SOUVENIR

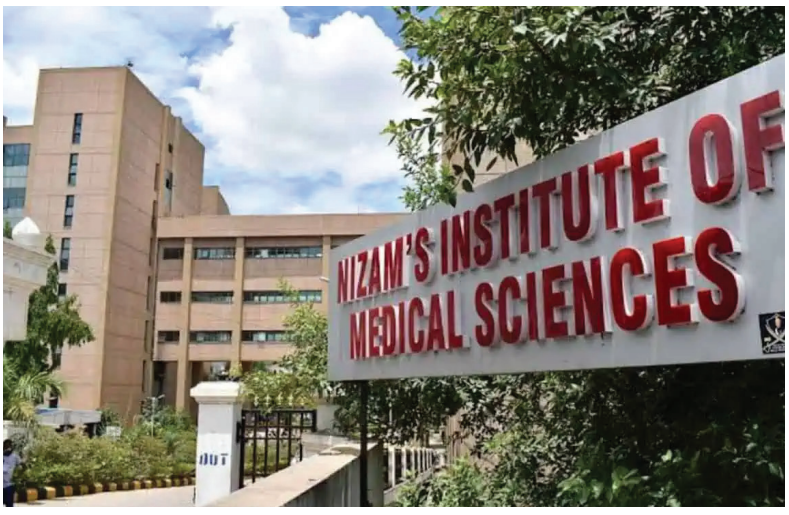
7th International Conference on Inborn Errors of Immunity

Gene discoveries to new therapies

Organised by:
Foundation for Primary Immunodeficiency diseases in collabration with Indian Society for Primary Immunodeficiencies and Department of Clinical Immunology and Rheumatology Nizam's Institute of Medical Sciences.

March 8th-10th, 2025

ITC Kohenur Hotel, Hyderabad



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ISPID Indian Society For Primary Immune Deficiency

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ICIEI 2025

7th International Conference on Inborn Errors of Immunity

8TH – 10TH MARCH 2025 – HYDERABAD, INDIA

MESSAGE FROM THE HEALTH SECRETARY

Message from Dr. Christina Z Chongthu
Secretary, Health Medical and Family Welfare
Government of Telangana

For the 7th International Conference on Inborn Errors of Immunity (ICIEI 2025) Souvenir

Dear Delegates, Esteemed Experts, and Distinguished Guests,

It is with great pride and privilege that I extend my warmest greetings to all participants of the 7th International Conference on Inborn Errors of Immunity (ICIEI 2025). This prestigious gathering, centered around the theme "From Gene Discovery to New Therapies," marks an important milestone in advancing our understanding and treatment of inborn errors of immunity (IEI).

The remarkable progress in genomic medicine and immunology has opened new frontiers in the diagnosis and management of IEI, offering hope to patients and families worldwide. As Telangana continues to emerge as a hub for cutting-edge medical research and innovation, we are honored to host this esteemed assembly of global experts, researchers, and clinicians committed to transforming healthcare through scientific advancements.

The Government of Telangana remains steadfast in its support for groundbreaking medical research and improved healthcare delivery. We believe that collaborations forged in conferences like ICIEI 2025 will not only drive scientific breakthroughs but also enhance patient care and public health policies on a larger scale.

I commend the Department of Clinical Immunology and Rheumatology, Nizam's Institute of Medical Sciences (NIMS) for their dedication in organizing this significant event. I extend my best wishes to all participants and encourage meaningful discussions that will pave the way for future innovations in immunology.

May ICIEI 2025 be a platform for inspiration, knowledge-sharing, and global collaboration in our shared mission to combat immune disorders and improve lives.

Best Regards,

Dr. Christina Z Chongthu
Health Secretary, Government of Telangana

MESSAGE FROM THE FPID FOUNDER

Dear Esteemed Colleagues and participants:

It is with great excitement and anticipation that I welcome you to the 7 th International Conference on Inborn Errors of Immunity. This gathering serves as a pivotal platform for researchers and clinicians to advance our understanding and therapy of IEIs. As we come together, we are reminded of the profound impact that collaborative efforts can have on improving the lives of individuals affected by IEIs.

With current 555 IEIs, 508 disease causing genes, and 67 novel monogenic defects and 2 phenocopies that have been discovered in just the last two years, the need for innovative research and clinical practices have never been greater. Although individual IEI are rare, collectively IEIs are not, and they represent a significant health burden. A recent study reported that the incidence of IEIs in the USA was 6 per 10,000 people.

This conference aims to foster dialogue, share breakthroughs, and highlights the latest advancements in discovering disease causing genes, and therapeutic strategies including gene transfer and gene editing for IEI. Throughout this event, you will have an opportunity to engage with leading experts, participate in interactive poster sessions, and explore the latest research findings through presentations and panel discussions. I encourage you to take full advantage of this unique forum to exchange ideas, establish new collaborations, and inspire one another in our shared mission.

I extend my personal gratitude to speakers who have taken time from their busy schedule to share their cutting-edge research. My thanks to Drs. Casanova and Notarangelo for helping me to organize this conference. My very special thanks to Dr. Liza Rajasekhar, organizing secretary and her team for an outstanding organization of this event. I also Thank our sponsors for their unwavering support, which makes this event possible.Together, we can continue to elevate the standard of care and enhance the quality of those living with IEI.

I look forward to a stimulating and productive conference.

Sincerely,

Sudhir Gupta, MD, Ph.D., D.Sc., MACP
Founder and Chairman, Board of Directors, FPID
Professor of Medicine and Chief of Basic and Clinical Immunology
University of California at Irvine, California

MESSAGE FROM THE ISPID PRESIDENT

Dear Colleagues, and Esteemed Participants

It is with great honor and enthusiasm that I extend my warmest greetings to all attendees of the 7th International Conference on Inborn Errors of Immunity (ICIEI 2025). This prestigious event, organized by the Foundation of Primary Immunodeficiency Diseases, Indian Society of Primary Immune deficiency and hosted locally by the Department of Clinical Immunology and Rheumatology, Nizam's Institute of Medical Sciences, is a testament to the relentless pursuit of scientific advancements in the field of immunodeficiencies.

The theme of this year's conference Gene Discoveries to New Therapies focuses on the remarkable therapeutic potential of the understanding of the genetic basis of immune disorders. We are witness to a transformative era in the management of inborn errors of immunity. This conference brings to your doorstep a platform where clinicians, researchers, and industry leaders will exchange knowledge, discuss emerging therapies, that will shape the future of immunological care.

I extend my heartfelt gratitude to the distinguished speakers, researchers, and delegates who bring their expertise and dedication to this forum.

A special note of appreciation to the Department of Clinical Immunology and Rheumatology, Nizam's Institute of Medical Sciences, and the organizing committee for their tireless efforts in hosting the global experts to create an enriching academic experience.

Together, let us work towards a future where cutting-edge research translates into life-changing therapies for patients worldwide.

Wishing you a successful and inspiring conference!

Amita Aggarwal
Professor and Head
Department of Clinical Immunology and Rheumatology
Sanjay Gandhi Institute of Medical Education and Research
President, Indian Society for Primary Immunodeficiency
Website: www.ispid.org.in

MESSAGE FROM THE ISPID SECRETARY

Dear Colleagues, and Esteemed Participants

It is with great enthusiasm that I extend my best wishes for this landmark international conference on Inborn Errors of Immunity being organised at Hyderabad. This gathering is not just a scientific meeting; it is a testament to how far Immunology in India has come—once a niche subject, now a dynamic and rapidly evolving field!

Over the years, our understanding of immune deficiencies has deepened, diagnostic capabilities have improved, and treatment options have expanded. Yet, the journey is far from over. For every patient diagnosed, there are many more still awaiting recognition. For every therapeutic breakthrough, there remain challenges in accessibility and affordability.

This conference brings together the best minds in the field, fostering collaboration, innovation, and a shared commitment to improving patient outcomes. May the discussions here inspire new research, new policies, and new hope for those living with immune deficiencies.

Wishing the Congress grand success!

Dr. Sagar Bhattad
Secretary, Indian Society for Primary Immune Deficiency

MESSAGE FROM THE DIRECTOR, NIMS

Dear Delegates, Senior scientists, and Colleagues,

It gives me a great sense of pride to welcome you all to the 7th International Conference on Inborn Errors of Immunity, ICIEI 2025, which is organised in Hyderabad by the Department of Clinical Immunology and Rheumatology of our Institute

As I understand, this conference comes to our city after a decade of a remarkable journey between the Foundation of Primary Immunodeficiency, USA, and NIMS. The support by FPID for diagnostic support to the underserved of the state has been furthered to bring together a remarkable gathering of experts, clinicians, and researchers dedicated to advancing the understanding of inborn errors of immunity.

