LONG-TERM EFFICACY AND SAFETY THROUGH TO END-OF-STUDY

AUTHORS

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Objective:
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) is an ultra-rare inborn error of immunity, characterised by immune deficiency and dysregulation. Leniolisib is a PI3Kδ inhibitor approved to treat APDS in patients ≥12 years old in the United States (US), United Kingdom, Israel and Australia, based on the results of a 12-week, placebo-controlled clinical trial (NCT02435173). A single-arm, open-label extension (OLE) study (NCT02859727) evaluated the long-term safety and efficacy of leniolisib. Results of interim analyses (2.0 and 3.0 years median leniolisib exposure) have previously been published; here, final study results are reported.

Design and method:
From Sep 2016–Aug 2021, patients with APDS aged ≥12 years, who had completed NCT02435173 or other PI3Kδ inhibitor studies were enrolled in the OLE. Participants received 70 mg leniolisib twice daily and remained in the OLE until transition to either commercial leniolisib (US participants) or investigational leniolisib through an early access programme (European participants). Primary endpoint: long-term safety, reported as adverse events (AEs); secondary efficacy endpoints: infection frequency (reported as AEs), and anti-infective comedications use (immunoglobulin replacement therapy [IRT] and antibiotics).

Results:
In total, 37 participants enrolled in the OLE (26 previously treated with leniolisib, Table 1). By study closure (Jan 2025), median leniolisib exposure was 4.3 years (range: 1.2–7.0 years) with 23 participants (62%) followed up for ≥4 years.

AEs were reported in 34 (92%) participants (Figure 1); the most common were SARS-CoV-2 infection (n=12; 32%), upper respiratory tract infection (n=10; 27%), pyrexia (n=9; 24%) and headache (n=8; 22%). Serious AEs were experienced by 10 (27%) participants, including one grade 3 transitional cell carcinoma; those leading to death or treatment discontinuation included a cardiac arrest and a grade 3 Hodgkin's lymphoma, respectively (both previously reported). In total, 181 infections were reported, 120 being respiratory, in 31 (84%) and 28 (76%) respective participants. Per additional year of leniolisib therapy there were nominally significant 25% reductions in both infection rates (1-sided p=0.0005 and 0.0017, respectively). Of the 27 (73%) participants receiving IRT at the start of the OLE, 10 (37%) discontinued IRT. For participants completing at least one full year of follow-up (Figure 2), IRT consumption (in grams) decreased by 11% with each year of treatment (n=27, one-sided p=0.0095) and days of antibiotic therapy were stable with a 2% decline each year (n=33, one-sided p=0.1934).

Conclusions:
The long-term use of leniolisib was well-tolerated and infectious complications of APDS and IRT requirements were reduced over time.

POSTER 217 - RESULTS OF A PHASE 3 OPEN-LABEL, SINGLE-ARM, 12-WEEK STUDY EVALUATING LENIOLISIB IN PAEDIATRIC PATIENTS AGED 4–11 YEARS WITH ACTIVATED PHOSPHOINOSITIDE 3-KINASE DELTA SYNDROME

AUTHORS

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Objective:
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) is an ultra-rare inborn error of immunity characterised by immune deficiency and dysregulation. Leniolisib is a PI3Kδ inhibitor approved to treat APDS in patients aged ≥12 years and ≥45 kg in the United States, United Kingdom, Israel and Australia. Data on the safety and efficacy of leniolisib in paediatric patients (<12 years) with APDS are limited; here, interim data from an ongoing paediatric clinical trial are reported.

Design and methods:
Paediatric patients aged 4–11 years with APDS, weighing ≥13–<45 kg, were enrolled in a two-part, international, prospective, open-label, single-arm study evaluating the safety and efficacy of bodyweight-adjusted doses of leniolisib (NCT05438407). In Part 1, leniolisib was administered orally twice daily (BID) for 12 weeks; BID doses ranged from 20 to 50 mg based on body weight at baseline. Part 1 co-primary endpoints were change from baseline (CFB) in log10-transformed sum of product of diameters (SPD) of index lymph nodes and % of naïve B cells (CD19+CD20+IgD+CD27-) out of total B cells. Safety was assessed through investigator-reported adverse events (AEs).

Results:
Of the 26 patients screened, 21 were enrolled (Table 1); all patients completed Part 1 of the study. After 12-weeks leniolisib exposure, both co-primary endpoints were met (Figure 1): mean CFB in log10-transformed index lymph node SPD was –0.1956 (n=19) and mean CFB in % of naïve B cells was 8.6% (n=11); the corresponding CFB in % of CD19+CD27-CD10- naïve B cells was 33.3%. Additional outcomes also showed improvement: mean CFB in log10-transformed spleen volume was –0.1222 (n=21) and mean CFB in the sum of log10-transformed volumes of non-index lymph nodes was –3.1000 (n=9). Mean immunoglobulin (Ig) levels at baseline (n=14) and week 12 (n=15) were: IgM, 2.7 and 1.6 g/L; IgG, 10.1 and 11.1 g/L; and IgA, 0.88 and 0.83 g/L. Leniolisib was generally well-tolerated (Figure 2): 20 patients had treatment-emergent AEs, which were either Grade 1 (n=20, 95.2%) or Grade 2 (n=8, 38.1%); none were serious. Five patients had treatment-related AEs, including headache, palpitations, abdominal pain, diarrhoea, nausea, pruritus, fatigue, decreased neutrophil count and increased aspartate aminotransferase. No AEs led to discontinuation of study treatment.

Conclusion:
Overall, leniolisib was generally well-tolerated and met the co-primary endpoints, reducing lymphoproliferation and increasing % of naïve B cells in paediatric APDS patients aged 4–11 years; data are consistent with those in patients ≥12 years old.

POSTER 218 - A SEMI-QUANTITATIVE EVALUATION OF LENIOLISIB TREATMENT RESPONSE THROUGH A PHYSICIAN SURVEY OF PATIENTS WITH ACTIVATED PHOSPHOINOSITIDE 3-KINASE DELTA SYNDROME UNDER AN EARLY ACCESS PROGRAMME

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Objective:
Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) is an ultra-rare inborn error of immunity characterised by both immune deficiency and dysregulation. Leniolisib is an oral, selective PI3Kδ inhibitor approved to treat APDS in patients aged ≥12 years and ≥45 kg in the United States, United Kingdom, Israel and Australia. In clinical trials in patients ≥12 years with APDS (NCT02435173 and NCT02859727), leniolisib was well-tolerated and efficacious, reducing lymphadenopathy and increasing the proportion of naïve B cells vs placebo over 12 weeks, and reducing infection rates over time with longer-term treatment. Real-world data can provide further evidence of the clinical benefits of leniolisib. Here, the findings from a global physician survey evaluating treatment response to leniolisib across clinically relevant domains in patients with APDS receiving leniolisib through an early access programme (EAP) are reported.

Design and methods:
From Sep–Oct 2023, 30 physicians treating 40 patients with APDS (children, adolescents and adults) with leniolisib in a global EAP were surveyed by an anonymised questionnaire. Infections and hospitalisations were reported as annual rates prior to and during leniolisib; treatment responses in non-infectious APDS complications were categorical (remission, meaningful improvement, no change, worsening, or new manifestation).

Results:
A total of 21 physicians treating 30 EAP patients responded; 16, 4 and 10 patients had received leniolisib for <1, 1–2 and >2 years, respectively. Treatments pre-leniolisib included steroids (40% of patients), rituximab (30%) and sirolimus/rapamycin (57%).

Reported mean annual infection and hospitalisation rates were lower during leniolisib treatment than pre-treatment (Figure 1).

For non-infectious complications, leniolisib was associated with at least clinically meaningful improvements in 53% (pulmonary) to 87% (organomegaly) of affected domains (Table 1). Additionally, 80% and 92% of affected patients had at least clinically meaningful improvements in chronic fatigue and lymphoproliferation, respectively. Despite the progressive nature of APDS, no worsening of complications and few new complications were recorded. One patient developed lymphoma (assessed as unrelated to leniolisib); among three patients who had a history of lymphoma, none recurred.

Physicians reported that 29/30 patients (1/30 left blank) tolerated leniolisib treatment well and had derived clinical benefits, supporting continued treatment.

Conclusion:
These contemporary, real-world survey data from physicians using leniolisib to treat patients with APDS in an EAP suggest that leniolisib has benefits across the spectrum of APDS manifestations, supporting and expanding on clinical trial data.

POSTER 219 - TREC-BASED NEWBORN SCREENING FOR SEVERE COMBINED IMMUNODEFICIENCY (SCID): 20-MONTH EXPERIENCE IN THE COMMUNITY OF MADRID

AUTHORS

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Objective:
T-cell receptor excision circles (TRECs) are small circular DNA fragments produced during T-cell receptor rearrangement, correlating with thymic output and T-cell maturation in newborns. The implementation of TREC-based newborn screening (NBS) for severe combined immunodeficiency (SCID) has been heterogeneous across regions in Spain, largely due to differences in healthcare policies and available resources.

This study aims to evaluate the outcomes of a TREC-based SCID screening program in the Community of Madrid, focusing on its effectiveness for early diagnosis and treatment after 20 months of its implementation.

Design & methods:
Screen-positive infants born between September 2023 and May 2025 in Madrid underwent confirmatory laboratory testing coordinated by the Immunology Division and clinical follow-up by pediatric immunologists at Hospital General Universitario Gregorio Marañón.

Immunology confirmatory laboratory tests included:

- T, B and NK lymphocyte counting, and T-cell subsets (CD3+CD45RA+/CD4+CD45RA+CD31^{+}/CD4+ and CD8+ HLA-DR+ /CD3+TCRγδ+) analysis in peripheral blood by flow cytometry.

-Serum IgG, IgM, IgA and IgE levels

-In vitro mitogen-based lymphoproliferation assay.

-Clinical exome (targeted to genes associated with primary immunodeficiencies) by NGS or CGH array, as appropriate, in patients meeting SCID criteria or with other suspected inborn errors of immunity (IEIs).

Results:
During the 20 months period of study, 83,543 newborns were screened in the Community of Madrid and 49 positive cases were identified. Among them, one case of typical SCID was confirmed (autosomal recessive ARTEMIS deficiency) and one Di George syndrome was diagnosed. Furthermore, 12 infants were classified as non-SCID T-cell lymphopenia, two of whom also showed an abnormal PHA response in the CD4^{+} compartment.

Conclusion:
We have identified one typical SCID case during the neonatal period, enabling early diagnostic confirmation within the first month of life and referral for urgent and specialized management. Additionally, several cases of T-cell lymphopenia and one DiGeorge syndrome were detected, with all patients continuing pediatric immunology follow-up that may provide significant clinical benefits through ongoing monitoring and timely interventions.

Our results demonstrate the feasibility and effectiveness of population-based TREC screening in a European public health system, with performance metrics comparable to well-established programs and supporting the recent expansion of SCID newborn screening across Spain.

POSTER 220 - CASE REPORT: INTRAVENOUS IMMUNOGLOBULIN ADVERSE REACTION WITH INTERLEUKIN-6 ELEVATION IN A PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY AND ITS CLINICAL MANAGEMENT

AUTHORS

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Introduction:
Intravenous immunoglobulin (IVIG) administration is a well-established treatment for patients with common variable immunodeficiency (CVID). While flu-like symptoms are commonly reported with IVIG, the association with significant IL-6 release and muscle spasms is poorly documented. IL-6 elevation has been described after the first infusion, suggesting an inflammatory response. We describe a case of a rarely reported reaction with elevated IL-6 levels and muscle spasms following IVIG infusion.

Case description:
We describe the case of a 55-year-old woman diagnosed with CVID at age 50. She had experienced recurrent respiratory infections and tonsillitis since childhood. IVIG therapy was initiated at another hospital in 2019 (400 mg/kg every 21 days) with clinical improvement. She experienced infusion-related reactions, including painful muscle spasms and neck stiffness, leading to inconsistent treatment adherence. The symptoms typically began within 30 minutes of infusion, persisted despite premedication and remained after treatment, with muscle pain and a major impact on her quality of life.

At our hospital, IVIG was reinitiated under monitoring along with the Department of Allergology: Flebogamma® at 500 mg/kg with paracetamol and cetirizine as premedication. The patient experienced similar symptoms, which partially improved with benzodiazepines. Blood tests during the episode revealed elevated IL-6 (86.7 pg/mL, ref. <7pg/mL) as the only abnormal finding. Baseline IL-6 was normal.

Given the suspicion of an infusion reaction with cytokine release, a desensitization protocol was established with premedication: paracetamol 1g/8h and alprazolam 0.25 mg/day from the day before, dexchlorpheniramine 5mg, methylprednisolone 40mg, and famotidine 40mg IV prior to infusion. Adherence to Singulair® was improved, and hydration was ensured during infusion (100 mL/h of NS simultaneously).

Despite improved tolerance with premedication, a decision was made to switch to subcutaneous therapy (Hizentra® 16g/2 weeks). This has allowed for withdrawal of premedication, with no recurrence of symptoms or laboratory abnormalities.

Conclusions:
Infusion-related reactions were reproducible, with muscle rigidity and spasms, partially relieved with benzodiazepines. IL-6 levels increased only during the reaction, supporting a cytokine-mediated mechanism.

The implementation of a desensitisation protocol together with the Department of Allergology was crucial for clinical management. Transitioning to subcutaneous immunoglobulin therapy has enhanced the patient's adherence and quality of life.

This case illustrates that cytokine profiling, including IL-6, may be useful in the evaluation of atypical infusion reactions. Further research is needed to better characterise these responses and guide treatment.

POSTER 221 - EVALUATION OF ALLERGIC AND IMMUNOLOGIC DISORDERS IN PATIENTS WITH MULTIPLE ENDOCRINOPATHIES

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Aim:
The endocrine system orchestrates numerous metabolic and homeostatic functions, operates in close interplay with the immune and nervous systems: neural and hormonal signals influence immune responses, while immune mediators modulate endocrine and neural activity.

Immune dysregulation is a hallmark of Inborn Errors of Immunity. It is associated not only with recurrent infections but also with a heightened risk of allergic conditions, autoimmunity, autoinflammation, and malignancies.

This study aimed to investigate the relationship between multiple endocrinopathies and immune dysregulation. We evaluated the presence and frequency of allergic and immunological conditions across three patient groups:

Patients with autoimmune thyroid disease (Hashimoto's thyroiditis or Graves' disease),
Patients with autoimmune thyroid disease plus additional endocrine disorders,
A control group.

Method:
This prospective cross-sectional study was conducted at the Internal Medicine and Endocrinology outpatient clinics of Ankara University.

A total of 420 adult participants were enrolled and evenly distributed into three age- and gender-matched groups:

Group 1: Healthy controls without endocrine disease (n = 140)

Group 2: Patients with only autoimmune thyroid disease (n = 140)

Group 3: Patients with autoimmune thyroid disease and at least one additional endocrinopathy (n = 140)

Each participant completed a 24-item data collection form, including demographic characteristics, clinical features, history of allergic, autoimmune, and autoinflammatory diseases, malignancy, known primary immunodeficiency (PID), and responses to the "10 warning signs of PID." Data were analyzed using SPSS version 27.0.

Results:
A higher burden of endocrine disease was significantly associated with an increased prevalence of autoimmune diseases ($p < 0.001$). Among patients with three or more endocrinopathies, the autoimmune disease prevalence reached 33.3% (Autoimmune endocrinopathies were NOT included in autoimmunity evaluation). Likewise, allergic diseases—particularly asthma—were significantly more common in patients with multiple endocrinopathies ($p < 0.001$).

Additionally, rate of positive responses to "10 warning signs of PID" was significantly higher in this group ($p = 0.038$), indicating a greater likelihood of underlying immune dysregulation in patients with a higher endocrine disease load.

One patient in the multiple endocrinopathies group had warning signs and she underwent immune work-up, which resulted in the diagnosis of CVID.

Conclusion:
This study reveals that immune dysregulation—including autoimmunity, allergic disease, and features suggestive of immunodeficiency—is significantly more prevalent in individuals with multiple endocrinopathies. Our findings underscore the importance of integrating immunological screening into the routine clinical assessment of patients with multiple endocrine disorders. These results may serve as a foundation for future research into the immunoendocrine interface.

POSTER 223 - İNBORN ERORS OF IMMUNITY IN AZERBAIJAN: FIRST NATIONAL EXPERIENCE

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Purpose:
Inborn errors of immunity (IEI) are a heterogeneous group of diseases with variable clinical phenotypes. This study was conducted to describe the epidemiology, clinical presentations, treatment, and outcome of IEI in Azerbaijan children.

Methods:
A retrospective data analysis was conducted for patients all age diagnosed with IEI from the pediatric Allergy, Immunology Division-based registry at Republican Pediatric Center - A.Garayev Children's Clinical Hospital, Baku, Azerbaijan, between 2023 and 2025.

Results:
A total of 90 patients, 62 (70 %) males and 28 (31%) females, were diagnosed with IEI. The mean age at symptom onset was 120 months , a positive family history of IEI was reported in 22%, and the consanguinity rate was 82.2 %. The most common IEI category was immunodeficiencies affecting cellular and humoral immunity at 41.1 %, followed by predominantly antibody deficiencies at 13.3%. The overall median diagnostic delay (range) was 72 months; patients with a positive family history of IEI had a statistically significant shorter diagnostic delay. Pulmonary and gastrointestinal clinical features were the most common at 82.2 % and 30 %, respectively. Of the patients, 90 had symptomatic treatment information: 63 (70%) received IG treatment, only IVIG (100%), and 4 (4.4%) patients were treated with biological drugs. HSCT has been performed in 5 (5.5%) patients, of whom 100% are currently alive. The overall mortality was 10 %; the highest rate was reported in combined immunodeficiency at 67 %.

Conclusions:
Here, we describe our first analysis of the epidemiological features of PID in Azerbaijan, allowing us to highlight the main challenges around PID diagnosis and treatment.

POSTER 225 - ANTIBODY RESPONSES AND IMMUNE MEMORY FORMATION AFTER COVID-19 VACCINATION IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY

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Objective:
Primary immunodeficient (PID) patients may have poor vaccination responses and high susceptibility to severe infections, including COVID-19. Our objective was to evaluate the SARS-COV-2-specific IgG, memory B cells (Bmem) and memory T cells (Tmem) following COVID-19 vaccination to ascertain whether third dose COVID-19 vaccination is effective in generating immune memory in PID patients.

Design and methods:
25 PID patients and 29 healthy controls were sampled one-month after doses two and three of the COVID-19 vaccination. Serum neutralizing antibody (NAb) titers were determined in live virus assays. Using recombinant spike receptor-binding domains (RBD), we analyzed plasma IgG by ELISA and Bmem by flowcytometry directed against ancestral and Omicron variants. Using overlapping peptide pools for the ancestral spike protein, we analyzed activation induced marker expression on the surface of CD4+ and CD8+ T cells.

Results:
Regardless of mRNA or adenoviral vector vaccine priming, ancestral RBD-specific IgG levels and Nab titers were significantly lower in PID patients than controls after both doses, with minimal boosting at dose 3. Ancestral RBD-specific IgG and Nab cross-recognition of Omicron BA.5 were lower in patients than controls after both doses, with boosting evident at dose 3 in both cohorts.

Despite normal total Bmem numbers, patients had fewer ancestral RBD-specific Bmem and reduced cross-recognition of both Omicron BA.2 and BA.5. Patients had increased frequencies of RBD-specific Bmem expressing CD71, and lower frequencies of IgG- and IgA-expressing RBD-specific Bmem.

Total and spike-specific CD8+ Tmem were lower in patients than controls after both doses, with significant boosting upon dose 3. Spike-specific CD4+ Tmem of patients expressed lower CD69 expression and contained lower frequencies of IFNγ+TNFα+ cells than controls.

Compared to patients who had seroconverted at dose 3, those patients lacking an NAb response exhibited a lower number of spike-specific CD4+ Tmem and RBD-specific Bmem. Whilst numbers spike-specific CD8+ T mem numbers were similar between both groups.

Conclusions:
Together, a large fraction of adult PID patients have an impaired vaccine responses to COVID-19. Most patients demonstrate an intact spike-specific CD4+ and/or CD8+ Tmem response, whereas antibody, NAb and Bmem responses are frequently reduced.

Therefore, measurement of cellular responses may better reflect immune competence, and are likely scalable for routine evaluation of responses to vaccination and infection. Furthermore, unlike antibody and NAb measurement, quantification of Tmem and Bmem responses are unaffected by receipt of immunoglobulin replacement therapy.

POSTER 226 - OPTIMIZING PATIENT CARE AFTER B-CELL-TARGETED THERAPIES: UPDATED DELPHI CONSENSUS RECOMMENDATIONS FOR THE MANAGEMENT OF SECONDARY HYPOGAMMAGLOBULINAEMIA IN PATIENTS WITH AUTOIMMUNE DISEASES

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Objective:
To revise and expand the 2019 consensus recommendations for the management of B-cell-targeted therapy (BCTT)-related secondary hypogammaglobulinaemia (SHG) in patients with autoimmune rheumatic disease (Wijetilleka et al. 2019, Rheumatology) through a Delphi consensus process.

Design and method:
A steering committee (N = 17, including patient advocates, immunologists, rheumatologists, other experts in relevant specialties and a voting Chair) was formed to design the B-cell therapies in Autoimmunity Secondary Immunodeficiency Consensus Study (BASICS). Following selection and recruitment of the wider Delphi panel (N = 69, international experts with experience in using BCTT for autoimmune diseases and/or immunoglobulin replacement therapy [IgRT]), the steering committee drafted statements informed by published evidence (clinical/real-world studies identified via systematic literature review; guidelines identified via supplementary search) and expert insight. Panel respondents provided their level of agreement on each statement anonymously via a 5-point Likert scale and free-text feedback for a maximum of two voting rounds. Consensus was accepted when a statement achieved a predefined census threshold of ≥ 75% agreement. Statements that did not reach consensus were refined by the steering committee considering feedback and submitted back to the panel for another review round.

Results:
The literature search outputs (186 publications and 154 guidelines) provided robust evidence which the steering committee discussed in the context of their expertise. These discussions informed the generation of 24 draft statements, which explored themes including: risk factors for/susceptibility of developing SHG; risk of SHG with newer BCTT drugs/biosimilars; monitoring SHG and other immunological assessments; role of antimicrobial prophylaxis/vaccination; role of clinical immunologists/multidisciplinary teams; IgRT utilization; and management of neonates/pregnant patients (Table 1). Statements were circulated to the full Delphi panel, for a total of two voting rounds (Figure 1). In round 1, 23/24 statements reached ≥ 75% consensus;12/24 reached ≥ 95% consensus (Table 2). Consensus was reached for all 24 statements in round 2.

Conclusions:
The expanded and revised consensus statements and recommendations derived from the BASICS Delphi initiative reflect recent evidence and are intended to improve clinical decision-making, harmonize care pathways and ultimately enhance outcomes for adult and paediatric patients at risk of SHG-related complications after treatment with BCTT for their autoimmune condition.

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POSTER 227 - GENETIC AND PHENOTYPIC CHARACTERIZATION OF A MONOCENTRIC COHORT OF ADULTS WITH CVID AND XLA

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Background:
Common variable immunodeficiency (CVID) is conceived as an umbrella diagnosis reflecting the diversity of the immunogenetic underpinnings. Genetic testing on CVID patients identified many genes associated with B-cells activation, signaling and immune-dysregulation. In these studies, a probable disease-causing variant has been identified in 20-50% of CVID individuals. Defects in numerous genes of many different cellular pathways can result in a similar CVID-phenotype. This heterogeneous genetic background may imply the broad immunological phenotypes, immune dysregulation, autoimmunity and lymphoproliferation.

Aim:
This study aims to characterize the genotype-phenotype relations of a monocentric CVID cohort of adults with CVID and XLA.

Patients & methods:
We enrolled 62 CVID and 5 XLA adults consecutively diagnosed at our ERN-RITA Centre for Inborn Errors of Immunity (IEI) in Milan, Italy. All the patients met the ESID criteria for CVID or XLA diagnosis and started with immunoglobulins replacement therapy. They underwent genetic analysis by whole exome sequencies (WES) through Illumina platform. The IUIS 2022 genes list for IEI was applied. Filtering, prioritization and analysis were performed by eVAI software (enGenome). Variants were classified in accordance with the American College of Medical Genetics and Genomics (ACMG) guidelines criteria. Variants of class 3 (variants-of-uncertain-significant:VUS), class 4 (likely-pathogenic:LP), and class 5 (pathogenic:P) were reported. Detailed clinical phenotypes have been recorded for genotype-phenotype assessment analysis.

Results:
All the patients, but two, are of Caucasians origin. None had parental consanguinity. Among the 67 patients, 47 (70%) were found carriers of a total of 93 variants on at least one of the IUIS genes list. The P/LP variants identified were 34 (36.6%) and 59 were VUS (63.4%).

Figure 1 details gene lists and the P/LP variants number identified.

Of the overall 93 variants, 21(22.3%) were on the TNFRSF13B (TACI)gene: 4P/LP, 2B/LB and 15VUS. Fourteen patients carried these variations. In two "CVID" adults a pathogenic variant on BTK gene was identified, which matched with immunological and clinical phenotype, resulting in XLA diagnosis. Hence, the study cohort consists of 60 CVID and 7 XLA.

The evaluation of genotype-clinical phenotype correlation is ongoing.

Conclusion:
This WES study shows that monogenic cause for CVID is poorly represented. Many VUS on one or more genes have been identified that have a described pathogenic key-role in CVID disorders. WES revealed in XLA patients further pathogenic variations on other genes influencing the phenotype. Further investigations are necessary to validate the VUS and elucidate the hypothesis of oligogenic and polygenic interactions.

POSTER 228 - PROLONGED ROTAVIRUS INFECTION DURING IMMUNE RECONSTITUTION FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN AN INFANT WITH CHEDIAK-HIGASHI SYNDROME

AUTHORS

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Objective:
To present a clinical case that provides insight into the immune mechanisms essential for overcoming rotavirus infections.

Design and method:
Rotavirus infection is one of the most common causes of diarrhoea in children under the age of 5. The global burden of disease remains very high—between 2013 and 2017, an estimated 122,000 to 215,000 children died annually from rotavirus gastroenteritis, with children under the age of 1 being the most at risk. In recent years, developed countries have reported different complications following administration of the live rotavirus vaccine in children with primary immune deficiencies, including prolonged rotaviral infection. We present a case of a newborn with a congenital immunodeficiency undergoing hematopoietic stem cell transplantation (HSCT) that was complicated by a prolonged rotavirus infection.

A three-week-old Roma boy was admitted to the hospital due to poor appetite, insufficient weight gain, and frequent bowel movements. Rotavirus infection was diagnosed. Due to phenotypic features (albinism) and pathognomonic changes in the differential blood count, Chediak-Higashi syndrome was suspected and later confirmed by genetic testing. The gastrointestinal symptoms resolved spontaneously. By the age of three months, rotavirus was no longer detectable in stool samples. At five months, the boy underwent myeloablative allogeneic HSCT. Stem cell source was peripheral blood of an HLA matched related donor. Soon after he began passing increasing volumes of stool, up to 100 ml/kg body weight per day. There were no signs of systemic infection or graft-versus-host disease (GVHD). In stool samples rotavirus was detected, with low cycle threshold values on PCR and viral particles seen on electron microscopy. To reduce viral replication, additional treatment with nitazoxanide was initiated. With the goal of accelerating immune reconstitution, immunosuppressive therapy was rapidly tapered. Three months post-transplant, as T lymphocytes and NK cells showed significant recovery, stool output gradually decreased, and rotavirus infection was cleared. (Figure 1)

Results and conclusion:
We present a case of a child with profuse diarrhoea during the period of immune reconstitution following HSCT. Differentiating between infectious causes and GVHD is crucial for appropriate adjustment of immunosuppressive therapy in patients with severe diarrhoea. Detailed microbiological monitoring allowed for faster reduction of immunosuppression, leading to earlier reconstitution of immunity and clearance of rotavirus infection. Adaptive immunity (T lymphocytes, particularly cytotoxic CD4+ T cells) plays a key role in limiting and eliminating rotavirus infection.

POSTER 229 - FROM PHENOTYPE TO MECHANISM: STRATIFYING COMMON VARIABLE IMMUNODEFICIENCY PATIENTS BASED ON TYPE 1 FOLLICULAR HELPER T CELLS

AUTHORS

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Objective:
Common variable immunodeficiency (CVID) is the most prevalent symptomatic primary immunodeficiency and displays a wide spectrum of clinical manifestations. Up to 60% of patients develop non-infectious complications such as autoimmune cytopenias, lymphoproliferation or malignancies, which are associated with increased morbidity and mortality. Previous studies have characterized these complications by clinically stratifying patients and subsequently analyzing their immunophenotype, identifying an expansion of type 1 follicular helper T cells (Tfh1) in peripheral blood. In this study, we propose a reverse approach: instead of starting from clinical features, we stratify patients based on the proportion of Tfh1 cells and explore whether this immunological parameter can identify a subgroup of patients with increased risk of immune dysregulation. This strategy aims to uncover mechanistic insights into CVID pathogenesis and evaluate the utility of Tfh1 cells as a potential biomarker for disease stratification.

Methods:
Detailed data were collected from the medical records of 41 CVID patients and non-infectious complications were grouped into: lymphoproliferation/granulomas, autoimmune events, gastrointestinal problems and malignancy. Determination of different T and B lymphocyte subpopulations in peripheral blood was performed in 41 patients and 20 healthy controls by flow cytometry. GraphPad Prism 8 software was used for statistical analysis.