At NIMS, we remain committed to fostering academic excellence, innovative research, and collaborative learning in all fields and the field of immunology. It is our privilege to co-host this prestigious event, providing a platform for meaningful discussions, knowledge exchange, and groundbreaking discoveries that will have a lasting impact on patient care.

I extend my deepest appreciation to the distinguished speakers, esteemed delegates, and young researchers whose contributions will enrich this conference. I wish the Department of Clinical Immunology and Rheumatology and the organizing committee for their dedication and meticulous planning in making ICIEI 2025 a grand success.

Warm regards,

Bheerappa Nagari
Director, Nizam's Institute of Medical Sciences (NIMS)
Website: www.nims.edu.in
ICIEI 2025 Website: www.iciei2025.org

MESSAGE FROM THE ORGANISING SECRETARY

Dear Friends,

It is my proud privilege to welcome you to the 7th International Conference on Inborn Errors of Immunity (ICIEI 2025).
The theme of this year's conference, "Gene Discoveries to New Therapies," underscores the rapid advancements in our understanding of inborn errors of immunity (IEI) and the transition from genetic discoveries to groundbreaking therapeutic strategies. Over the years, research in this field has led to significant improvements in early diagnosis, precision medicine, and innovative and improving treatment options, improving the lives of patients worldwide.
This conference is bringing together leading researchers, young scientists, and clinicians to share insights, discussthe latest developments, to address the challenges in immunodeficiency disorders. Through keynote lectures, research presentations and panel discussions, we have created a programme that will provide a stimulating environment fostering learning and improvement in skills.
I extend my heartfelt gratitude to Prof Gupta, ISPID, our distinguished speakers, participants, and sponsors for their invaluable support and contributions. A special thanks to the organizing team, faculty members, and volunteers whose dedication and hard work have made this event possible.
Please make the most of this unique event which will hopefully allow each one of us to be enriched with knowledge that will advance our research and clinical practices.

Wishing you a fruitful and inspiring conference experience!
Warm regards,

Liza Rajasekhar
Organizing Secretary, ICIEI 2025
Dean, Senior Professor and Head
Department of Clinical Immunology and Rheumatology
Nizam's Institute of Medical Sciences (NIMS)
Website: www.nims.edu.in
ICIEI 2025 Website: www.iciei2025.org

7th INTERNATIONAL CONFERENCE ON INBORN ERRORS OF IMMUNITY

Theme-From gene discovery to new therapies

ITC Kohenur Hotel, Hyderabad, India March 8-10, 2025

DAY-1	8th March		8:00 AM Registration
SESSION - I	**TOPIC**	**SPEAKER**	**CHAIRPERSONS**
9:00-9:40 AM	The Immunopathological landscape of human pre-TCRα deficiency: From rare to common variants	**Vivian Beziat** Institut Imagine, Paris, France	Jean Laurent Casanova, Manisha Madkaikar
9:40-10:10 AM	Regulators of genome superstructure in T-cell development	**Kushagra Bansal** Molecular Biology & Genetics unit at Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India	
10:10-10:50 AM	Life and Death by Thousand Bites	Sudhir Gupta University of California, Irvine, US	Murali Dharan Bhasyam, Suma Balan
10:50-11:30 AM	Coffee Break		
11:30-12:00 PM	INAUGURATION FUNCTION		
SESSION - II			
12:00-12:40 PM	Platform Presentations (3)	Rashi, Kanmani K, Umair Ahmed Bargir	Amita Aggarwal, Amit Rawat, Manisha Madkaikar, Suma Balan
12:40-1:30 PM	**Poster View**/Lunch Break	Two groups of Judges for poster walk	Stu Tangye, Biman Saikia, Narender Mehra, Sanjib Mondal
SESSION - III			
1:30-2:00 PM	Innovations in T cell assays: Application in infections and immune deficiency disorders	**Nimesh Gupta** National Institute of Immunology,India	Sudhir Gupta, Gautam Saharia
2:00-2:40 PM	IgM autoantibodies in CVID patients, origins and implications	**Neil Romberg** USA-Children's Hospital of Philadelphia (CHOP), USA	
2:40-3:20 PM	Dysregulation of IgE in IEI	**Stu Tangye** Garvan Institute of Medical Research, UNSW, Sydney, Australia	Surjit Singh, Ashwin Kotnis
3:20-3:50 PM	Unravelling the Link Between Autoimmune Cytopenias, Benign Lymphoproliferation, and Inborn Errors of Immunity	Priyanka Setia National Institute of Immunohaematology, Mumbai, India	
3:50-4:30 PM	Coffee Break		
4:30-5:15 PM	Sudhir Gupta Oration- Dissecting congenital T-cell lymphopenia: A journey into T-cell and thymus development	**Luigi Notarangelo** Chief of the LCIM, NIAID, NIH, Bethesda, USA	Amita Aggarwal Sagar Bhattad
5:15 PM	Adjournment/EB meeting		
6:00 PM	Reception/Dinner		

7th INTERNATIONAL CONFERENCE ON INBORN ERRORS OF IMMUNITY

Theme-From gene discovery to new therapies

ITC Kohenur Hotel, Hyderabad, India March 8-10, 2025

DAY-2 **9th March**

SESSION - IV	TOPIC	SPEAKER	CHAIRPERSONS
9:00-9:40 AM	Human Genetic and Immunological determinants of severe infections	**Jean-Laurent Casanova** The Rockefeller University, New York, USA.	Geetha Govindaraj, Umabala, Tara Roshni Pal
9:40-10:00 AM	Viral infection as clue to Inborn errors of Immunity	**Mukesh Desai** Wadia Hospital, Mumbai, India	
10:00-10:20 AM	Clinical and molecular spectrum of CGD in India	Vignesh Pandiarajan Allergy and Immunology Unit, Advanced Pediatrics Centre, PGIMER, Chandigarh, India	
10:20-10:40 AM	Coffee Break		
SESSION - V			
10:40-11:20 AM	IKAROS family proteins in Infection, Autoimmunity and Malignancy	**Tomohiro Morio** Tokyo Medical and Dental University (TMDU), Japan.	Neil Romberg, Ashwin Kotnis
11:20-11:50 AM	Platform presentations (3)	Abhikarsh Gupta, Umair Ahmed Bargir, Kavitha Ganesan	Amita Aggarwal, Amit Rawat, Manisha Madkaikar, Suma Balan
11:50-1:50 PM	**Poster View**/Lunch Break		Stu Tangye, Biman Saikia, Narender Mehra, Sanjib Mondal
SESSION - VI			
1:50-2:30 PM	IEI in patients with herpes virus infections in CNS	**Trine Mogensen** Aarhus University, Department of Biomedicine Clinical Medicine and Infectious Diseases, Denmark	Vijay V Yeldandi, Revathi Raj
2:30-2:50 PM	Experience with Interleukin 1β activation disorders at PGIMER:Challenges in diagnosis and management	**Deepti Suri** Postgraduate Institute of Medical Sciences Chandigarh, India	Ashwin Dalal, Vijaya Gowri
2:50-3:30 PM	New and old therapies for IL-1 mediated autoinflammatory diseases	**Hal Hoffman** University of California, San Diego (UCSD), USA	
3:30-4:00 PM	Platform presentations (3)	Kavitha Ganesan, Lavina Temkar, Sanghamitra Machua	Amita Aggarwal, Amit Rawat, Manisha Madkaikar, Suma Balan
4:00-4:30 PM	Coffee Break		
4:30-5:10 PM	New Frontiers in Targeted Therapy : Dispatch From Bethesda	Dan Kastner National Human Genome Research Institute NIH, USA	Sudhir Gupta, Liza Rajasekhar
5:10 PM	Adjourn /GBM meeting		