Results:
Tfh1 levels were significantly elevated in patients with non-infectious complications, especially autoimmunity and lymphoproliferation, with an AUC of 0.82. Patients were stratified based on the proportion of circulating Tfh1 cells using a ROC-derived cutoff of 36.15%, identifying two groups: Tfh1-high (NIC group) and Tfh1-low (NC group). The NIC group showed reduced counts of major lymphocyte subsets, expanded CD21low B cells ($p < 0.001$), and decreased Treg compared to NC and healthy controls. Serum free kappa chains were also reduced ($p = 0.01$). A two-tier decision tree using Tfh1 (>49.75%) and Treg (<4.785%) achieved 87.5% accuracy (AUC = 0.948) in identifying high-risk patients.

Conclusions:
Tfh1 expansion strongly correlates with immune dysregulation features and, when combined with Treg frequency, provides a simple, high-performance tool for identifying patients at risk of non-infectious complications. Our findings suggest a mechanistic link in CVID between elevated Tfh1, reduced Treg, and expanded CD21low B cells, potentially driving immune dysregulation and non-infectious complications. The associated drop in serum free light chains may reflect impaired B cell maturation. This hypothesis requires validation through functional assays and longitudinal studies to confirm causality and clinical utility.

POSTER 230 - ELEVATED ARGINASE-1 AND IL-6 LEVELS AS BIOMARKERS OF IMMUNE DYSREGULATION IN COMMON VARIABLE IMMUNODEFICIENCY

AUTHORS

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AFFILIATIONS

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Objective:
This study aimed to investigate serum levels of arginase-1 (ARG1) and interleukin-6 (IL-6) in patients with Common Variable Immunodeficiency (CVID), with a specific focus on their association with non-infectious complications (NIC) and systemic inflammatory markers. The goal was to assess whether these molecules reflect underlying immune dysregulation.

Design and method:
A prospective case-control study was conducted at Ankara University Faculty of Medicine between December 2024 and March 2025. Forty-five adult CVID patients and 41 age- and sex-matched healthy controls were enrolled. Serum ARG1 and IL-6 levels were measured by ELISA prior to immunoglobulin replacement therapy in patients. Clinical characteristics, immunologic parameters, and comorbidities were recorded. Statistical analyses were performed to compare biomarker levels between groups and examine their relationships with inflammatory markers and NIC.

Results:
Mean serum ARG1 (21.5 ± 16.2 ng/mL vs. 11.8 ± 7.5 ng/mL, $p < 0.001$) and IL-6 levels (4.4 ± 13.3 pg/mL vs. 1.1 ± 3.3 pg/mL, $p = 0.003$) were significantly higher in CVID patients compared to controls. A positive correlation was observed between IL-6 and ARG1 levels ($\rho = 0.312$, $p = 0.037$). ARG1 concentrations remained elevated even after excluding individuals with high C-reactive protein. Notably, both IL-6 and ARG1 levels were significantly higher in patients with NIC. All individuals with IL-6 ≥ 5 pg/mL belonged to the NIC-positive group ($p = 0.036$), and ARG1 levels were markedly elevated in patients with hepatomegaly or splenomegaly ($p = 0.006$). No significant relationship was found between ARG1 or IL-6 levels and frequency of infections or immunoglobulin levels.

Conclusions:
CVID patients exhibit significantly increased serum ARG1 and IL-6 levels, particularly those with non-infectious complications. These findings support a potential role for ARG1 and IL-6 as biomarkers of immune dysregulation and subclinical inflammation in CVID. Further research is warranted to explore their prognostic value and mechanistic roles in disease pathogenesis.

POSTER 231 - IMMUNE-MEDIATED COLITIS AND CMV SUPERINFECTION IN CTLA-4 HAPLOINSUFFICIENCY: INDIVIDUALIZED IMMUNOMODULATORY MANAGEMENT

AUTHORS

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Objective:
To describe the multidisciplinary therapeutic approach in a patient with CTLA-4 haploinsufficiency and immune-mediated colitis complicated by CMV reactivation, highlighting the clinical challenges of balancing immunosuppression and infection control in the context of a primary immune regulatory disorder.

Design and method:
We report a 32-year-old man from Pakistan, living in Barcelona since age 17, with recurrent otitis media, pyogenic skin infections, and EBV/CMV mononucleosis at 18. Persistent CMV viremias followed, partially controlled with antivirals. Diagnosed with common variable immunodeficiency (CVID) in 2013, he started Immunoglobulin replacement therapy (IGRT) with improvement of infections. In 2019, he was found to be a carrier of vaccine-derived poliovirus, treated with pocapavir. Genetic testing by NGS of a primary immunodeficiency gene panel detected a heterozygous pathogenic variant in the CTLA4 gene (c.473_474del / p.P158RfsX3), confirming immunodeficiency. Abatacept led to clinical benefit but was discontinued due to refractory oral ulcers; sirolimus was started. His course included chronic giardiasis, non-cirrhotic portal hypertension with nodular regenerative hyperplasia, splenomegaly, and cryptogenic pneumonia.

Results:
He presented with diarrhea, abdominal pain, and fever. Hospitalized, he was initially treated for parasitosis without improvement. Histopathology revealed lymphoplasmacytic colitis with CMV inclusions. Ganciclovir 5 mg/kg every 12 hours was initiated. After five days without response, abatacept 10 mg/kg was added with corticosteroids and aminosalicylates, achieving normalization of stool frequency within 48 hours and fever resolution by day three.

Conclusions:
Autoimmune enteropathy in CTLA-4 haploinsufficiency poses major management challenges, requiring a coordinated multidisciplinary approach. Evidence supports abatacept as first-line immunomodulator. When CMV colitis coexists, collaboration between immunology, gastroenterology, and infectious diseases is critical to optimize therapy and prevent complications. In this case, weekly abatacept and valganciclovir prophylaxis were maintained to control immune-mediated complications and minimize viral reactivation risk. Therapy will be reassessed based on clinical evolution and follow-up endoscopy, considering its use as a bridge to hematopoietic stem cell transplantation due to the progressive nature of complications and anticipated need for intensified immunomodulation.

POSTER 232 - A CASE OF CHRONIC MUCOCUTANEOUS CANDIDIASIS WITH STAT1 GAIN-OF-FUNCTION MUTATION PRESENTING WITH SEVERE PULMONARY COMPLICATIONS

AUTHORS

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Objective:
Chronic mucocutaneous candidiasis (CMC) is characterized not only by recurrent Candida infections, but also by susceptibility to other microbial pathogens, which may result in severe pulmonary complications. Recent advances in genetics have significantly expanded our understanding of the genetic defects and immunological pathways underlying CMC. Identifying the causative mutations and associated immunopathogenic mechanisms offers opportunities for targeted therapy in patients with inborn errors of immunity. This report aims to raise awareness of the importance of targeted treatments in CMC associated with STAT1 gain-of-function (GOF) mutations.

Design and methods:
This case report was prepared in accordance with ethical standards, and written informed consent was obtained from the patient.

Results:
We present the case of a patient with CMC, marked by recurrent infections with multiple pathogens—most notably Candida species—beginning in the neonatal period. Despite a history of Candida sepsis, frequent hospitalizations, and repeated antifungal and antibiotic treatments until the age of 24, an immunodeficiency evaluation was delayed, and follow-up was inconsistent across multiple centers. Upon presenting to the pulmonology clinic with progressive dyspnea, the patient was found to have diffuse bronchiectasis and was subsequently referred to the immunology clinic for further evaluation of an underlying immunodeficiency. Based on clinical findings, a preliminary diagnosis of CMC was made, and treatment was initiated with prophylactic itraconazole, trimethoprim-sulfamethoxazole, and immunoglobulin replacement therapy. Genetic analysis revealed a STAT1 GOF mutation. Due to severe pulmonary damage and oxygen dependency, hematopoietic stem cell transplantation (HSCT) was considered high risk. As Ruxolitinib—a Janus kinase 1/2 inhibitor—has shown efficacy in treating STAT1 GOF mutations, it was introduced as a targeted therapy. Therefore, Ruxolitinib was added to the patient's treatment regimen as a targeted therapeutic agent. The patient was monitored closely for eligibility for both lung transplantation and HSCT.

Conclusion:
This case underscores the importance of early recognition and targeted treatment in CMC, especially in cases with delayed diagnosis and severe complications. The patient faced a therapeutic dilemma: advanced lung disease limited HSCT eligibility, while severe immunodeficiency contraindicated lung transplantation. Ruxolitinib functioned as a bridging therapy, enabling clinical stabilization and potential eligibility for both interventions. This case illustrates how targeted therapeutics can play a transformative role in managing complex immunodeficiency disorders.

POSTER 233 - IMMUNE DYSREGULATION IN CHILDREN WITH DOWN SYNDROME AND ITS IMPACT ON QUALITY-OF-LIFE

AUTHORS

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Individuals diagnosed with Down syndrome exhibit a wide range of clinical manifestations, which include autoinflammatory and autoimmune diseases, as well as an increased vulnerability to infections. In this study, we will present the results of an investigation into the immune dysregulation present in individuals with Down syndrome and their implications on quality-of-life. The aim of this study is to analyze the clinical characteristics associated with the aforementioned symptoms, and thereby obtain information about the frequency and severity of infectious, inflammatory, and autoimmune manifestations.

The proposed methodology involves the editing of online clinical and quality-of-life questionnaires using the Sphinx tool. The study focuses on a cohort of 278 individuals with Down syndrome, ranging in age from 4 to 21 years, who completed the questionnaires with the assistance of their parents or legal guardians. The clinical questionnaires collected information on the prevalence and severity of autoinflammatory and infectious processes using an adapted version of the IDDA (Immune Deficiency and Dysregulation Activity Score) scoring system for children with Down syndrome. On the other hand, the quality-of-life of the respondents was assessed through the KidsLife-Down scale (Gómez LE et al. 2017), which addresses social inclusion, self-determination, emotional well-being, physical well-being, material well-being, rights, personal development, and interpersonal relationships.

This study constitutes the initial phase of a broader research initiative that aims to elucidate the pathophysiology underlying these immunological alterations and to identify an effective treatment that will result in a significant enhancement in the quality-of-life of these individuals.

POSTER 234 - ADULT-ONSET IMMUNODEFICIENCY PRESENTING AS CHRONIC, TREATMENT-RESISTANT DERMATOPHYTIC INFECTION WITH STAT1 GAIN-OF-FUNCTION VARIANT: A CASE REPORT

AUTHORS

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Objective:
To highlight the diagnostic significance of chronic, treatment-refractory dermatophytic infections as a potential early manifestation of adult-onset primary immunodeficiencies, particularly those associated with STAT1 gain-of-function (GOF) mutations.

Design and method:
This case report was prepared in accordance with ethical standards, and written informed consent was obtained from the patient.

Case p resentation / results:
A 63-year-old male with no notable history of recurrent infections was referred for evaluation of an 8-year, treatment-resistant dermatophytic infection (tinea corporis), confirmed through multiple skin biopsies. Immunologic work-up revealed lymphopenia (absolute lymphocyte count: 970%E2%80%931340/%C2%B5L), marked B-cell lymphopenia (CD19+: 1%) with a predominance of na%C3%AFve B cells and decreased class-switched memory B cells. CD4 and CD8 T-cell percentages were 69% and 21%, respectively. While vaccine-specific antibodies were generally preserved, mumps IgG was absent. IgG2 was low (1.15 g/L; ref: 1.69%E2%80%937.86), with total IgG, IgA, and IgM within normal limits. Genetic analysis identified a heterozygous STAT1 GOF variant (c.821G>A; p.Arg274Gln). Further evaluation, prompted by known STAT1 GOF phenotypes, revealed pulmonary fibrotic changes, ground-glass opacities, and imaging findings suggestive of chronic liver disease with elevated GGT. Given the association of STAT1 GOF with autoimmune hepatitis and vascular complications, broader screening and close clinical follow-up were initiated. Systemic antifungal therapy was intensified, with consideration of targeted treatment such as JAK inhibitors if needed.

Conclusion:
This case underscores the importance of considering inborn errors of immunity in adults with chronic, refractory mucocutaneous infections, even in the absence of classical infection histories. STAT1 GOF mutations are associated with a broad clinical spectrum, including fungal and viral infections, autoimmunity, and organ-specific complications due to impaired Th17 responses and cytokine dysregulation. Early immunologic and genetic evaluation can guide appropriate surveillance and management, potentially improving patient outcomes.

POSTER 235 - UNMASKING IMMUNE DYSREGULATION: IS EOSINOPHILIC ESOPHAGITIS AN EARLY CLUE TO INBORN ERRORS OF IMMUNITY?

AUTHORS

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Objective:
Although allergic diseases are commonly observed in patients with inborn errors of immunity (IEI), eosinophilic gastrointestinal disorders (EGID) have been rarely reported. This study aims to characterize the clinical features of inborn errors of immunity (IEI) in patients who develop EGID either as an initial manifestation or during the follow-up, with the goal of elucidating the underlying mechanisms of immune dysregulation.

Design and method:
Nine patients diagnosed with IEI and histopathologically confirmed EGID (Figure 1) at Hacettepe University Pediatric Immunology Department during 2009-2025 period were retrospectively reviewed.

Results:
Male/female ratio was 7/2. Six (P4-P8) had eosinophilic esophagitis (EoE) and three (P1, P2, P3, P9) had EGIDs. Median ages at the EGID and IEI diagnoses were 2 years (9 months–14 years) and 7 years 7 month (9 months–18 years), respectively. The IEI diagnoses are given in Figure I. Concomitant atopic diseases were present in 5 patients (55.5%); asthma in 3(33.3%), food allergy in 3(33.3%), allergic rhinitis in 2 (22.2%), and atopic dermatitis in two (22.2%).

P7 presented with alopecia, Hashimoto's thyroiditis and urticaria, others` first symptom at EoE diagnoses were gastrointestinal symptoms (Table 1). All EoE patients were treated with dietary elimination, proton pump inhibitors, and systemic corticosteroids. Two of them (with DOCK8 deficiency and CGD) underwent hematopoietic stem cell transplantation (HSCT), and complete clinical remission was achieved for both EGIDs and underlying IEI.

Conclusions:
These findings support the hypothesis that eosinophilic esophagitis (EoE) may result from complex immunological dysregulation involving multiple immune pathways, ultimately promoting a Th2-skewed inflammatory response. Contributing mechanisms may include antibody deficiencies, impaired regulatory T cell function, and altered innate immune responses. Given emerging evidence that HSCT can offer a curative approach for EoE in the context of certain IEI and that EoE may represent as an initial manifestation of IEI, a thorough immunological evaluation should be considered in all patients diagnosed with EoE.

POSTER 236 - PRELIMINARY RESULTS OF THE PROJECT "SELECTIVE SCREENING OF HOSPITALIZED PATIENTS WITH SERIOUS BRONCHOPULMONARY INFECTIONS FOR SERUM ANTIBODIES IGG, IGM, AND IGA"

AUTHORS

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Background:
Inborn errors of immunity (IEI) are a heterogeneous group of disorders that often present with recurrent or severe infections, particularly affecting the respiratory tract. However, due to the lack of pathognomonic clinical features, early diagnosis remains a global challenge, especially in resource-limited settings, where access to advanced immunological diagnostics is restricted and diagnostic delays are common.

Methods:
We conducted selective screening of serum IgG, IgA, and IgM levels using turbidimetric analysis in patients meeting specific inclusion criteria: hospitalization for pneumonia, but additionally, history of recurrent/chronic sinusitis. The study was performed at three clinical sites in Ukraine: Kyiv City Children's Hospital No. 1 (17 patients), the Institute of otolaryngology named after O.S. Kolomiychenko (16 patients), and Sarny Central Departmental Hospital (27 patients).

Results:
A total of 60 patients were included: 50 children (under 18 years, including 3 infants) and 10 adults. The inclusion criteria were hospitalization for pneumonia or a history of recurrent or chronic sinusitis. Of the 60 patients, 40 were hospitalized with pneumonia, and 18 were outpatients with recurrent or chronic sinusitis. One additional patient had chronic lung disease, and one had limb phlegmon. Three patients (5%) were found to have immunoglobulin abnormalities. A 17-year-old adolescent with recurrent sinusitis and a prior history of pneumonia was diagnosed with common variable immunodeficiency (CVID), with IgA 0.04 g/L, IgM 0.05 g/L, and IgG 1.16 g/L. A second patient had significantly reduced IgG (0.06 g/L), his final diagnosis is pending. A 2-year-old child with pneumonia was diagnosed with selective IgA deficiency (IgA 0.06 g/L). Importantly, all patients with immunoglobulin abnormalities had pneumonia either as the presenting complaint or in their medical history. Among patients hospitalized with pneumonia (n=40), the detection rate of clinically significant immunodeficiency was 5% (2 out of 40). The screening process and recruitment of patients are still ongoing.

Conclusion:
Selecting patients hospitalized with pneumonia or presenting with recurrent sinusitis as a target group for screening yields a meaningful detection rate of immunodeficiency (5%). Targeted immunoglobulin testing in these populations is a low-cost, high-yield strategy that facilitates earlier diagnosis and management of IEI. Simple laboratory tests, such as serum immunoglobulin measurement, can serve as effective initial screening tools in appropriately selected patients.

Funding:
This study was supported by a grant from IPOPI, delivered to the Ukrainian Association of Pediatric Immunology.

POSTER 237 - UNMET NEEDS IN WORK ACTIVITIES IN ADULTS WITH INBORN ERRORS OF IMMUNITY IN ITALY: A CROSS SECTIONAL NATIONAL STUDY PROMOTED BY AIP AND IMMUNITA

AUTHORS

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Background and aims:
Due to the rarity of the condition and the scarce 'visibility', patients with inborn errors of immunity (IEI) may face difficulties in having their health status and their work rights recognised.

Methods:
A cross-sectional study on IEI adults to investigate work-related difficulties and unmet needs. A digital survey including the Work Productivity and Activity Impairment (WPAI-GH) questionnaire, the CVID_QoL, and the General Health Questionnaire-12 (GHQ-12) was sent to affiliates of the Italian Association of Patients with Primary Immunodeficiencies (AIP). The initiative was also implemented with the support of the members of the ImmunITA Italian scientific society.

Results:
The survey started on May 27, 2025 and is still running. The preliminary analysis of the first 200 patients who returned the questionnaires showed that the patients' employment rate was 80%, with about 70% of workers employed full-time, working fixed hours, and exclusively on-site. The median number of working days lost due to health issues was 15 per-year. About 60% of participants reported having limited access to specific job-related facilities or felt unsafe due to inadequate infection prevention measures while working. Seventy percent reported a negative impact of IEI on usual working activities and 50% reported a deleterious effect on career opportunities. One fifth of patients did not disclose their health status to the employer. Among those who revealed their diagnosis, 15% experienced changes to their job duties and 5% were dismissed. Three out of five patients reported of being embarrassed by claiming work permissions,and perceiving limited respect from their coworkers about the risk of infections. WPAI-GH impairment was more affected in patients with the worst health status measured by CVID_QoL and with higher mental burden assessed by GHQ. The percentage of work time missed due to health impairment while working was influenced by the occurrence of acute IEI manifestations or by spending working days for diagnostic exams, whereas the time spent on treatments has a limited impact. Older age was the main factor affecting the unemployment status. Unemployed patients reported more frequently perceived difficulties in daily non job-related activities compared to those who were employed.

Conclusion:
Despite a high employment rate, adults with IEI face many difficulties in the workplace in terms of recognition of their rights and career development. This survey could help to define inclusion policies for patients with IEI and help them to reach their full professional and personal potential.

POSTER 238 - CLINICAL AND LABORATORY CHARACTERISTICS OF ARTEMIS DEFICIENCY: A SİNGLE-CENTER EXPERINCE

AUTHORS

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Objective:
Severe combined immunodeficiencies (SCID) and combined immunodeficiencies represent a genotypically and phenotypically heterogeneous group of diseases. ARTEMIS, encoded by the DCLRE1C gene, is a component of the non-homologous DNA end-joining pathway and is involved in helicase unwinding and DNA double-strand break repair during the V(D)J recombination process.

Design and method:
The demographic, clinical, immunologic, and genetic characteristics of five patients (three girls and two boys) with confirmed DCLRE1C variants were collected retrospectively.

Results:
All patients were born to consanguineous parents. Two patients (P1 and P2), who presented with recurrent sinopulmonary infections in the first six months of life, were diagnosed with T-B-NK+ SCID (severe combined immunodeficiency). Both are awaiting hematopoietic stem cell transplantation. The other three patients (P3, P4, and P5) presented after the age of two years with a combined immunodeficiency phenotype. P3 had disseminated varicella infection at 2 years of age, along with recurrent otitis media and pneumonitis since then. He exhibited mild CD3+ T cell lymphopenia, low IgG and IgA levels, and normal IgM levels. He underwent hematopoietic stem cell transplantation (HSCT) at the age of 7 from a matched unrelated donor. P4 presented with granulomatous dermatitis and was found to have a mild decrease in IgM levels at the age of 6 years. Genetic analysis revealed a TACI (C104R) mutation, leading to a diagnosis of common variable immunodeficiency (CVID). He began to experience recurrent sinopulmonary infections at the age of 10. Lymphocyte subsets and immunoglobulin levels were near age-related normal levels. Due to his severe clinical phenotype, genetic tests were repeated. During this period, he developed diffuse large B-cell lymphoma. Hematopoietic stem cell transplantation (HSCT) was performed as soon as remission for the lymphoma was achieved. The last patient (P5) presented with autoimmune hemolytic anemia at the age of 13. Her CD3 levels were normal, but she had extremely low recent thymic emigrants and a low in vitro T cell proliferative response to PHA. She underwent matched-sibling donor (MSD) HSCT.

Conclusion:
Early diagnosis, radiation avoidance, and careful preparation for transplantation contribute to minimizing complications, enhancing life expectancy, and improving the patient's quality of life.

POSTER 240 - EVALUATING OXIDATIVE STRESS, BONE DENSITY, COGNITIVE FUNCTION, AND SERUM 25-HYDROXYVITAMIN D LEVELS IN PEDIATRIC PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISORDERS

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Background and aims:
Vitamin D is essential for bone mineralization, immune function, and neurological health. Deficiencies in serum 25-Hydroxyvitamin D [25(OH)D] are increasingly recognized among children with Primary Immunodeficiency Disorders (PIDs), potentially contributing to bone fragility, oxidative stress, and neurocognitive symptoms. This study aims to evaluate the interrelationship between serum 25(OH)D levels, bone mineral density (BMD), oxidative stress markers, and cognitive function in pediatric patients diagnosed with PIDs.

Methods:
This cross-sectional study included 482 pediatric patients with confirmed diagnoses of PID. Infants with illness durations exceeding 10 days or a history of steroid therapy or vitamin D/calcium supplementation were excluded to minimize confounding variables. Serum 25(OH)D levels were quantified using electrochemiluminescence immunoassay. Oxidative stress markers, including malondialdehyde (MDA), vitamin C, and vitamin E, were assessed. Bone mineral density (BMD) measurements of the lumbar spine and femoral neck were conducted using dual-energy X-ray absorptiometry (DEXA). Cognitive and motor function were evaluated using the Functional Ambulation Classification (FAC) scale and the Pittsburgh Sleep Quality Index (PSQI).

Results:
Infants with PID had significantly lower serum 25(OH)D levels than age-matched healthy controls ($P < 0.001$). A positive correlation was observed between vitamin D levels and FAC scores ($p = 0.001$), suggesting improved motor function with higher vitamin D status. MDA levels were inversely correlated with antioxidant vitamins (C and E) and positively associated with oxidative stress severity. Patients with lower vitamin D levels experienced a higher frequency of falls ($P = 0.05$), increased insomnia ($P = 0.01$), and elevated scores on the PSQI ($P = 0.01$), anxiety ($P = 0.001$), and depression scales ($P = 0.05$). Additionally, significant reductions in BMD were recorded at both the lumbar spine ($P = 0.01$) and femoral neck ($P < 0.001$) in patients with vitamin D deficiency.

Conclusion:
Pediatric patients with Primary Immunodeficiency Disorders exhibit notable vitamin D deficiency, increased oxidative stress, lower bone density, and impaired cognitive and sleep parameters. These findings underscore the potential value of vitamin D supplementation and antioxidant therapy as adjunctive interventions in the comprehensive management of PID.

POSTER 241 - DOCK2 DEFICIENCY IN SAUDI CHILDREN: CLINICAL FEATURES AND TRANSPLANTATION OUTCOMES — A SINGLE-CENTER CASE SERIES

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Background:
DOCK2 deficiency is a rare autosomal recessive form of combined immunodeficiency caused by biallelic mutations in the DOCK2 gene. This defect disrupts Rac-mediated cytoskeletal remodeling essential for immune cell migration, synapse formation, and antiviral responses. Affected individuals typically present in infancy with recurrent severe infections, profound T, B, and NK cell lymphopenia, and adverse reactions to live vaccines such as BCG, MMR, and varicella. Fewer than 40 cases have been reported globally, and only one previously from Saudi Arabia(P2).

Objective:
To describe the clinical, immunological, and transplantation outcomes of four Saudi pediatric patients with genetically confirmed DOCK2 deficiency, and to highlight diagnostic and therapeutic challenges in a high-consanguinity population.

Methods:
This retrospective case series was conducted at King Faisal Specialist Hospital & Research Centre. All four patients, from unrelated consanguineous families, were found to carry homozygous pathogenic variants in DOCK2 (including nonsense, frameshift, and splice-site mutations). Data collected included clinical presentation, immunologic profiles, genetic findings, infectious complications, and outcomes following hematopoietic stem cell transplantation (HSCT). Immune reconstitution and donor chimerism were monitored longitudinally.

Results:
All patients presented before 12 months of age with recurrent infections involving bacterial, viral (e.g., adenovirus, varicella), and mycobacterial pathogens. Two developed disseminated BCGitis and one experienced vaccine-related seizures. Immunological workup consistently revealed T- and B-cell lymphopenia with variable immunoglobulin levels.

Three patients underwent HSCT: two from matched related donors and one from a haploidentical donor. All achieved full myeloid and lymphoid engraftment. Two patients discontinued IVIG and immunosuppression within 10–16 months, showing robust immune reconstitution and positive vaccine responses. The haploidentical recipient demonstrated delayed T-cell recovery but maintained full donor chimerism. The fourth patient remained on supportive care due to family refusal of HSCT.

Functional validation studies using Western blot and qPCR are underway, as all four DOCK2 variants are novel and unreported in existing literature.

Conclusion:
DOCK2 deficiency should be suspected in infants presenting with early-onset lymphopenia, recurrent infections, and adverse vaccine responses, especially in consanguineous populations. Early HSCT offers curative potential, with favorable outcomes when performed before the onset of irreversible infections or immune dysregulation. This case series expands the global understanding of DOCK2 deficiency and represents the first multi-patient report from Saudi Arabia, contributing valuable insight into clinical heterogeneity and transplant strategies in resource-limited or high-consanguinity settings.

POSTER 242 - SEVERE LOCAL ADVERSE REACTION IN A PATIENT TREATED WITH SUBCUTANEOUS IMMUNOGLOBULINS: A CASE REPORT

AUTHORS

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Introduction:
Subcutaneous immunoglobulins (IgSc) are used to treat various immunological and hematological diseases, such as primary and secondary immunodeficiency. They are generally well-tolerated but can cause local adverse effects. This case describes a severe local adverse reaction in a patient who received 20% IgSc treatment, highlighting the importance of close monitoring and proper management of these events.

Objective:
To present a case of a severe adverse reaction at the injection site of 20% subcutaneous immunoglobulin, describing its clinical evolution, diagnosis, and management.

Methods:
A 51-year-old female patient with a history of CVID with bronchiectasis, ITP, polyadenopathic syndrome, neurological involvement (myelitis), and atopic dermatitis, who started treatment with IgSc in 2015. The patient administers 20% subcutaneous immunoglobulin using a bifurcated 26Gx9mm line in the chosen abdominal area. A detailed clinical evaluation was performed after the appearance of a severe local reaction at both puncture sites, characterized by erythema, edema, pruritus, and intense pain in both areas. No laboratory tests were conducted, but follow-up was done through imaging.

Results:
The patient presented with severe inflammation characterized by erythema, edema, intense pain, pruritus, and redness at the puncture site, which evolved into second-degree ulcers. After evaluation, an acute local inflammatory reaction was diagnosed, requiring local treatment for 6 months. Initially, corticosteroids were used to reduce inflammation and topical antibiotics to prevent infection. When the condition did not improve and evolved into an ulcer, the treatment was changed to a hydrogel that provided absorption, debridement of necrotic and fibrotic tissue. After a few weeks of favorable evolution, the granulation phase was reached, during which a skin regenerating agent was used to promote an optimal moist environment and prepare the wound bed to facilitate the natural healing process. This severe local process resolved in 6 months, and the IgSc treatment continued with adjustments in application conditions.

Discussion:
This case highlights the possibility of severe local adverse reactions to subcutaneous immunoglobulins, despite being a generally safe therapy. Underlying causes may include factors such as application technique, administration rate, and patient characteristics. Timely evaluation and treatment are essential to prevent major complications, and alternatives should be considered in recurrent cases.

Conclusion:
Severe local reactions to subcutaneous immunoglobulins, although rare, must be recognized and managed appropriately. This case emphasizes the importance of rigorous clinical evaluation and close follow-up to ensure the safety and effectiveness of the treatment.

Keywords:
Subcutaneous immunoglobulins (IgSc), local adverse reaction, immunotherapy, clinical management, side effects.

POSTER 243 - MACHINE LEARNING-DRIVEN ANALYSIS OF EPIGENETIC SIGNATURES IN PRIMARY IMMUNODEFICIENCY DISORDERS: INVESTIGATING HISTONE MODIFICATION DYNAMICS

AUTHORS

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Objective:
This study aims to investigate the role of histone modifications in the pathophysiology of Primary Immunodeficiency Disorders (PIDs), an emerging yet underexplored area of epigenetic research. The primary goal is to identify epigenetic biomarkers associated with disease onset and severity, using machine learning techniques to uncover regulatory patterns that may inform diagnosis and therapeutic strategies.