7th INTERNATIONAL CONFERENCE ON INBORN ERRORS OF IMMUNITY

Theme-From gene discovery to new therapies

ITC Kohenur Hotel, Hyderabad, India March 8-10, 2025

DAY-3	10th March		
SESSION - VII	**TOPIC**	**SPEAKER**	**CHAIRPERSONS**
9:00-9:40AM	Stem cell therapy for PID-A personalized perspective	**Andy Gennery** University of Newcastle upon Tyne, UK	Vijay Kumar Kutala, A V M Narendra
9:40-10:20AM	HSCT as a treatment for autoinflammatory conditions	**Marco Gattorno** Rheumatology and Autoinflammatory diseases, IRCSS Istituto Giannina Gaslini, Genova, Italy	
10:20-10:40AM	Coffee Break		
10:40-11:00 AM	HSCT in SCID experience and challenges	**Ramya Uppuluri** Apollo Cancer Hospitals, Chennai, India	Able Lawrence, Geeta Govindaraj
11:00 -11:20AM	Tailoring Transplants-The immunologists role in navigating immunodeficiencies	**Sagar Bhattad** Aster CMI Hospitals, India	
11:20-12:00 PM	Thymus transplantation for congenital athymia	**Alexandra Kreins** Great Ormond Street Hospital for Children, London, UK	
12:00-1:00 PM	Lunch Break		
SESSION - VIII			
1:00 -1:40PM	Universal correction strategies to correct PID mutations: How do we get to patients ?	**Matthew Porteus** Stanford University, Stanford Cancer Institute, Institute for Stem Cell Biology and Regenerative Medicine, USA	Shagun Aggarwal, Vijaya Lakshmi
1:40PM :3:30PM	Panel discussion on challenging cases	Moderator- Dr Sunitha Kayidhi, Dr Anjani Gummadi	Panelists: Hal Hoffman, Nita Radhakrishnan, Rudrarpan Chatterjee, Prajyna Ranganath, Amit Rawat
3:30 PM	Closing and Coffee		

PRE-CONFERENCE WORKSHOP ON APPROACH TO IEI CONDUCTED AT NIMS ON 23-02-2025

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ORAL PRESENTATIONS

OP-1

Abstract Title:

STAT3 Loss of Function in Hyper-IgE Syndrome: Unveiling Molecular Mechanisms of Bone Dysregulation

Abstract no: 5

All authors: Rashi[1], Abha Tiwari[1], Harshika Choudhary[1], Ankur Jindal[1], Amit Rawat[1], Deepti Suri[1], Surjit Singh[1], Biman Saikia[1]

Complete details of Institute including city state -

[1] Postgraduate Institute of Medical Education & Research, Chandigarh, India

Presenting Author email- rashigarg2007@gmail.com

Abstract:

Background:

Hyper IgE syndrome (HIES) is a rare disorder caused majorly by a mutation in the STAT3 gene. Up to 70% of patients experience skeletal and craniofacial abnormalities. Previous studies from our centre have shown that STAT3 plays a role in osteoclastogenesis (unpublished data). Recent studies using mouse models have demonstrated that STAT3 knockdown in osteoblasts (OB), but not osteoclasts (OC), leads to similar skeletal defects. Despite these findings, the role of STAT3 in mediating OB-OC crosstalk remains unclear.

Objective:

To decipher osteoblastic-osteoclastic dysregulation in STAT3-LOF-HIES patients by analysing 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. Patient and control PBMC-derived MSCs were differentiated into osteoblasts. To assess the STAT3-osteogenesis pathway, ALP activity, mineralisation (Alizarin Red staining), and RNA sequencing were analysed. Upregulated and downregulated genes were validated with RT-PCR.

Results:

The osteogenic potential of patients was significantly reduced compared to controls, as evidenced by lower Alizarin Red staining and decreased ALP activity levels. RNA sequencing analysis revealed 2,459 genes downregulated and 231 genes upregulated by more than 1.5-fold in patients compared to controls. Gene ontology analysis of significantly downregulated genes showed enrichment in biological processes involved in osteoblast differentiation that correlate with the skeletal abnormalities observed in patients. Key affected genes included RUNX2, DLX5, STAT3, and COL2A1, validated using RT-PCR and found to be significantly downregulated in patients compared to controls ($p = 0.0286$*).

Conclusions:

Our study showed significant downregulation of patients' genes involved in the STAT3-osteogenesis pathway. RUNX2 and DLX5 are crucial regulators of osteoblast differentiation, with RUNX2 governing bone formation and DLX5 driving early osteoblast development. Col2A1, a cartilage matrix component, reflects extracellular matrix defects critical for osteogenesis. The downregulation of these genes suggests impaired osteoblast function, potentially driven by defective STAT3 signalling.

OP-2

Abstract Title:

A study on children with autoimmune cytopenias and their association with inborn errors of immunity

Abstract no: 15

All authors: Dr Kanmani K[1], Dr Meena S[1], Dr Arathi Srinivasan[1], Dr Julius Scott[1]

Complete details of Institute including city state:

[1] KKCTH, 12 A Nageshwara road, Chennai, Tamil Nadu, India

Presenting Author email: drkanmanikannan03@gmail.com

Abstract:

Background:

Autoimmune cytopenias are a group of disorders having the hosts immune system attack their own blood cells causing low counts. Genetic predisposition, rheumatic disorders, infections and some malignancies can be the causes but Autoimmune cytopenia can be the initial or sometimes the only finding.

Objective:

To evaluate cases of autoimmune cytopenias and their association with inborn error of immunity.

Methods:

We included a hospital-based data from KKCTH hospital, Chennai from the past 4 years 2020-2024 of children(Age 0-21) diagnosed with immune thrombocytopenia and autoimmune haemolytic anemia. A retrospective analysis with immune cytopenias, disease profile and outcome were entered.

Results:

A study population of 186 children were enrolled with immune cytopenias including 43 children(23.11%) of AIHA and 143 children(86.88%) of ITP. The mean age were 8.5 years of AIHA and 8.9 years of ITP. 24 out of 43 children(55.81%) with AIHA were girls and 19 out of 43(44.18%) were boys. Likewise, 66 out of 143 children(46.15%) with ITP were girls and 76 out of 143(53.14%) were boys. Out of these isolated AIHA were 34 out of 186 (18.27%), isolated ITP were 138 out of 186(74.19%).

Children diagnosed with IEI were 14 children out of 186(7.5%) out of which, 1 in 14(7.14%) presented with isolated AIHA, 2 in 14(14.28%) had AIHA with systemic manifestations like neonatal diabetes and pneumonia, 9 out of 14(64.28%) presented with autoimmune anemia and thrombocytopenia while 2 out of 14(14.28%) presented with isolated thrombocytopenia.

8 out of 14(57.14%) children with IEI had age of onset less than one year and 4 were of age group 1-2 years. The most common IEI noted were WAS i.e, 6 in 14(42.85%) followed by LRBA, 3 out of 14(21.42%). The other genetic disorders noted were SCID, ALPS and CARD11(-) mutations

Conclusions:

IEI can present with children with immune cytopenias who have a baseline immunological profile normal and is more commonly seen in children with initial age of presentation less than 2 years. Use of genetic tests can benefit the children by helping in early diagnosis and intervention in the form of targeted therapies and transplants showing better outcomes.

OP-3

Abstract Title:

Investigating the molecular underpinnings of functional defects in Familial Hemophagocytic Lymphohistiocytosis-4 (FHLH-4) patient T cells.

Abstract no: 22

All authors: Abhikarsh Gupta[1], Monika Vig[1]

Complete details of Institute including city state:

[1]Tata Institute of Fundamental Research, 36/P Gopapally, Serilingampally, Hyderabad, Telangana, India.

Presenting Author email: gabhikarsh@tifrh.res.in

Abstract:

Background:

Familial Hemophagocytic Lymphoistiocytosis-4 (FHLH-4) is a life threatening, hyperinflammatory, autosomal recessive disorder. The primary defect lies in CD8 T and NK cells which fail to effectively degranulate and eliminate the pathogenic challenge resulting in chronic activation of macrophages (histiocytes). Histiocytes in turn secrete excessive cytokines leading to autoimmunity and organ damage unless intervened by bone marrow transplants (BMT).

FHLH-4 results from mutations in a Q-SNARE, known as Syntaxin-11. Like other Q-SNAREs, mutations in Syntaxin-11 are associated with defective exocytosis, despite lack of concrete molecular evidence. Interestingly, the disease also presents with excessive secretion of cytokines, which is contrary to and cannot be reconciled with defective exocytosis. We have found that an FHLH-4 patient with a deletion frameshift mutation harbours a severe defect in store-operated calcium entry (SOCE) from Orai1. We present mechanistic dissection of the defect and propose alternatives to BMT.

Objective:

To dissect the molecular mechanism of FHLH-4 in human patients harbouring mutations in Syntaxin-11.
Rescue the functional defects in FHLH4 and STX11 deficient T cells.

Methods:

Measurement of degranulation in T cells derived from FHLH4 patients.
Measurement of SOCE and NFAT activation in FHLH4 patient T cells and STX11 depleted Jurkat T cells.
Measurement of IL-2 transcription in FHLH4 patient T cells by Q-PCR.
Use of calcium ionophore or in-silico designed CRAC channel agonists to rescue FHLH4 T cell defects.