Background:
PIDs are a diverse group of inherited immune disorders often linked to monogenic mutations. However, clinical heterogeneity among patients with similar genetic defects suggests that non-genetic factors, such as epigenetic modifications, may also play a role in disease progression. Histone modifications are key regulators of gene expression, and their dysregulation may influence immune cell function, inflammatory pathways, and susceptibility to immune-related complications. Despite their relevance, the epigenetic landscape of PIDs—particularly histone modifications—remains poorly characterized.

Methods:
The study utilized chromatin immunoprecipitation sequencing (ChIP-seq) data from neuronal precursor cells derived from 250 PID patients and matched healthy controls. Analysis focused on key histone modifications (e.g., H3K4me3, H3K27ac) at regulatory immune-related gene loci. These datasets were integrated with whole-genome sequencing and clinical metadata. Convolutional Neural Networks (CNNs) were applied to detect spatial patterns of histone modification peaks, while a Random Forest (RF) model was used to predict disease onset and severity by integrating epigenetic, genomic, and clinical variables. Stratified cross-validation was used to evaluate model performance and ensure reproducibility.

Results:
Distinct histone modification patterns were observed in PID patients with early disease onset and more aggressive progression. These alterations were especially pronounced near genes involved in neuronal signaling and immune regulation. The combined CNN-RF model achieved 88% accuracy in distinguishing early- from late-onset PID, with an area under the curve (AUC) of 0.94 and a mean absolute error of 2.3 years in predicting disease onset. A subset of patients with specific epigenetic signatures exhibited a 30% higher rate of disease progression.

Conclusion:
This study highlights the potential of machine learning tools to decode the epigenetic architecture of PIDs. Histone modification profiles may serve as early biomarkers and therapeutic targets, offering new avenues for personalized immunological care and advancing our understanding of PID pathogenesis.

POSTER 244 - TH-2 MONOCLONALS AND JAK INHIBITORS TO TREAT INBORN ERROR OF IMMUNITY WITH ALLERGIC DYSREGULATION: THE ATO-PID PROJECT

AUTHORS

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Background:
Although IEI is typically associated with recurrent and/or severe infections, patients often experience other symptoms, including severe atopic dysregulation. Anti-TH2 biologics and JAK inhibitors (JAKi), which are effective in immunocompetent individuals, are potential therapies, but there is little data on their use in IEI. This systematic review and meta-analysis aimed to assess their efficacy and safety in patients with IEI.

Methods:
A systematic review of international medical databases on the use of anti-TH2 biologics and JAKi in IEI patients with atopic manifestations was conducted in May 2025.

Results:
Ninety-nine papers and 139 patients (54% <18 years old; Fig.1) were identified. Data on 149 treatment courses were collected, including anti-IL4/R (n=92), anti-IgE (n=26), JAKi (n=27), and anti-IL5/R (n=4). The most frequent diagnoses were Netherton syndrome (NS) and STAT3-LOF (Fig.2). Treatment was primarily indicated for dermatological manifestations (75%), followed by a combination of more than one manifestation (11%; Fig.3). Six patients were treated to improve their HSCT outcome, having received dupilumab or JAKi as treatment for GVHD or as bridging therapy. A positive outcome was observed in five of these patients. Hyper-IgE syndromes, disorders of the epithelial barrier and primary antibody deficiencies were mainly treated with anti-IL4R, anti-IgE and anti-IL5/IL5R. In contrast, disorders of the JAK/STAT pathway were primarily treated with JAKi (Fig.3). Treatment was effective in 97% of patients. Eight patients who experienced symptom failure or incomplete control achieved better control by switching to other monoclonals/JAKi, and one patient achieved better control by adding a second biologic. Adverse events (AEs) occurred in 15% of patients, mostly mild or moderate, without treatment discontinuation. JAK-is were associated with the highest frequency of AEs, including two severe AEs. Three patients died while receiving JAKi: two due to infection and one due to progression of pulmonary GVHD (Fig.3). The subanalysis conducted in dupilumab recipients (Fig.4) showed improvement rates of 82% and 93% for patients with NS and STAT3-LOF, respectively. All the manifestations generally responded after a median of five weeks, with NS showing a faster response than AD-HIES. The target dose was 300 mg beweekly in 70% of patients. Dupilumab-related AEs were reported in 10% of patients, most of which were mild.

Conclusions:
The available data suggest that anti-TH2 biologics and JAKi are highly effective in treating atopic dysregulation in IEI. However, the safety profile of JAKi requires careful individual assessment. Larger, prospective studies are crucial to establishing definitive conclusions.

POSTER 245 - HOW DOES GENETIC TESTING CHANGE THE CLINICAL DECISION IN INBORN ERRORS OF IMMUNITY

AUTHORS

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Background:
Over the past two decades, genetic testing has profoundly transformed the diagnosis, classification, and treatment of inborn errors of immunity. Genetic tests not only complete the final stage of diagnosing inborn errors in immunity after a routine immunological examination but they can also be useful when routine immunological examination does not allow for an accurate diagnosis as well as for differential diagnosis with other non-immunological causes of recurrent infections.

Aim:
to analyze how the genetic result changes therapeutic decision-making based on the cohort of patients examined within genetic diagnostic project sponsored by Biopharma Plasma.

Design:
Since 2022 the Ukrainian Association of Pediatric Immunology with the sponsorship of Biopharma Plasma has launched a project for genetic diagnostics of patients with clinical suspicion of PID. To assess the suitability of clinical cases submitted by doctors from all over Ukraine a commission was created. Inclusion criteria are: clinical signs of immunodeficiency, availability of results of immunological examination, negative HIV test, absence of immunosuppressive therapy or other causes for secondary immunodeficiency. The Invitae PID panel was used for genetic testing. In total, for the period of 2022-2024, the 147 clinical cases were considered, 84 patients underwent genetic testing, others 63 were rejected or postponed due to non-compliance with the criteria or insufficient immunological work-up before genetic testing.

Results:
Of the tested 84 patients, the diagnosis of PID was genetically verified in 37, in 25 the diagnosis was rejected, in 22 patients with uncertain genetics the diagnosis was still established according to the ESID working criteria. The genes with identified pathogenic disease-caused variants include TACI (TNFRSF13B) – 12, KMT2D, SAMD9, GATA2 – 3, PIK3CD, PI3K, CYBB, TBX1, STAT3, IGLL1, CARD11 - 3, FAS, SON, BTK - 3, CD40L – 2, FANCD2, TCF3, AICDA - 2. One patient was diagnosed with cystic fibrosis. According to the results of genetic examination in 11 patients the management tactics was confirmed, in 14 the treatment was modified, in 6 changed (BMT was recommended for 4 patients, BMT was rejected for 2 patients), in 6 patients with a detected pathogenic variant in the absence of full manifestation careful clinical and laboratory monitoring was suggested as well as family members screening.

Conclusions:
Genetic testing is crucial for the choice of therapeutic approach in the majority of cases. It enables more precise, personalized, and predictive medicine. Genetic diagnosis helps to provide the prognostic education and family testing and remove the misdiagnoses.

POSTER 246 - THE DILEMMA OF X-LINKED AGAMMAGLOBULINEMIA CARRIERS

AUTHORS

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Background:
Many patients with X-linked agammaglobulinemia (XLA) nowadays have reached adulthood, as well as their sisters, possibly carriers of a deleterious Bruton tyrosine kinase variant. Studies on motherhood outcomes in families with XLA are lacking.

Objective:
We sought to investigate adherence to carrier status screening, interest in preconception and prenatal genetic counseling, and reproductive decisions in relatives with XLA.

Methods:
In this multicenter, retrospective cohort study, we collected a 3-generation pedigree and data on mothers and sisters of patients with XLA, including carrier status and pregnancy outcome.

Results:
Data on 53 adults with XLA, 52 mothers, and 33 sisters were collected. All XLA sisters received genetic counseling. Forty percent of the sisters chose to undergo carrier status determination, and 60% of them chose invasive prenatal testing. The main reasons for the sisters to decide not to undergo genetic testing were their young age and the willingness to carry on with the pregnancy regardless of the outcome of the genetic test, followed by the willingness to postpone the decision at the time of pregnancy and the decision to not have children. Prenatal testing resulted in 5 XLA diagnoses, with 2 pregnancy terminations, 1 miscarriage, and 2 XLA live births. Three carriers refused prenatal testing and had 6 live births, including 3 XLA-affected sons. One sister was diagnosed as a carrier after the birth of an XLA-affected son. In total, 9 XLA diagnoses were made, including 6 live births.

Conclusions:
A number of XLA sister carriers decided to carry on with their pregnancy after receiving the diagnosis of an affected fetus or after refusing prenatal testing. We propose to initiate a more extensive collaborative study to verify the effect of genetic counseling on families with XLA in other cohorts from different countries.

POSTER 247 - COMPLEMENT FACTOR I DEFICIENCY MAY PRESENT WITH RECURRENT SEIZURES AND ENCEPHALITIS

AUTHORS

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Introduction:
Complement factor I (CFI) deficiency is an immunodeficiency disorder, which is inherited in an autosomal recessive manner and caused by mutations in the CFI gene(1). We aimed to contribute to the literature by describing a complement deficiency that was diagnosed in adulthood, as well as its rare clinical presentation.

Case presentation:
A 21-year-old female patient was admitted to the hospital due to recurrent seizures and encephalitis. Her parents were first-degree cousins. She was admitted to the intensive care unit at six months of age with a fever, loss of consciousness, and right-sided convulsions. She experienced frequent otitis and sinusitis infections. At age 17, she developed weakness, loss of strength in her right arm and leg, impaired speech. Brain imaging revealed asymmetric, bilateral signal changes in the periventricular white matter, consistent with gliosis. There was severe cortical atrophy in the cerebral and cerebellar hemispheres. These finding were consistent with previous encephalitis (Figures 1). The autoimmune encephalitis panel, viral PCR assays, and metabolic investigations were all negative. She received intravenous immunoglobulin and pulse steroid therapy, which resulted in clinical improvement.

Whole-exome sequencing (WES) was performed due to her history of fever, encephalitis, and recurrent seizures. This revealed a homozygous c.1A>G p.(Met1Val) mutation in the CFI gene (NM_000204.4)(Figures 2-3). Familial segregation confirmed the heterozygosity in the parents and health sibling (Figure 4). Cerebrospinal fluid was negative for microorganisms. Laboratory tests showed low C3 (0.508 g/L) with normal C4 (0.393 g/L). Trimethoprim-sulfamethoxazole prophylaxis was started. She was vaccinated against encapsulated bacteria.

Discussion:
In our case, a patient with homozygous CFI mutation developed refractory seizures secondary to recurrent encephalitis episodes. CFI deficiency can lead to destructive cerebral inflammation due to uncontrolled complement activation. However, encephalitis associated with CFI deficiency has rarely been reported in the literature. Unlike previous reports describing compound heterozygous CFI deficiency with severe CNS involvement (2,3). Our patient shows homozygous inheritance. The same CFI start codon mutation has also been reported with atypical HUS. This start codon mutation likely results in loss of function due to impaired translation initiation.

Conclusion:
CFI deficiency should be considered in the differential diagnosis of patients with recurrent encephalitis and seizures. An early diagnosis is essential to prevent infectious and inflammatory sequelae. This case underscores the need for raising awareness that complement system defects can affect central nervous system.

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POSTER 248 - VACCINE HESITANCY IN ADULTS WITH 22Q11.2 DELETION SYNDROME AND THEIR CAREGIVERS: RESULTS OF A SELF-REPORTED SURVEY

AUTHORS

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Background:
22q11.2DS is the most frequent microdeletion in humans, responsible for heterogeneous clinical pictures, including congenital structural disease, neuropsychiatric, and different degrees of immunodeficiency, leading to reduced immunogenicity of vaccines and difficulty in sustaining long-term protective responses. In addition, many patients develop chronic comorbidities, including metabolic and respiratory diseases. Immunizations are therefore an important tool to protect these patients from preventable infections. Low insight of immunodeficiency and of the benefits of vaccination and reluctance to be vaccinated are the principal barriers to immunisation especially for self-managing adults, who make health decisions independently of their caregivers. The purpose of this study was to assess reasons and predictors of vaccine hesitancy in a population of adults living with 22q11.2DS and their caregivers.

Methods:
Cross-sectional survey research was conducted on a sample of 85 adults living with 22q11.2DS followed up in the Referral Care Centre of Sapienza University of Rome, Italy and their caregivers. Data were collected using a digital survey and phone interview between July and November 2024. Patients were asked about their hesitancy to be vaccinated due to their genetic disease. For not-sufficient patients, caregivers completed the survey. Data were analyzed using bivariate odds ratios and cumulative logit model.

Results:
Seventy-five participants completed the survey, mostly care-givers (75%). Sixty-two percent of the caregivers and 41% of the patients considered people with 22q11.2DS to be at moderate to high risk of infection. Eighty-seven percent of the caregivers and 62% of patients thought vaccines would be useful for people with 22q11.2 DS. Reasons for hesitancy were contradictory in patients and caregivers as caregivers were to be worried for immune system overstimulation, anaphylaxis, and negative long-term effects whereas patients were reluctant due lack of confidence in the science behind the vaccines and concerns about possible allergy or negative long term effects. Multivariate analysis found vaccine hesitancy to be related to education, employment. Moreover, having a major congenital heart disease and a history of recurrent respiratory infections was negatively associated with hesitancy.

Conclusion:
Findings suggest 22q11.2DS population heterogeneity may account for vaccine hesitancy. Whereas caregivers showed limited hesitancy, the high levels of reluctance in self-managing adult patients suggests that communications on risk of infections and benefits of vaccinations should be emphasized to improve the confidence with immunizations.

POSTER 249 - GATA2 DEFICIENCY PRESENTING WITH HYPOGAMMAGLOBULINEMIA AND HEARING LOSS

AUTHORS

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Introduction:
GATA2 deficiency is a disorder with a broad clinical spectrum, including lymphedema, hearing loss, and pulmonary dysfunction, but it primarily affects the immune and hematologic systems. It results from mutations in the GATA2 gene, which encodes a zinc finger transcription factor playing a crucial role in hematopoiesis. In these patients, monocytes, dendritic cells, natural killer cells, and B lymphocytes are significantly reduced or absent.

Objective:
We present a case with a heterozygous pathogenic mutation in the GATA2 gene with autosomal dominant inheritance.

Findings:
A 14-year-old male patient was initially evaluated at 30 months of age due to recurrent fever and upper respiratory tract infections (URTIs). His history revealed that he was born at term to a 33-year-old mother, with no need for neonatal intensive care. After 8 months of age, he experienced frequent URTIs and acute otitis media approximately three times per month, along with diarrhea lasting up to 30 days after the age of one. Physical examination revealed low-set ears, hypertelorism, ptosis. Bilateral hearing loss was present, and his speech was not age-appropriate.

Laboratory findings included WBC:
10,500/mm³, ANC: 2,290/mm³, ALC: 7,970/mm³, Hb: 11.7 g/dL, PLT: 360,000/mm³. Concurrent lymphocyte subset analysis showed CD3+: 83.6%, CD19+: 12%, CD4+: 64%, CD8+: 18%, CD16+56+: 2.8%. Immunoglobulin levels were IgG: 432 mg/dL, IgA: 40 mg/dL, IgM: 90 mg/dL, and total IgE: 8 kU/L. Immunoglobulin replacement therapy was initiated. At age 13, during a febrile episode, the patient developed lymphopenia for the first time and was evaluated by the pediatric hematology department, where viral suppression was considered. At age 14, mild thrombocytopenia was noted, and genetic testing revealed a heterozygous pathogenic mutation in the GATA2 gene: c.1084C>T (p.Arg362Ter). Bone marrow aspiration biopsy demonstrated dyserythropoiesis with <1% blast cells.

Throughout follow-up, IgG levels remained persistently low, and even during periods without lymphopenia, CD19+ B cells decreased to as low as 5%. Previous studies have reported a 75% prevalence of myeloid neoplasia in individuals with GATA2 deficiency, with a median age at diagnosis of 19.7 years. Due to the high risk of developing MDS/AML associated with GATA2 mutations, the patient underwent hematopoietic stem cell transplantation (HSCT).

Conclusion:
GATA2 deficiency can present at different ages with various clinical manifestations, including monocytopenia, hypogammaglobulinemia, susceptibility to mycobacterial infections, and lymphedema. A definitive molecular diagnosis can be achieved through genetic analysis.

Given the high risk of progression to myeloid neoplasia, HSCT is recommended in these patients.

POSTER 250 - LONG-TERM IMMUNOLOGICAL CHANGES AFTER CORRECTIVE CARDIAC SURGERY

AUTHORS

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Background:
Infants with congenital heart disease (CHD) often undergo thymectomy during corrective cardiac surgery (CCS). The long-term immunological effects remain controversial, with concerns regarding increased susceptibility to infections, allergies, autoimmunity due to compromised immune tolerance mechanisms. This study aims to elucidate the long-term immunological effects of early thymectomy.

Methods:
We enrolled 22 patients who underwent thymectomy in infancy and were followed up in the Pediatric Allergy and Immunology Clinic at Marmara University. We performed demographic characteristics and detailed immunological evaluation, including immunoglobulins, vaccine responses, lymphocyte subset analyses, upregulation, proliferation of T cells and T-cell receptor excision circles (TRECs).

Results:
Sixteen patients had a history of infection, including 6 serious infections, all in the first year. Lymphopenia was observed in 27% of patients, with a significant decrease in naive CD4+ and CD8+ T-cell counts and an increase in the proportion of memory T-cells, indicating premature immune senescence. Low levels of IgG, IgA and IgM were found in 36%, 40% and 22% of patients respectively. Vaccine responses were positive in 90% of patients. TREC levels were low in all 10 patients analyzed. Seven of 9 patients had normal proliferation. 22% of patients had allergic disease, autoimmunity was not observed.

Conclusion:
Early thymectomy leads to permanent immunological changes that are indicative of early immunosenescence. It is recommended to preserve thymic tissue during surgery and requires long-term follow-up in terms of findings such as allergy and autoimmunity as well as infections due to impaired immune tolerance mechanisms.

Key Words:
Congenital heart defect, early thymectomy, immunodeficiency, immunosenescence, lymphopenia, T-cells, thymus.

POSTER 251 - DIAGNOSTIC DELAY IN ADOLESCENTS AND YOUNG ADULTS WITH 22Q11.2 DELETION SYNDROME: ARE WE DOING ENOUGH?

AUTHORS

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Background:
22q11.2 deletion syndrome (DS) is the most common genomic disorder characterized by a diverse and highly variable array of clinical manifestations, which may lead to diagnostic delay, late access to care and inadequate prenatal counselling.

Methods:
Single-centre retrospective study in 22q11.2DS adult patients grouped according to their age at the time of genetic diagnosis. The primary outcome was to determine the diagnostic delay and to define whether atypical clinical phenotypes might justify a late diagnosis. Multiple linear regression models with a stepwise procedure identified factors influencing the diagnostic delay.

Results:
Eighty 22q11.2DS adult patients were included. The median diagnostic delay, defined as the age at 22q11.2DS genetic diagnosis, was 15 years (IQR: 4-23): 21% of patients were diagnosed at <1 year of age, 16% during childhood (1-9 years), 26% during adolescence (10-18 years), 29% during early adulthood (19-35 years), and 8% during adulthood (>35 years). The primary indications for the genetic testing were a congenital heart disease (CHD) in the first year of life, a delayed psychomotor in childhood, a psychiatric illness in adolescence and early-adulthood (<35 years), and a positive familiar history in adulthood (>35 years). In patients diagnosed <1 year of age, the prevalent symptoms were CHD and dysmorphism. Frequencies of ENT congenital problems, neurodevelopmental delay, learning and speech difficulties, and neonatal hypocalcemia were similar over the groups diagnosed at different age intervals, except for patients diagnosed >35 years, who showed a less severe phenotype. Most patients diagnosed in adolescence and adulthood had at least three manifestations attributable to 22q11.2DS during childhood. Major CHD and a combination of signs of immunodeficiency plus dysmorphism and/or neurodevelopmental problems were associated with a shorter diagnostic delay.

Conclusion:
Patients with 22q11.2 experienced a diagnostic delay, in particular when CHD and immunodeficiency were non present. Dissemination of the warning signs among practitioners should be encouraged to improve access to treatment, quality of life for patients and their families and to reduce the diagnostic burden.

POSTER 252 - CLINICAL, IMMUNOLOGICAL, AND GENETIC CHARACTERISTICS OF 15 PATIENTS WITH MENDELIAN SUSCEPTIBILITY TO MYCOBACTERIAL DISEASE

AUTHORS

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Introduction:
Mendelian Susceptibility to Mycobacterial Disease (MSMD) is a rare primary immunodeficiency caused by defects in the IL-12/IFN-γ signaling pathway. It predisposes patients to severe infections with weakly virulent mycobacteria and other intracellular pathogens. This study aims to evaluate the clinical, immunological, and genetic features of 15 MSMD patients followed at a tertiary referral center.

Methods:
We conducted a retrospective review of medical records of 15 patients diagnosed with MSMD between 2004 and 2024 at the Pediatric Immunology Department of Ege University Faculty of Medicine. Demographic data, infection history, laboratory findings, immunological assessments, and genetic test results were analyzed.

Results:
The mean age of the patients was 12 ± 7.4 years, and 66% were male. The average age at symptom onset was 56.4 ± 54 months. Parental consanguinity was noted in 66%, and 40% had a family history of primary immunodeficiency. All patients had received BCG immunization. The most common presenting symptoms were BCG lymphadenitis and atypical mycobacterial infections. Additionally, 86% of the patients reported frequent respiratory tract infections.

Lymphocyte and neutrophil counts were within normal ranges, while hypergammaglobulinemia was found in 80%. Pathogens identified included M. bovis (n=8), M. avium-intracellulare (n=1), M. elephantis (n=1), and Salmonella enteritidis (n=2). Genetic analysis revealed IL12RB1 mutations in 6 patients, IFNGR1 defects (2 complete, 2 partial) in 4 patients, IFNGR2 mutations in 3 patients, and single cases with NEMO and STAT1 mutations. Recombinant IFN-γ therapy was administered to 5 patients. Hematopoietic stem cell transplantation was performed in 2 cases; 1 patient died. At the final follow-up, 12 patients were alive.

Conclusion:
MSMD is a rare but potentially treatable immunodeficiency. Early recognition through targeted immunological and genetic evaluations is essential. Recombinant IFN-γ therapy may offer clinical benefit in selected cases. Due to the genetic heterogeneity of MSMD, comprehensive molecular testing is critical in patients presenting with suggestive clinical features.

POSTER 253 - AUTOIMMUNE POLYENDOCRINOPATHY-CANDIDIASIS-ECTODERMAL DYSTROPHY (APECED): A CASE STUDY EMPHASIZING THE CRUCIAL ROLE OF IMMUNODEFICIENCY AND GENETIC EVALUATION IN RECURRENT CANDIDIASIS AND SKIN RASHES

AUTHORS

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Introduction:
Apeced is a rare, genetically inherited immunodeficiency caused by mutations in the AIRE gene, which plays a crucial role in central immune tolerance. AIRE deficiency leads to autoreactive T-cells and autoantibodies against multiple tissues. APECED is diagnosed based on at least two of the three key clinical features: chronic mucocutaneous candidiasis (CMC), primary hypoparathyroidism, and adrenal insufficiency. Early signs may include non-endocrine autoimmune manifestations such as enamel hypoplasia, recurrent skin rashes, and CMC, which are vital for early diagnosis.

Material and methods:
This study presents the clinical and genetic characteristics of a one-year-old female diagnosed with APECED at the Pediatrics Clinic III of the Children's Emergency Hospital "Louis Țurcanu" Timișoara, Romania.

Results:
The patient, from non-consanguineous, apparently healthy parents, presented with urticarial-like rashes, enamel hypoplasia, seborrheic dermatitis, and localized hair loss due to fungal infection. Over one year, she experienced CMC, recurrent rashes, pneumonia, and an episode of septicemia. Laboratory tests revealed autoimmune markers and persistent hypergammaglobulinemia. Due to recurrent CMC, a. primary immunodeficiency was suspected. Whole Exome Sequencing identified AIRE mutations suggestive of APECED.

Conclusion:
Apeced may first appear with CMC and non-endocrine autoimmune signs. Immunodeficiencies should be considered in young patients with such symptoms to ensure early diagnosis and treatment.

POSTER 254 - CHRONIC GRANULOMATOUS DISEASE WITH MULTISYSTEM INVOLVEMENT IN AN ADULT PATIENT WITH A CONFIRMED CYBB MUTATION: A DIAGNOSTIC AND THERAPEUTIC

AUTHORS

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Objective:
To present a rare case of late-diagnosed chronic granulomatous disease (CGD) in adulthood, with progressive multisystem complications including pulmonary fibrosis, gastrointestinal inflammation, hepatopathy, and recurrent infections.

Design and method:
This case involved longitudinal follow-up of a male patient from early childhood to adulthood, including clinical assessments, laboratory investigations, imaging, and genetic testing.

Results:
We report a 35-year-old male with a history of hepatosplenomegaly, recurrent infections, and failure to thrive since early childhood. Liver biopsy revealed granulomatous hepatitis of unknown etiology. Idiopathic nanosomia was diagnosed at the age of four. Family history of primary immunodeficiency was negative. The initial nitroblue tetrazolium (NBT) test was within normal limits. Throughout childhood and adolescence, the patient experienced frequent complicated sinopulmonary infections, recurrent furuncles, and chronic diarrhea. Abdominal MRI and liver function tests were unremarkable at that time. At age 24, due to recurrent otitis media, he underwent tympanoplasty and myringoplasty. Despite intermittent treatment with antibiotics, glucocorticoids, and short-term interferon-gamma, the disease progressed, leading to multiple hospitalizations. At age 29, dihydrorhodamine (DHR) testing confirmed CGD. Clinical exome sequencing identified a rare hemizygous missense variant c.1583C>G (p.Pro528Arg) in the CYBB gene on the X chromosome. Over time, the patient developed progressive complications: pulmonary fibrosis with impaired lung function (DLCO 36%, FEV1/FVC 88%), chronic gastritis, colitis, recurrent fungal and bacterial infections, and cutaneous abscesses. In the past year, the patient's respiratory condition further deteriorated, with increased dyspnea and fatigue. Sputum cultures repeatedly grew Candida tropicalis and Streptococcus spp. Long-term antifungal therapy with voriconazole was initiated, and interferon-gamma therapy was reintroduced due to worsening lung function and recurrent infections.

Conclusions:
CGD should be considered in adults presenting with recurrent infections caused by catalase-positive organisms. This case highlights the diagnostic and therapeutic challenges associated with late-diagnosed CGD due to a hypomorphic CYBB mutation and progressive multisystem involvement. Early genetic testing and individualized immunomodulatory treatment are essential for improving outcomes in such patients.

POSTER 255 - THE SPECTRUM OF HEPATIC FINDINGS IN COMBINED IMMUNODEFICIENCY PATIENTS

AUTHORS

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Objective:
Patients with combined immunodeficiency (CID) are susceptible to a broad spectrum of infections, autoimmune disorders, malignancies, and organ-specific complications. Among these, hepatic involvement represents a clinically significant yet frequently underrecognized manifestation that may impact overall disease prognosis. A comprehensive understanding of the spectrum, etiology and clinical features of liver complications in patients with CID is crucial for effective management. This study aimed to investigate the causes and clinical characteristics of liver involvement in patients with CIDs.

Design and methods:
Patients with CID who were followed at the Pediatric Immunology Department of Hacettepe University between 2010 and 2021 were retrospectively evaluated. Only those with documented liver involvement were included. Demographic data, characteristics of hepatic involvement, laboratory findings, treatment approaches, and clinical outcomes were recorded.

Results:
Hepatic involvement was observed in 13.9% of 344 patients with CID (Table 1). The median age of the patients was 15.7 years (IQR: 6.2–26.6), and 50% were male. Hepatomegaly and splenomegaly were present in 87.2% and 60.4% of patients, respectively. The most frequent cause of liver involvement was infection (29.6%), including CMV hepatitis (n = 5), chronic hepatitis B virus (HBV) infection (n = 4), fungal infections (n = 2), and tuberculosis (n = 2). Hepatic tumors were detected in nine patients (16.6%). In four of these, liver involvement resulted from metastasis, all associated with non-Hodgkin lymphoma. One patient developed fibro-lamellar hepatocellular carcinoma while in remission following treatment for hepatic embryonal sarcoma. Other hepatic tumors included high-grade malignant epithelial neoplasia, hemangioma, and adenoma. Sclerosing cholangitis was diagnosed in five patients (9.2%), most frequently in those with DOCK8 deficiency. One of these patients progressed to end-stage liver disease. Additional hepatic pathologies included HLH-related hepatitis (n = 3), lymphoproliferative infiltration (n = 3), autoimmune hepatitis (n = 2), drug-induced hepatotoxicity, graft-versus-host disease (GVHD), Budd–Chiari syndrome, and granulomatous hepatitis. Secondary choledocholithiasis due to autoimmune hemolytic anemia and resulting cholestasis was observed in two patients, and one patient had a choledochal cyst. No identifiable etiology for liver involvement could be determined in 10 patients. A definitive diagnosis was established through liver biopsy in 47.9% of cases. Three patients died due to acute liver failure, and four developed cirrhosis; one of them underwent liver transplantation following HSCT.

Conclusion:
Liver involvement in patients with CID encompasses a wide spectrum of etiologies. Early recognition and targeted management of liver complications are crucial to improve outcomes in this high-risk population.