Results:

T-cells isolated from a 4-year-old Iranian FHLH-4 patient who had developed all the typical symptoms of FHLH-4 showed significant defects in SOCE (Figure 1).
Ectopic expression of Syntaxin-11 rescued the defect in SOCE (Figure 1).
Syntaxin-11 deficient Jurkat and FHLH-4 patient T cells show impaired nuclear translocation of NFAT and IL-2 transcription.
IL-2 transcription in STX11 deficient T cells could be rescued by using Ionomycin, a calcium ionophore.
Defective degranulation in FHLH-4 patient T-cells could be rescued using Ionomycin.

Conclusions:

We propose that design and early administration of CRAC channel agonists to FHLH-4 patients with mutations

in STX11 could correct functional defects in T cells and prevent the establishment of chronic infections and development of autoimmunity.

Reference: https://www.biorxiv.org/content/10.1101/2024.10.25.620144v1

Figures, tables:

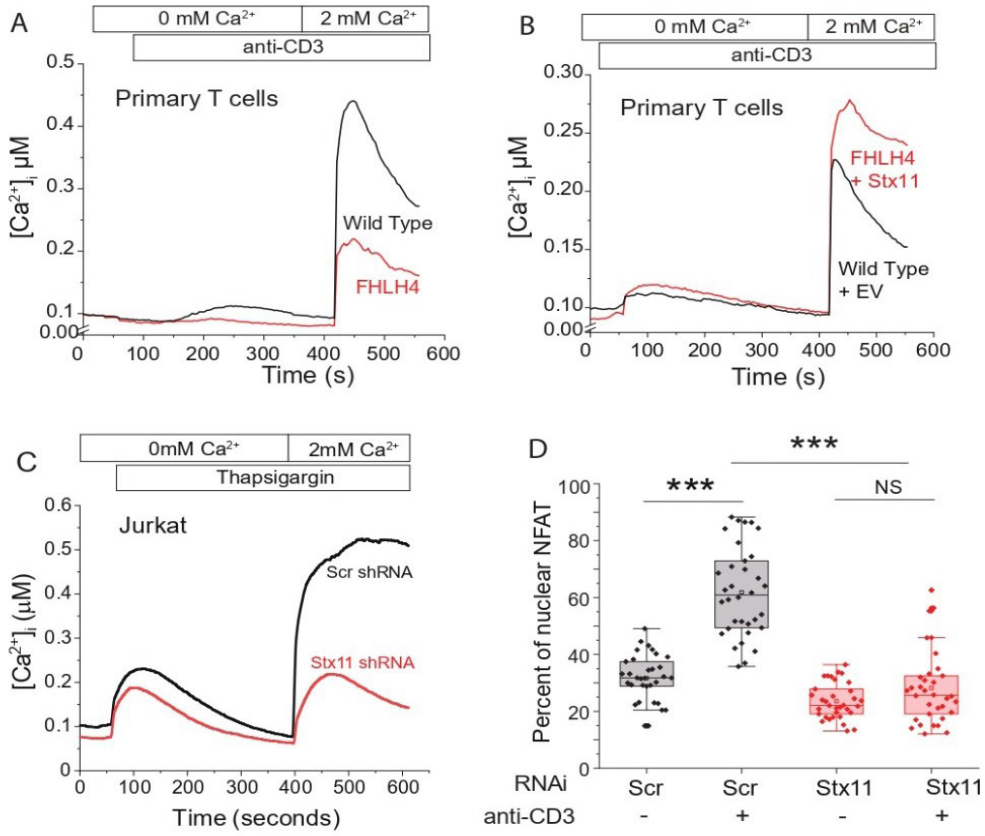

Figure 1. (A) Fura-2 calcium imaging assay measuring anti-CD3 induced SOCE in healthy donor and FHLH4 T cells. (B) Fura-2 calcium imaging assay measuring SOCE in healthy donor and FHLH4 T cells expressing either empty vector (EV) or wildtype human STX11, respectively. (C) Measurement of thapsigargin (TG) induced SOCE in Jurkat T cells after shRNA mediated depletion of STX11. (D) Box and whisker plot showing percent nuclear NFAT, post activation in control (grey box) and Stx11 depleted (red box) Jurkat T cells quantified from 40-50 cells. *P<0.05; **P<0.01; ***P<0.001 using two-tailed Student's t test.

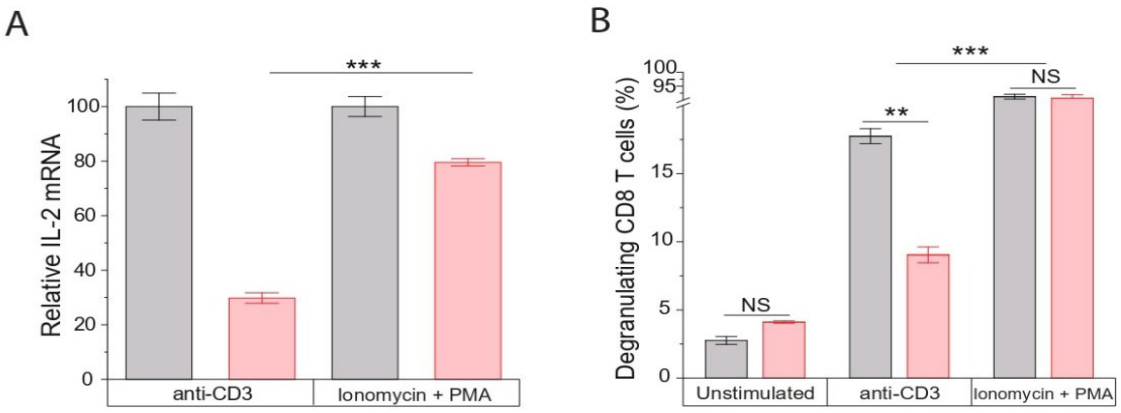

Figure 2. (A) Analysis of IL-2 expression in control and FHLH4 T cells. In vitro cultured healthy donor (grey bars) and FHLH4 patient T cells(pink bars) were rested and stimulated with either plate coated anti-CD3 + soluble anti-CD28 or PMA + Ionomycin for 6 hours. Total RNA was extracted and subjected to quantitative PCR analysis using Taqman probes for IL-2. (B) Quantification of granule release assay performed on the *in vitro* cultured healthy donor (grey bars) and FHLH4 patient CD8 T cells (pink bars). PBMCs were periodically stimulated with (2ug/ml) PHA and IL-2 for expansion and pre-activation of cells. On the day of assay, cells were restimulated with plate coated anti-CD3+ anti-CD28 or PMA + Ionomycin and analyzed. *P<0.05; **P<0.01; ***P<0.001 using two-tailed Student's t-test.

OP-4

Abstract Title:

Fifteen years follow up of haploidentical HSCT for children with IEI – TCR-αβ/CD 19 depleted or T replete graft with post-transplant cyclophosphamide in children undergoing haploidentical hematopoietic stem cell transplant for inborn error of immunity

Abstract no: 25

All authors: Kavitha Ganesan[1], Anupama N[1], Vijayashree M[1], Nithya S[1], Minakshi B[1], Anurag NR[1], Ramya U[1], Revathi R[1]

Complete details of Institute including city state:

[1] Apollo Speciality Hospital, Annalsalai, Teynampet, Chennai, Tamil Nadu, India.

Presenting Author email: kavitha5293dr@gmail.com

Abstract:

A haploidentical-related donor is readily available for children with inborn errors of immunity (IEI) requiring hematopoietic stem cell transplantation (HSCT) as alternative donors for those with no matched family donors, with TCRαβ/CD19-depletion and post-transplant cyclophosphamide (PTCY) being the predominant techniques for T-cell depletion. Our study aimed to analyze the outcomes of TCRαβ/CD19 depleted graft and T-replete graft with PTCY in children with IEIs.

Methods:

We conducted a retrospective analysis of the children with IEI who underwent haploidentical donor HSCT at our center between April 2009 to September 2024 over a 15-year period. We collected data on the underlying diagnosis, donor source, conditioning, engraftment, graft versus host disease (GVHD), viral reactivation, and survival from chart reviews and performed statistical analysis using SPSS software. The study was approved by our Institutional Ethics Committee.

Results:

From April 2009 to September 2024, we performed HSCT for 230 children with inborn errors of immunity, of which 105(45%) children had a haploidentical HSCT. We used a TCR deplete technique in 65(62%) children while T cell replete transplant was done in 40(38%) children.