POSTER 256 - SMART-CVID: A PID COMMUNITY-OWNED, AI-ENHANCED APP TO IMPROVE QUALITY OF LIFE IN PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY

AUTHORS

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Introduction:
Patients with Common Variable Immunodeficiency (CVID) face substantial reductions in health-related quality of life (HRQoL), influenced by fatigue, recurrent infections, emotional distress, and social isolation. Existing clinical care often lacks proactive, personalized support. We developed SMART-CVID, the first digital health application specifically for CVID, designed with ethical AI and decentralized data ownership. Crucially, the app is managed by AEDIP (the Spanish Association for Primary Immunodeficiencies), ensuring long-term sustainability, patient autonomy, and alignment with community needs.

Methods:
A six-month observational pilot was conducted with 48 CVID patients (mean age 49.5 years; 70.8% female). The app enabled real-time collection of symptoms, immunoglobulin replacement therapy (IgRT) data, HRQoL scores (using the validated CVID-QoL questionnaire), and treatment adherence. Built on the Raito platform, it guaranteed GDPR-compliant data privacy and ownership. SMART-CVID also included personalized alerts, appointment reminders, and an AI-powered assistant based on ChatGPT technology.

Results:
In this study, the baseline mean CVID-QoL score was 47.8/128, indicating a moderate impact on quality of life among participants. Of the 48 patients included, 5 were receiving subcutaneous immunoglobulin (SCIg) and 43 intravenous immunoglobulin (IVIg). Patients treated with IVIg exhibited better quality of life outcomes compared to those on SCIg. The digital health application demonstrated high user engagement, with strong adherence to symptom tracking and active patient participation. All collected data were fully anonymized, facilitating both individual-level monitoring and population-level analyses, and laying the groundwork for future predictive modeling strategies

Conclusions:
SMART-CVID is a pioneering, patient-governed mobile application that integrates ethical AI and decentralized health data technologies to address the complex needs of individuals with CVID. It supports proactive, personalized care while preserving human connection. Results from this pilot show promising impacts on patient empowerment, clinical monitoring, and HRQoL improvement. With its modular design and community ownership model, SMART-CVID offers a scalable blueprint for digital health innovation in rare diseases.

POSTER 257 - PROFILE OF PATIENTS WITH INBORN ERRORS OF IMMUNITY MANAGED IN AN ADULT TRANSITION CLINIC

AUTHORS

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Objective:
Inborn errors of immunity (IEI), or primary immunodeficiencies (PID), are congenital disorders that increase susceptibility to infections, autoimmunity, and malignancy. Advances in care have improved survival, leading to more patients needing lifelong follow-up. Transition clinics ensure structured transfer from pediatric to adult services, supporting continuous management during this phase. This study describes the baseline demographic and clinical characteristics of patients with IEI recently transitioned to our new adult PID transition clinic. The aim is to emphasize the importance of transition practices and outline age, gender, and IUIS classification in this group.

Design and methods:
We collected and analyzed demographic and clinical data of patients with PID who transitioned from pediatric to adult care and are now followed in our transition clinic.

Results:
A total of 78 patients were included in the analysis. The median age was approximately 39.8 years (range: 18–68 years). Of the patients, 42 (53.8%) were female and 36 (46.2%) were male. According to our grouping, out of 78 patients, 47.4% were classified as Predominantly Antibody Deficiencies, 20.5% as Combined Immunodeficiencies (CID), 11.5% as Diseases of Immune Dysregulation, 5.1% as Combined Immunodeficiencies with Syndromic Features, 3.8% as Defects in Intrinsic and Innate Immunity, 2.6% as Defects in Phagocyte Number/Function, 2.6% as Complement Deficiencies, 1.3% as Phenocopies and Secondary Immunodeficiencies, and 5.1% were classified as Other(Figure1). Of the total 78 patients, 30.8% had CVID, 16.7% CID, 5.1% immune dysregulation, 2.6% had Hyper IgM syndrome, 2.6% Hyper IgE syndrome, 2.6% XLA, 2.6% CGD, and the remaining patients represented syndromic forms, complement deficiencies, and rare variants. A genetic mutation was identified in 29 out of 78 patients (37.2%) and these are illustrated in the figure2. In our cohort of 78 adult patients with primary immunodeficiencies, 86.4% had at least one additional comorbidity. The most common were chronic lung diseases (48%), autoimmunity (36%), and infection-related complications (24%). Furthermore, 14% had a history of lymphoproliferative disorders or malignancy. These results demonstrate that the burden of comorbidities in adult PID patients is substantially higher than in pediatric patients. 70% of adult PID patients have recurrent respiratory infections, with 35% developing bronchiectasis. Opportunistic viral infections (HSV, HPV) occur in 25%, fungal infections in 15%, and severe bacterial or rare opportunistic infections (TB, atypical mycobacteria, PJP) in 9 %.

Conclusions:
In conclusion, transition clinics are essential and must be multidisciplinary, as these patients represent a high-risk group with significant comorbidity burden.

POSTER 258 - CROSS-BORDER ACCESS TO GENE THERAPIES FOR RARE PRIMARY IMMUNODEFICIENCIES: REAL-WORD EXPERIENCE AND INSIGHTS FROM A QUALIFIED TREATMENT CENTER

AUTHORS

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For rare diseases, timely access to effective treatment frequently depends on highly specialized expertise, which is typically concentrated in a few expert centers globally. Given the low prevalence, clinical complexity and specific therapeutic requirements of these conditions, the centralization of care is imperative to ensure patient safety and optimize clinical outcomes. This consideration is especially pertinent for rare primary immunodeficiencies (PID) that necessitate advanced therapies available only at select EU centers.

This case exemplifies a distinctive experience with a medicinal product derived from genetically modified HSPCs that was commercially available, presenting multiple challenges concerning reimbursement, treatment accessibility and logistics involving treatment centers, referring physicians, patients, and caregivers.

EU legislation supports access to such specialized care through Regulation (EC) No 883/2004 and the S2 funding route. However, access remains uneven, as national implementation often requires that the therapeutical pathway be fully reimbursed in the country of residence (not always possible for ultra-rare therapies offered only abroad).

We report our experience as qualified treatment center administering gene therapies for rare diseases, including PID and specifically as the only QTC in the EU for the administration of the ex-vivo gene therapy for ADA-SCID, approved by the European Commission in 2016.

Between 2017 and 2024, 22 patients from the EU were referred to us, 15 of whom had a PID and came from 9 different European countries. Of these, 7 patients obtained S2 approval without major issues. In 1 case S2 was approved only after delays and in 1 case after targeted advocacy (the country initially refused but later approved after advocacy efforts). Among the approved access, the interval from referral to effective access to treatement is largely variable. In 3 other cases, S2 requests were denied outright, due to lack of response, legal issues or cost concerns. 1 patient was able to access treatment only thanks to a crowdfunding initiative. In 2 additional cases, the families opted for alternative treatment routes (matched donor transplant).

Reimbursement of follow-up (FU) care also proved to be inconsistent. While 5 patients obtained S2 for FU visits without issues, 2 experienced delays. One patient from Norther Europe had post-treatment FU partially obtained. Another patient from Eastern Europe was denied support for FU visits. This emphasizes the need for more harmonized implementation of EU legislation, streamlined S2 approval processes and recognition of the specific needs of patients with PID requiring centralized, highly specialized treatment.

POSTER 259 - SRPRA MUTATION CAUSING SEVERE CONGENITAL NEUTROPENIA: A SHWACHMAN-DIAMOND-LIKE PHENOTYPE

AUTHORS

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Shwachman-Diamond syndrome (SDS) is a rare inherited bone marrow failure syndrome characterized by neutropenia, exocrine pancreatic insufficiency, and skeletal abnormalities. Approximately 90% of patients with SDS harbor biallelic pathogenic variants in the SBDS gene.

SRPRA (Signal Recognition Particle Receptor Alpha-subunit) encodes the soluble subunit of the SRP receptor (SRPR), an endoplasmic reticulum (ER) membrane protein involved in the co-translational targeting of nascent polypeptides to the ER. It interacts with SRP54 as part of the SRP-ribosome complex to mediate proper protein translocation.

Pathogenic variants in SRP54, DNAJC21, and EFL1—genes involved in ribosome biogenesis and protein synthesis (Fig.1)—have been identified in patients with SDS-like phenotypes, characterized primarily by severe congenital neutropenia (SCN). Dysfunction in these pathways may lead to defective protein trafficking and promote apoptosis, potentially contributing to similar clinical manifestations.

We describe a 25-year-old female patient diagnosed with SCN. Since a young age, she has been diagnosed with mononucleosis, neutropenic peritonitis (requiring appendectomy, ileostomy due to necrotic loop and ICU). Throughout the patient's childhood and adolescence, she had two pneumonias with hospitalizations, up to two otitis per year, recurrent gastroenteritis, five orbital cellulitis, and cutaneous abscesses in the buttocks and extremities. Paediatric evaluations showed low weight and height percentiles. She maintains treatment with granulocyte colony-stimulating factor, with fluctuating values between 100-2000 cells/mm3. Currently, the frequency of infections has decreased, although Periodontitis persists and remains difficult to manage.

From an immunological perspective, the levels of immunoglobulins and subclasses of T, B, and NK lymphocytes have remained within normal parameters. Furthermore, the determination of antineutrophil antibodies was negative, and the study of phagocytosis and oxidative metabolism of neutrophils was found to be normal.

Clinical exome identified a heterozygous variant of uncertain significance (VUS) in the SRPRA gene (c.1390C>G, p.Gln64Glu). This mutation was recently published as a pathogenic variant, causing SCN with recurrent pulmonary infections and growth deficiency, both in human and animal models, which may suggest a clinical presentation similar to SDS.

This highlights the importance of functional validation in VUS variants, which could directly influence the treatment and clinical management of patients.

POSTER 261 - RECURRENT RESPIRATORY INFECTIONS AS A WARNING SIGN OF PRIMARY IMMUNODEFICIENCIES: EXPERIENCE FROM A PEDIATRIC CENTER IN THE REPUBLIC OF MOLDOVA

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Objective:
To describe the clinical characteristics and diagnostic course of children with recurrent respiratory infections who were subsequently diagnosed with primary immunodeficiencies and to evaluate the associated microbiological and radiological patterns in a low-resource national setting.

Design and method:
We conducted a retrospective observational study at the Institute of Mother and Child, Pulmonology Clinic, Moldova. We analyzed the medical records of 26 children diagnosed with primary immunodeficiencies. Data included infection history, number of hospitalizations, chest imaging findings, immunological profiles, and microbiological cultures from respiratory samples. The time from the onset of first symptoms to diagnosis was calculated for each patient.

Results:
All children had at least three respiratory infections per year before diagnosis. Pneumonia was the most common presentation (73%), followed by otitis media (42%) and sinusitis (27%). The median delay from initial symptoms to referral was 18 months. Radiological evaluation revealed structural lung lesions in 46% of patients, including bronchiectasis, fibrosis and persistent atelectasis. Pathogens isolated from sputum or bronchoalveolar lavage included Staphylococcus aureus (42%), Klebsiella pneumoniae (27%) and Pseudomonas aeruginosa (19%). Immunological classifications predominantly included antibody deficiencies (16 patients), combined immunodeficiencies (5 patients) and congenital neutropenia (2 patients). Delayed recognition of immunodeficiency was associated with an increased frequency of hospitalization and chronic pulmonary complications.

Conclusions:
Recurrent respiratory infections are an early clinical feature of pediatric primary immunodeficiencies and should be actively recognized as a potential warning sign, especially in health systems with limited access to immunology. Timely referral, appropriate microbiological investigations, and early initiation of immunoglobulin therapy are crucial to prevent irreversible lung damage. Our findings highlight the need for increased awareness among pediatricians and the development of national protocols to support earlier diagnosis of primary immunodeficiencies in children.

POSTER 263 - NEUROLOGIC INVOLVEMENT IN X-LINKED AGAMMAGLOBULINEMIA: INSIGHTS FROM A SLOVENIAN COHORT

AUTHORS

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Objective:
Neurologic manifestations are increasingly recognized as an important comorbidity in X-linked agammaglobulinemia (XLA) but not well understood. They were observed in one third of XLA patients, with several cases of progressive neurodegenerative disorders without causative microorganisms reported (1,2). This study evaluated neurologic and neuropsychiatric symptoms in a Slovenian XLA cohort.

Design and method:
In this retrospective cohort study, patients with genetically confirmed XLA were identified via the national immunodeficiency registry. Clinical and demographic data were collected from medical records. Telephone interviews were conducted with patients or their parents/caregivers, using a structured questionnaire designed in collaboration with pediatric and adult neurologists, clinical immunologists and a clinical psychologist to assess neurologic and neuropsychiatric symptoms. Only chronic/repetitive symptoms were considered, except for cerebral paroxysms, where also single episodes were included.

Results:
14 patients were identified and 13 agreed to participate (age 6-61 years). The median age at diagnosis of XLA was 4.8 years (range 0.2-10.9 years). Self-reported neurologic symptoms of individual patients are presented in Table 1. At the time of data collection, 3 patients were deceased (at 18, 36 and 61 years). Four (30%) patients reported no neurologic symptoms. Patient 5 presented at 18 years with epilepsy, his brain MR showed generalized cerebral atrophy. Patient 9 had enteroviral meningitis at 21 years. Patient 11 initially presented at 8 years of age with reading and writing difficulties, followed by generalized weakness, loss of motor function, and cognitive decline by age 18; he died at 36 years of age. The definitive cause of neurologic decline was not identified, and autopsy was not performed. Apart from patient 11, so far, none of the patients reported motor impairment.

Conclusion:
Two thirds of patients in our cohort reported neurologic and neuropsychiatric symptoms. Based on this and two notable cases—one with progressive neurologic decline and another with cerebral atrophy—there is a clear need for close neurologic monitoring and further research into central nervous system involvement in XLA patients.

Literature:
1. Hernandez-Trujillo et al, J Clin Immunol 2023
2. Kasahara et al, Front Pediatr 2020

POSTER 264 - COMMON COMORBIDITIES IN CHILDREN WITH PRIMARY IMMUNODEFICIENCIES: FOCUS ON CHRONIC PULMONARY DAMAGE AND GROWTH DISORDERS IN A PEDIATRIC COHORT FROM MOLDOVA

AUTHORS

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Objective:
Evaluation of the prevalence and clinical patterns of chronic pulmonary complications and growth failure in children diagnosed with primary immunodeficiencies in a pediatric center in the Republic of Moldova.

Design and method:
This retrospective observational study included 26 pediatric patients diagnosed with primary immunodeficiencies at the Institute of Mother and Child, Pulmonology Clinic. We reviewed clinical records for the history of recurrent infections, radiological evidence of chronic lung disease, anthropometric data, immunological profiles, and nutritional status at the time of diagnosis and during follow-up. Growth was assessed using WHO Z-scores for weight and height.

Results:
Chronic pulmonary complications were identified in 12 of 26 patients (46%), including bronchiectasis (31%), persistent atelectasis (19%), and interstitial fibrosis (12%). These complications were associated with recurrent pneumonia, delayed diagnosis, and lack of early immunoglobulin replacement therapy. Radiological findings were confirmed by chest computed tomography in all cases. Growth failure was observed in 15 children (58%), of whom 8 (31%) had weight-for-age Z scores below -2 standard deviations. Height deficit was documented in 7 cases (27%), often in association with chronic respiratory disease, malabsorption, or frequent hospitalizations. The median delay in diagnosis for this subgroup was 19 months. Most of patients with comorbidities belonged to the predominantly antibody-deficient or combined immunodeficiency subgroup. Nutritional rehabilitation and immunoglobulin therapy resulted in partial recovery of growth in some cases during follow-up.

Conclusions:
Chronic lung injury and growth failure are common and clinically relevant comorbidities in children with primary immunodeficiencies. These complications often reflect delayed diagnosis and inadequate disease control. Early recognition, systematic respiratory assessment, and multidisciplinary care, including nutritional and pulmonary support—are essential to improve outcomes in pediatric patients with chronic lung disease. Our findings underscore the importance of proactive screening for comorbidities in low-resource settings.

POSTER 265 - A CASE OF TWO RARE PATHS: PNH AND AN INBORN ERROR OF IMMUNITY

AUTHORS

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Background:
Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired clonal hematopoietic stem cell disorder characterized by intravascular hemolysis, bone marrow failure, and thrombosis. Inborn errors of immunity (IEI) can rarely co-occur with PNH, complicating diagnosis and management. Here, we present a patient with combined immunodeficiency and chronic hemolytic anemia, eventually diagnosed with PNH.

Case presentation:
A 43-year-old female with a 5-year history of episodic abdominal pain, vomiting, anorexia, and constipation was found to have hemolytic anemia (reticulocytosis, elevated LDH, low haptoglobin, indirect hyperbilirubinemia). Evaluation for red cell membrane defects revealed normal G6PD and pyruvate kinase activity, decreased 5′-nucleotidase level (0.89 U/10^{12} erythrocytes), and normal osmotic fragility; Coombs tests were negative. Folic acid was initiated with partial clinical improvement. One year prior, she was referred due to newly diagnosed panhypogammaglobulinemia. Her history included parental consanguinity, recurrent sinusitis, and a single urinary tract infection. Immunophenotyping showed normal lymphocyte subsets, absent transitional and plasmablast B cells, and borderline elevated CD4+ TEM and TEMRA cells. IVIG therapy (0.8 g/kg every 21 days) was initiated. During follow-up, recurrent abdominal pain and intermittent dark-colored urine were noted. Abdominal MRI revealed bilateral renal signal changes consistent with hemosiderosis, suggestive of chronic intravascular hemolysis. FLAER-based flow cytometry identified a PNH clone: 33.61% in erythrocytes, 78.65% in monocytes, and 91.32% in granulocytes. Eculizumab therapy was planned. Clinical exome sequencing revealed a heterozygous TCF3 c.1513G>A (p.Glu505Lys) variant (VUS), previously reported in autosomal dominant agammaglobulinemia. Whole exome sequencing is pending.

Conclusion:
This case highlights the diagnostic complexity in patients presenting with overlapping features of IEI and acquired hemolytic disorders. Longitudinal immunologic and genetic evaluation is crucial. Clinicians should remain alert for PNH in patients with unexplained hemolysis and renal findings, even in the context of immunodeficiency.

POSTER 266 - CEREBRAL ATROPHY IN A YOUNG ADULT PATIENT WITH X-LINKED AGAMMAGLOBULINEMIA: A CASE REPORT

AUTHORS

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Objective:
Although frequently reported, neurologic manifestations in X-linked agammaglobulinemia (XLA) remain poorly understood. We present a case of a young XLA patient with diffuse cerebral atrophy and epilepsy.

Design and method:
Patient's clinical and demographic data were retrospectively obtained from institutional medical records.

Results:
The patient was diagnosed with agammaglobulinemia at 6 months of age following recurrent viral and middle ear infections. Genetic analysis confirmed XLA. He was treated with intravenous immunoglobulins (IVIG) since 6 months of age until age 9, then transitioned to subcutaneous immunoglobulins, without any treatment interruptions or complications. Perinatal history was unremarkable, as well as family history for immunologic and neurologic disorders.

Despite regular immunoglobulin substitution with median IgG trough levels of 9.4 g/l (range 6.62 – 12 g/l), he had multiple infections. He had a several years long chronic Haemophilus influenzae conjunctivitis until 8 years of age. He had skin abscess 2 times, impetigo, and recurrent otitis media with chronic tympanic membrane perforation. He had multiple lower respiratory tract infections (pneumonias and bronchitides with H. influenzae often isolated). CT thorax scans revealed bronchial wall thickening without bronchiectasias. Between ages 13 and 16, he had recurrent episodes of epididymitis and orchitis that responded to antibiotic therapy.

At 15, the patient experienced isolated self-limited tension-type headaches for one year, with normal EEG and neurologic findings.

At 18 (2024), he had two generalized seizures during a period of stress and sleep deprivation; EEG showed bifrontal 3 Hz slow waves in otherwise normal activity for age and state of alertness. There was no history of central nervous system infection, inflammation, or head trauma. MRI revealed diffuse cerebral atrophy, with no epileptogenic lesions described. After the introduction of valproate, he had no further seizures, nor other neurologic or neuropsychiatric symptoms. Additional neurological testing is currently in progress.

Conclusion:
This case adds to previously reported neurologic complications in XLA, including cases of chronic meningitis with no identified cause – possibly an unrecognized or atypical infection affecting the central nervous system. It stands out due to recurrent eye and sinopulmonary infections as well as epididymo-orchitis, despite immunoglobulin substitution. Notably, there were no suspicious neurologic symptoms prior to the onset of seizures and diagnosis of cerebral atrophy. This highlights the need for careful neurologic monitoring in XLA, even in the absence of clear clinical warning signs.

POSTER 267 - COMPARISON OF CAPILLARY DRIED BLOOD SPOT AND CAPILLARY MICROTUBES VERSUS VENOUS IMMUNOGLOBULIN G LEVELS FOR ROUTINE DIAGNOSTICS

AUTHORS

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Objective:
Patients with primary antibody deficiencies receiving immunoglobulin replacement therapy require frequent monitoring of immunoglobulin G (IgG) levels. Capillary IgG measurements from dried blood spots (DBS) or microtubes offer several advantages over samples obtained by venipuncture, including facilitating remote self-sampling. However, the validity of this alternative method utilizing turbidimetry in total laboratory automation is still unknown. We evaluated the comparability of IgG levels measured in venous samples with capillary blood samples collected on DBS cards and in microtubes.

Design and method:
Paired venous and capillary finger-stick DBS and microtube samples were collected from 100 patients. IgG was extracted from DBS with phosphate buffered saline and measured with a Siemens Atellica CH. For method comparison, we performed Deming regression analysis. Absolute mean bias and limits of agreement were calculated with Bland-Altman analysis. Relative mean differences were compared to a 10.9% total allowable error (TEa).

Results:
Method comparison of venous versus capillary DBS samples resulted in an R of 0.77 (Figure 1A). Mean bias was 0.23 g/L with limits of agreement of -4.06 g/L to 4.53 g/L (Figure 1B). Method comparison of venous versus capillary microtube samples resulted in an R of 1.00 (Figure 2A). Mean bias was -0.11 g/L with -0.67 g/L to 0.46 g/L limits of agreement (Figure 2B). Relative mean differences were 2.2% for DBS sampling and -0.6% for capillary sampling, both fall within 10.9% TEa.

Conclusions:
IgG measurements from DBS demonstrated a good correlation, but excessively broad limits of agreement. The bias in this method makes it unsuitable to accurately determine IgG levels. This result hampers implementation of DBS in routine diagnostics. Conversely, capillary microtube samples demonstrated a strong correlation and a low bias with narrow limits of agreement. Hence, capillary microtube samples could be a viable alternative to venipuncture.

POSTER 268 - ANTIBODIES AGAINST IL-6 AS A CAUSE OF CHRONIC STAPHYLOCOCCUS AUREUS OSTEOMYELITIS IN A GIRL

AUTHORS

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IL-6 is a pleiotropic cytokine that participates in inflammation, hematopoiesis, and in the response against viral, parasitic, fungal, and bacterial infections.

A 10-year-old girl with a history of cystitis, chickenpox, and otitis media presented for the first time with a 50% muscle tear of the right adductor magnus, diagnosed by ultrasound with an intracomparative hematoma. She was placed in pelvic immobilization and administered clindamycin and ceftriaxone, changed to cephalothin. An MRI showed bone marrow edema in the epiphyseal, metaphyseal, and proximal segment of the right femur due to an inflammatory process. A bone scan showed a positive study for an infectious process in the right hip joint and soft tissues in the area. She presented a comminuted fracture of the right femoral head due to septic arthritis and osteomyelitis of the right hip joint. Surgical cleaning and arthrotomy were performed. Joint fluid culture showed growth of S. aureus sensitive to clindamycin. She required further surgical cleaning due to severe pain. The patient completed 42 days of treatment with clindamycin and cephalothin. Flow cytometry for lymphocyte populations, immunoglobulin levels, and the DHR test were reported normal. The patient was discharged home and, at age 11, presented with pain on flexion and limitation of movement in the right hip while undergoing rehabilitation. An MRI showed minimal intra-articular fluid and evidence of osteonecrosis. The patient began treatment with clindamycin and cephalothin for 42 days and underwent arthrotomy, curettage, and bioactive glass insertion in the right hip. Culture of the hip fluid was positive for hypervirulent S. aureus. The patient was discharged home and subsequently underwent right hip arthroscope surgery with ipilateral hip arthrodystasis with external fixator placement. The patient presented with sequelae such as ankylosis of the right hip and wears the sole of his right shoe, which is 6 cm wider than his left shoe. Femoral lengthening is planned. Since the onset of the condition, C-reactive protein was reported negative with neutropenia in all tests. Autoantibodies against IL-6 were reported positive by micro-ELISA technique. We did not find other positive autoantibodies. The patient presented with persistent moderate allergic rhinitis with biometry without eosinophilia, total IgE within normal ranges with allergic sensitization against Cupressus arizonica, and four tests with decreased C4 levels. A genetic study is pending.

To our knowledge, there are very few reported cases with anti-IL-6 autoantibodies and we must rule out an inborn error of immunity as a primary cause.

POSTER 269 - CLINICAL IMPACT OF CYBB MUTATION IN FEMALE CARRIERS: A CASE OF INTRAFAMILIAL VARIABILITY

AUTHORS

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Chronic Granulomatous Disease (CGD) is an Inborn Error of Immunity that mainly affects boys, as its most frequent form is caused by mutations in the CYBB gene, located on the X chromosome. Although studies suggest that female carriers of CYBB mutations may present clinical manifestations, these are generally milder. However, studies on symptoms in carriers of CYBB mutations remain limited, which is why this study seeks to contribute to a better understanding of the subject by reporting a family with 8 boys diagnosed with CGD and 5 female carriers.

Based on the diagnosis of CGD in an 8-month-old boy, genetic testing was offered to family members who were interested. In total, 25 individuals were tested, among whom another 7 boys with CGD and 5 carriers were identified. The carriers were interviewed about their clinical symptoms at the time of the genetic test and after a year through a follow-up phone call.

The variant identified in this family was CYBB:c.T769A:p.C257S. Overall, both the affected males and the carriers displayed significant phenotypic variability. The proband's mother (C2) was tested at the age of 31 and reported only joint pain and oral mucosal ulcers. The proband's grandmother (C1), tested at the age of 59, had recurrent oral mucosal ulcers, joint pain, and severe, treatment-resistant hidradenitis suppurativa. The other three carriers are the proband's maternal aunts, C5 being the oldest (38y.o), followed by C4 (37y.o) and C3 (32y.o). C5 experienced hidradenitis suppurativa, joint pain and frequent oral mucosal ulcers; C4 had mastitis, recurrent otitis since childhood and a history of hospitalization for diarrhea and skin infection. C3 reported 1 episode of pneumonia in childhood, asthma, oral mucosa ulcers and joint pain. The clinical data reveal considerable variation in symptom severity among the carriers, without a clearly defined pattern. Despite this, the results suggest a higher occurrence of symptoms affecting the joints, skin and oral mucosa, with high occurrence of joint pain, skin lesions and oral ulcers.

Despite the limited size of the cohort, the study demonstrates the heterogeneity of symptoms presented in a single family, highlighting the importance of recognizing clinical manifestations of carriers. Often, attention to CYBB mutation carriers focuses only on the risk of conceiving children with CGD. However, the symptoms presented by these women need to be acknowledged and managed appropriately. Providing information, treatment and support to these women is fundamental to prevent more severe complications and promote quality of life.

POSTER 270 - 6-YEAR-OLD BOY WITH AUTOIMMUNE LYMPHOPROLIFERATIVE IMMUNODEFICIENCY (ALPID)

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Presentation of a patient (born in 2018) with lymphadenopathy of still unclear origin. In 2021, incidental finding of hepatosplenomegaly as well as intrathoracic and inguinal lymph node enlargement. Only mild pulmonary infections have been reported. Two lymph node biopsies and a bone marrow examination revealed no evidence of malignancy, histologically unspecific lymphadenitis. No infectious cause detected. Exclusion of the following diseases: FAS/FAS-L-ALPS, Blau syndrome, septic granulomatosis, HLH, Langerhans cell histiocytosis, mast cell disease, IgG4 related disease, hereditary globular cell anaemia, Evans syndrome, Rosai-Dorfman disease. One-time trial of prednisolone therapy 03-05/2022: lymphadenopathy initially improved, but progression after completion of steroid-therapy. Conspicuous laboratory findings: mild anaemia (10/2021), persistent mild thrombocytopenia (150-160 Gpt/l), intermittent leukopenia (4.3-5.2 Gpt/l), persistently elevated sIL2 receptor (2024: 12,274 U/ml), elevated Vit B12 (2024: 968 ng/l) as an expression of lymphoproliferation. Normal findings for: proportion of DNT-cells, expression of XIAP in lymphocytes, NK cell degranulation after prestimulation with IL-2 and NK-sensitive target cells, CTL degranulation after stimulation with anti-CD3/CD28, expression of SAP in lymphocytes, HLA-DR expression of CD4+ and CD8+ T cells, perforin expression in NK- cells, sFasL, no evidence of oligoclonal expansion of T cells. B-lymphocytopenia with B-cell differentiation defect (so far without antibody deficiency), reduced CD4+RTEs and mild hypergammaglobulinaemia was detected. CRP, calprotectin S100 A8/A9 and SAA unremarkable. No genetic cause identified in the genetic examination (trio exome). In summary, we currently assume an autoimmune lymphoproliferative immunodeficiency (ALPID). In case of progressive mediastinal lymphoproliferation, the question arises as to whether and how the patient should be treated.


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