Engraftment rates were similar in both the groups. The rates of acute GVHD and chronic GVHD between TCRαβ/CD19-depletion vs PTCY were 5(7.5%) vs 6(15%) and 9(14%) vs 7(17%) respectively. Viral reactivation rates were 65% vs 45% respectively in TCRαβ/CD19-depleted vs PTCY cohorts. The overall survival in the TCRαβ/CD19-depleted cohort vs PTCY were 66% vs 55%.

The overall survival in this cohort was 62%, with most of the mortality secondary to viral infections. Mortality was higher among those with poor immune reconstitution. The individual variables under study have been listed in the table as below.

Conclusions:

The survival was superior in TCRαβ/CD19-depletion compared to PTCY with viral reactivation rated been extremely high in the former group. The promise of early engraftment and low morbidity during HSCT and low rates of graft versus host disease was offset by persistent viraemia. We need early diagnosis of IEI by raising awareness with timely interventions improves the overall outcomes. Letermovir prophylaxis and memory cell addback to improve immune reconstitution and viral specific T cell infusions will result in over 90% survival as seen in data from high income countries. Despite higher cost, the way forward for children with IEI would be haploidentical HSCT using TCRαβ/CD19-depletion.

Figures, tables:

Variables	TCR ALPHA BETA DEPLETED (N 65)	PTCY (N 40)
Total number of children	65	40
Median Age	2.2 year	5 years
Age range	2month-16 years	2month-14 year
Male:Female	3:1	4:1
Diagnosis: SCID Non SCID	 21 44	 5 35
Conditioning: MAC RIC No conditioning	 57 3 5	 7 31 2
Source stem cell: Bone marrow PBSC	 0 65	 7 33
CD34	11.2 times	6.4 times
Engraftment	58/65(89%)	34/40(85%)
Acute GVHD	5/65(7.5%)	6/40(15%)
Chronic GVHD	9/65(13.8%)	7/40(17.5%)
Viral Reactivation	42/65(64.5%)	18/40(45%)
Dead	22/65(34%)	18/40(45%)
Survival	66%	55%
Cause of death		

OP-5

Abstract Title:

Hematopoietic stem cell transplantation in children with neutrophil disorders: a single centre experience from South India

Abstract no: 26

All authors: Kavitha Ganesan[1], Anupama N[1], Vijayashree M[1], Nithya S[1], Minakshi B[1], Anurag NR[1], Ramya U[1], Revathi R[1]

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Abstract:

Introduction: Children with neutrophil disorders chronic granulomatous disease (CGD), leukocyte adhesion deficiency (LAD), and severe congenital neutropenia (SCN) present with recurrent life-threatening infections. Hematopoietic stem cell transplantation (HSCT) is an available curative option. We present our data on the outcome of children undergoing HSCT for neutrophil disorders.

Methods: We conducted a retrospective analysis and included children up to 18 years of age diagnosed to have genetic neutrophil disorders who underwent HSCT from March 2012 to October 2024 over twelve years.

Results: Forty-two children with neutrophil disorders underwent 44 transplants (CGD-27, LAD-11, SCN-6) were included with male to female ratio of 3.7:1 and the median age at HSCT was four years (range 3monts to 18 years). Among the children with CGD, all (100%) had received treatment for tuberculosis and/or disseminated BCGosis and at least 70% children had staphylococcal pneumonia. Among the 11 children with LAD, all children presented with non-healing ulcers and 50% of these required stabilization with anti-staphylococcal antibiotics and buffy coat infusions prior to HSCT. All six children with SCN had over 3 severe febrile illnesses per year. We used myeloablative conditioning based on fludarabine with busulfan, treosulphan or melphalan in 40 children (91%) and reduced-intensity conditioning in 4 children (9%). Twenty-one (47%) had haplo-identical HSCT, matched family donor in 14 (32%), followed by a matched unrelated donor in 9 (21%). Out of the children with haplo HSCT, 18 had TCR alpha beta depletion while three children had post-transplant cyclophosphamide. Peripheral blood stem cell was the predominant stem cell source in 37(86%). We documented engraftment in 42 children (96%), of which three children had secondary graft failure (7%). Viral reactivation was noted in 15 (35%) children cytomegalovirus (CMV) followed by adenovirus. Direct deaths related to CMV was noted in two children who succumbed to CMV pneumonia and CMV induced acute kidney failure. The incidence of acute GVHD was high at 16 (37%) in our cohort. Chronic skin GVHD was seen in eleven children (26%) with extensive skin and musculoskeletal GVHD in three children (7%). The overall survival in our cohort was 75% and each disease was 70% in CGD, 82% in LAD and 83% in SCN.

Conclusions: HSCT achieves a cure in children with neutrophil disorders with the best outcomes in SCN followed by LAD. Myeloablative conditioning results in engraftment with an overall survival of 75%. Haploidentical HSCT using TCR alpha beta depletion is safe in infants.

OP-6

Abstract Title:

Augmenting the Jeffery Modell Criteria for Optimizing screening for inborn errors of immunity: a retrospective analysis

Abstract no: 46

All authors: Lavina Temkar[1], Reetika Malik Yadav[1], Umair Bargir[1], Amruta Dhawale[1], Pallavi Gaikwad[1], Aparna Dalvi1, Shweta Shinde[1], Priyanka Setia[1], Neha Jodhawat[1], Disha Vedpathak[1], Ankita Parab[1], Nidhi Desai[1], Maya Gupta[1], Manisha Madkaikar[1]

Complete details of Institute including city state -

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Abstract:

Objective:

Next generation sequencing is often used as a tool parallel to immunological investigations for diagnosis of inborn errors of immunity (IEIs). The Jeffrey Modell criteria have been used to guide screening for IEIs. Our study explored JMF criteria along with additional presentations and some laboratory parameters and assessed their effectiveness for guiding molecular screening for IEI.

Methods:

We performed a retrospective analysis of molecularly characterized patients categorized into three – those with pathogenic/likely pathogenic variant (n=50), variants of uncertain significance (n=50), and no variant (n=50) identified in WES (control group). In addition to the JMF criteria, medical records of the patients were evaluated for presence of autoimmunity, autoinflammatory features, vaccine complications, persistent fever with bi-cytopenia, consanguinity, and laboratory parameters – low naïve T-cell(%) and hypogammaglobulinemia at initial presentation. Chi-square test was to shortlist additional criteria with p-value less than 0.25 for multi-variate analysis. A total of 28 models were considered with different combinations of additional presentations along with JMF score of two or more. The AIC and BIC of all models were compared to determine the best model, followed by determining the sensitivity and specificity of the best model. Data was analysed using Epi Info v7.2.5.0 and STATA v17.0.

Results:

The JMF scores of the pathogenic/likely pathogenic group (3.5 ± 1.93) and VUS (2.72 ± 1.68) groups were significantly higher than those of the control group (1.68 ± 1.38) ($p < 0.05$). Among the additional presentations, the odds of consanguinity and hypogammaglobulinemia were 5.57 (2.14-15) and 4.14 (1.39-12.34) times higher in the pathogenic compared to the no variants group. The best model with consanguinity, presence of autoimmunity, vaccine complications, and hypogammaglobulinemia as additional criteria to JMF, had a sensitivity and specificity of 84% and 86% respectively, compared to sensitivity and specificity of 84% and 52% for JMF criteria alone.

Conclusions:

Our study shows that presence of any two among the criteria parental consanguinity, presence of autoimmunity, vaccine complications and hypogammaglobulinemia increased the specificity of JMF criteria by 34% in guiding molecular screening for early diagnosis of IEIs. This may be validated in a larger cohort.

OP-7

Abstract Title:

Reduced TCR Beta Repertoire Clonality and Diversity in X-Linked Agammaglobulinemia Patients: A Next-Generation Sequencing-based Study from India

Abstract no: 57

All authors: Sanghamitra Machhua[1], Ankur Kumar Jindal[1], Rahul Tyagi[1], Gayathri CV[1], Hersh Parikh[2], Ruchi Saka[1],Saniya Sharma [1], Manpreet[1] , Dhaliwal[1], Rakesh Kumar Pilania[1], Vignesh Pandiarajan[1],Prateek Bhatia [1], Deepti Suri[1], Amit Rawat[1], Surjit Singh[1].

Complete details of Institute including city state-

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Abstract:

Background:

X-linked agammaglobulinemia (XLA) is a primary immunodeficiency disorder characterized by low levels or absence of immunoglobulins, mature B cells and recurrent infections. It results from a loss-of-function mutation in a single gene, Btk (Bruton's tyrosine kinase), arresting B cell differentiation at the pre-B cell stage in the bone marrow. The role of T cells in B cell development and differentiation is well described; however, the role of B cells in T cell development has not been as well defined. Patients with XLA represent a classic model for studying the impact of B cell deficiency on T cell immunity.

Aim: To study the T-cell receptor (TCR) beta repertoire in patients with XLA.

Methods:

This study included 15 XLA patients with confirmed BTK mutations and 13 age and gender-matched healthy controls. RNA was isolated from peripheral blood samples, and T-cell receptor (TCR) beta repertoire analysis was performed using the Oncomine TCR Beta-LR Assay by next-generation sequencing (NGS). An unpaired t-test was used to compare TCR diversity, clonality, and gene segment frequencies between XLA patients and controls. P-values < 0.05 were considered statistically significant.

Results:

Among the 15 XLA patients, pneumonia was observed in 66.67%, otitis media in 60%, and diarrhoea in 40%. Skin infections were noted in 33.33%, while empyema and meningitis were less common, affecting 13.33% and 6.67% of patients, respectively. Sepsis was observed in 13.33%, caused by Campylobacter jejuni and Staphylococcus aureus. TCR beta repertoire analysis revealed no significant differences in total reads, productive reads or rescued productive reads. However, XLA patients exhibited significantly fewer clones (20,336.13 ± 13,035.86) compared to controls (32,392.54 ± 14,550.70, p=0.02) and lower Shannon diversity (9.63 ± 2.12) compared to controls (11.53 ± 2.12, p=0.02). Notable differences in TRBV frequencies were observed: TRBV6-4 was reduced in XLA patients (0.0017 ± 0.0024) compared to controls (0.0063 ± 0.0054, p=0.006), TRBV6-8 was lower in XLA patients (0.00004 ± 0.00006) than in controls (0.00009 ± 0.00007, p=0.0188), and TRBV28 was higher in XLA patients (0.1280 ± 0.0981) compared to controls (0.0633 ± 0.0358, p=0.03).

Conclusion:

XLA patients exhibit reduced TCR beta repertoire clonality and diversity, indicating impaired T cell immune responses due to the underlying B cell defect, likely the cause of the high incidence of recurrent infections by

affecting the generation of diverse antigen-specific responses. The observed variations in TRBV gene segment frequencies further emphasize the critical role of B cells in maintaining effective T-cell immunity.

Figures, tables

Figure 1 (XLA Patient):

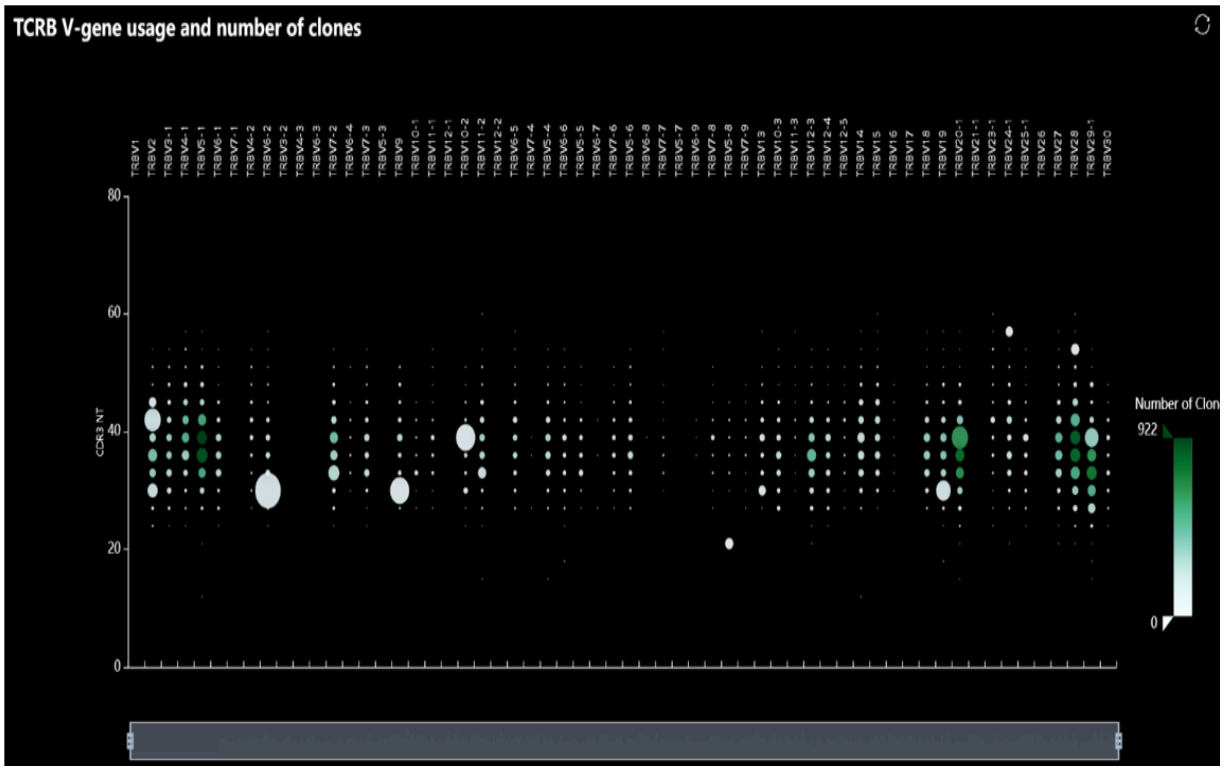
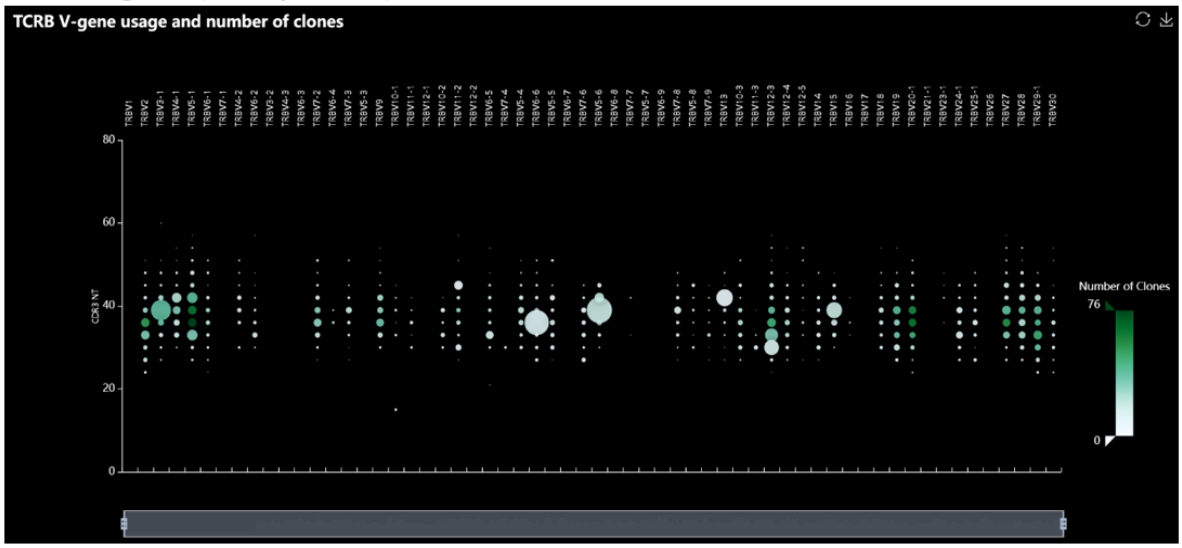


Figure 2 (Healthy Control):



Figures 1 and 2: The spectratyping plot displays the TCR beta repertoire, with clones represented as circles. The X-axis shows the variable gene identity, and the Y-axis represents the CDR3 nucleotide length. Circle size indicates the frequency of each clone, while color denotes the number of clones for a given variable gene-CDR3 NT combination. Reduced diversity and clonal expansion are observed in the patient compared to the control.

OP-8

Abstract Title:

Breaking Barriers: Immunodeficiencies Behind Fungal Vulnerability

Abstract no: 61

All authors: Umair Ahmed Bargir[1], Disha Vedpathak[1], Chandrakala CS[1], Aparna Dalvi[1], Shweta Shinde[1], Lavina Temkar[1], Priyankar Pal[2], Pranoti Kini[3], Ratna Sharma[3], Sujata Sharma[4], Manisha Madkaikar[1].

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Abstract:

Background:

Inborn error of immunity can lead to mild to severe fungal infections infections. Advances in next-generation sequencing have identified inborn genetic errors, such as defects in IL-17 immunity, which are linked to conditions like chronic mucocutaneous candidiasis. This study immunologically evaluated patients with recurrent fungal infections and screened for molecular defects to uncover genetic causes, highlighting the role of innate and adaptive immunity in infection resolution.

Objectives:

To establish a cohort of patients with increased predisposition to mucocutaneous fungal infections

To understand the underlying molecular defect and immunopathology of the patients with increased pre-disposition to fungal infections within the Indian population

Methods:

Peripheral blood samples were collected, processed, for immunological and genetic analysis. Initial investigations included clinical evaluation, CBC, lymphocyte subset analysis, and serum immunoglobulin levels. Extended immunophenotyping panels analyzed T, B, NK cells. In-vitro assays assessed Th1, Th2, and Th17 cytokine responses. DNA from patients with immunological abnormalities was extracted and screened for genetic defects using next-generation sequencing to identify underlying causes.

Results:

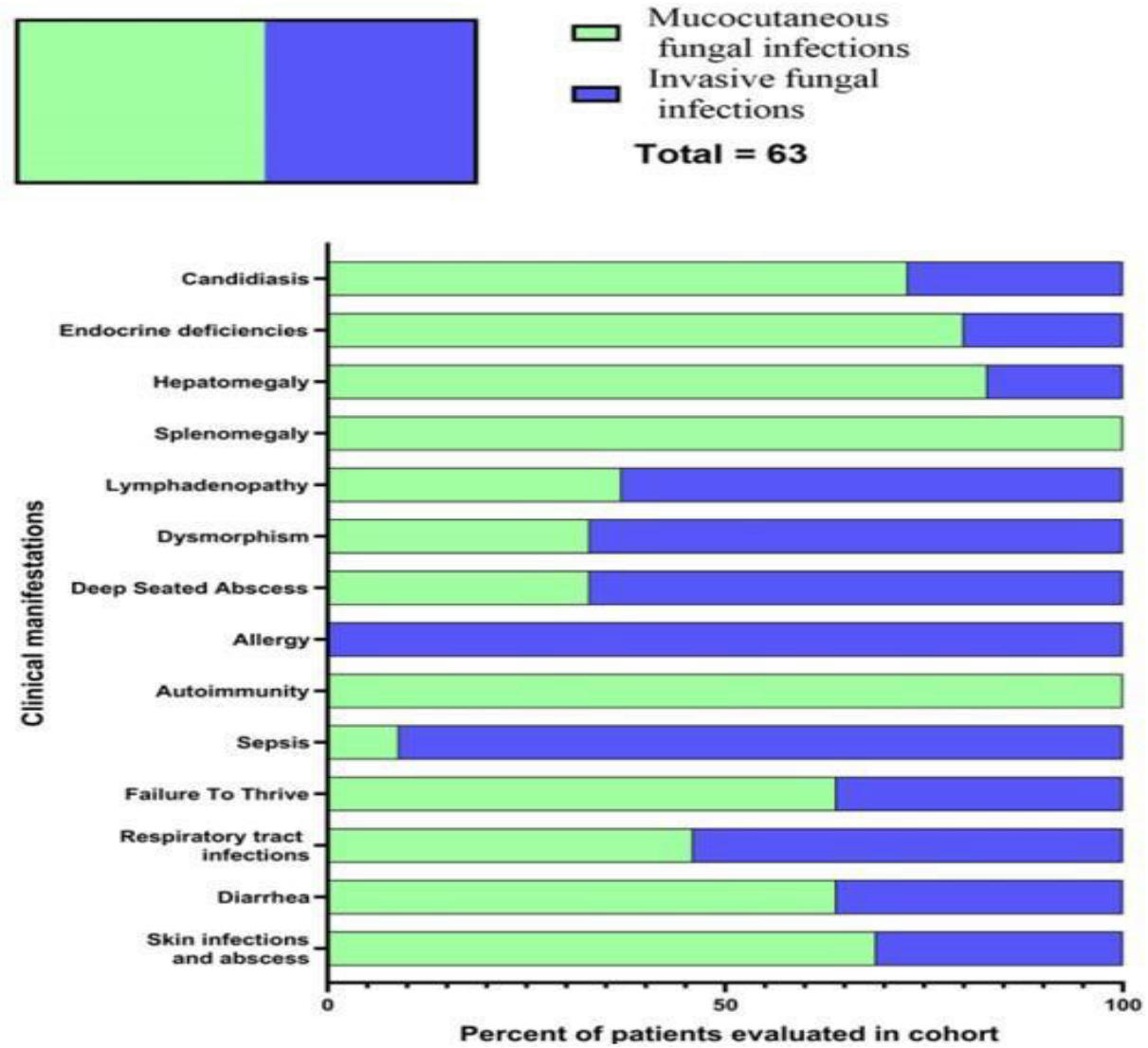
A total of 63 patients with recurrent fungal infections were studied, with 55% presenting mucocutaneous infections and 45% invasive infections. The female-to-male ratio was 0.5:1, and the median age of presentation was 0.7 years. Candida infections were most common (66%), with oropharyngeal candidiasis being the predominant manifestation, while non-candidal infections (34%) included Aspergillus, Cryptococcus, Mucor, and Dermatophytes, primarily causing pneumonia and meningitis. Common symptoms included respiratory infections, candidiasis, skin infections, failure to thrive, and sepsis. The immunological evaluation revealed T cell lymphopenia in 21% of patients, decreased naïve Th cells in 21%, neutropenia in 6.3%, low IgG/IgA levels in 11%, and elevated IgM/IgE levels in 4.7% and 14.2%, respectively. Defective phagocytic function and reduced ROS production were observed in three patients. Overall, 36 patients showed significant immunological abnormalities, and 17 were prioritized for whole exome sequencing. Molecular analysis identified 18 variants in

15 genes, classified into five IEI categories per IUIS guidelines. Commonly identified variants included NCF1, AIRE apart from individual cases of STK4, CD40L, RAG1 etc. In vitro assays showed reduced IFN-γ and IL-17 secretion by CD4+ T cells, highlighting their critical role in antifungal immunity alongside lymphocyte and neutrophil populations.

Conclusions :

We identified significant immunological abnormalities in 36 patients, of whom 17 were further analyzed for genetic defects using NGS analysis, which revealed variants in 15 genes associated with IEI suggesting an increased predisposition to fungal infections in these patients.

Figures, Tables:



OP-9

Abstract Title:

Machine Learning Models for Predicting Disease Severity in Common Variable Immunodeficiency

Abstract no: 62

All authors: Umair Ahmed Bargir[1] ,Priyanka Setia[1], Chandrakala CS[1], Mukesh Desai[2], Manisha Madkaikar[1]

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Abstract:

Background:

Common Variable Immunodeficiency (CVID) is a heterogeneous primary immunodeficiency disorder characterized by hypogammaglobulinemia and recurrent infections, autoimmunity, or malignancy. Predicting disease severity is critical for optimizing management strategies. Existing severity scores, such as Ameratunga's and VISUAL, rely on clinical and immunological parameters but face limitations in accessibility and interpretability. This study leverages machine learning (ML) models to predict CVID severity using readily available immunological data, aiming to provide a robust and accessible tool for clinical use.

Methods:

A cohort of 150 CVID patients diagnosed between 2009 and 2024 in India was analyzed. Patients were classified into severe and non-severe categories based on Ameratunga's severity score. Immunological parameters, including serum IgG, IgA, IgM, CD19, class-switched memory (CSW) B cells, CD4, Th:Tc ratio, and CD16, were used as predictors. The dataset (114 observations) was split into training (70%) and validation (30%) sets. Five ML models—Logistic Regression, Support Vector Machine (SVM), Random Forest (RF), Lasso Regression, and Extreme Gradient Boosting (XGBoost)—were trained and evaluated using 10-fold cross-validation. Synthetic Minority Over-sampling Technique (SMOTE) was applied to address class imbalance. Model performance was assessed using accuracy, F1 score, and positive predictive value (PPV).

Results:

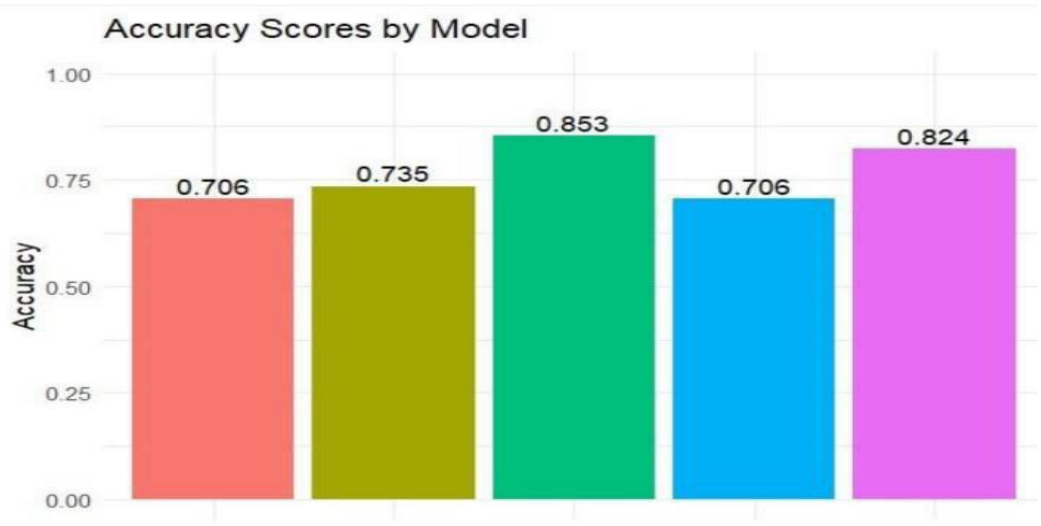
The Random Forest model outperformed other models, achieving an accuracy of 85.3% (95% CI: 84.0–86.6), an F1 score of 87.2% (95% CI: 85.9–88.5), and a PPV of 87.2% (95% CI: 85.9–88.5). XGBoost demonstrated comparable performance, with an accuracy of 82.4% and an F1 score of 83.3%. Feature importance analysis identified the Th:Tc ratio, CD19, and IgM levels as the most influential predictors. SVM achieved a higher F1 score than Logistic Regression, indicating better balance between precision and recall for the minority class.

Conclusion:

This study demonstrates the utility of ML models, particularly ensemble methods like Random Forest and

XGBoost, in predicting CVID severity using basic immunological parameters. These models provide a robust, accessible, and interpretable tool for clinical decision-making, addressing limitations of existing severity scores. Future research should focus on validating these models in larger, diverse cohorts to enhance their generalizability and clinical applicability.

Figures, Tables:



CHALLENGING CASES

CC-1

Abstract Title:

A Twisted Tale of Immunity: XLP1 Masquerading as Thrombotic Microangiopathy in the Kidney

Abstract no: 13

All authors: Mounika B[1], Dr Meena S[1],

Complete details of Institute including city state:

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Abstract:

Background:

X-linked lymphoproliferative syndrome type 1 (XLP1) is a rare primary immunodeficiency caused by mutations in the SH2D1A gene. It predisposes individuals to hemophagocytic lymphohistiocytosis (HLH) and Epstein-Barr virus (EBV)-associated lymphomas. The concurrent presence of HLH, thrombotic microangiopathy (TMA), and chronic kidney disease (CKD) in XLP1 is exceedingly rare and presents a complex clinical scenario.

Case description:

A 3-year-old boy, developmentally normal, first born to non consanguineous union presented with two weeks of fever, myalgia, headache, and splenomegaly. Initial investigations showed leukopenia (3900 cells/cu mm), proteinuria (2+), elevated urea (87 mg/dl), creatinine (2.46 mg/dl) and bilateral nephromegaly with increased cortical echogenicity in ultrasonography. Infectious disease workup was negative. Persistent fever, worsening cytopenia, renal dysfunction, and elevated LDH, ferritin, and D-dimers raised suspicion of autoimmune disorder with Macrophage activation syndrome. Bone marrow aspirate revealed hemophagocytes and he received Intravenous immunoglobulin and steroid, later escalated to Ruxolitinib due to refractory disease. His autoimmune workup was negative except for anticardiolipin antibody positivity prompting the initiation of Rituximab. His renal dysfunction worsened, necessitating dialysis.

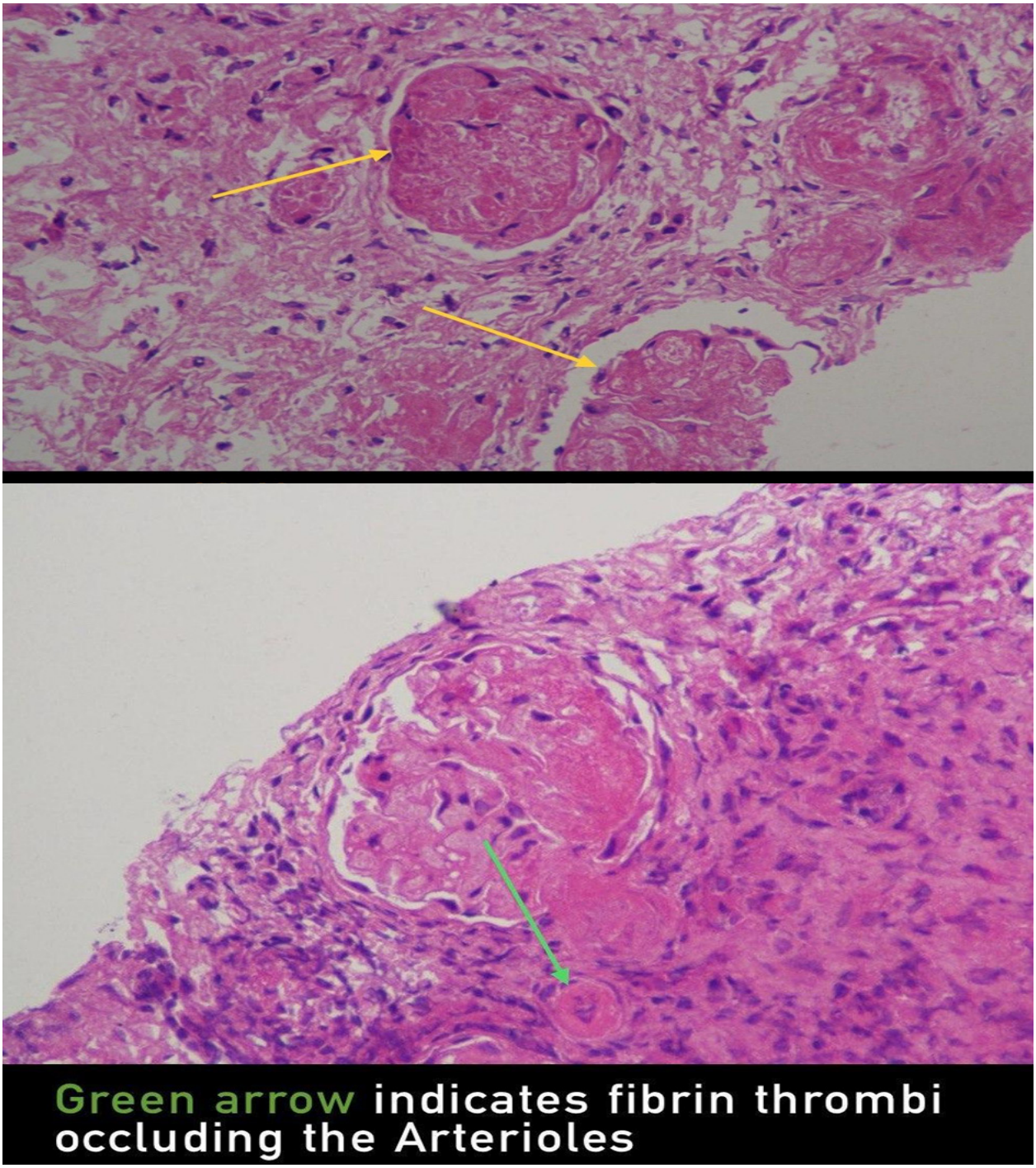
The child developed coagulopathy and gastrointestinal (GI) bleeding (melena), which was managed with multiple transfusions, Factor VII and endoscopic interventions followed by laser photocoagulation of the duodenal artery. Renal biopsy showed thrombotic microangiopathy (TMA) and global glomerulosclerosis despite the absence of schistocytes in repeated blood smears throughout the course of the disease. Dialysis dependency and severe hypertension persisted in spite of plasmapheresis, rituximab and eculizumab though his coagulopathy and hemodynamics improved. Genetic analysis identified a hemizygous nonsense mutation in SH2D1A, confirming X-linked lymphoproliferative syndrome type 1 (XLP1).

He underwent haploidentical hematopoietic stem cell transplantation with T-cell αβ/CD19-depleted peripheral blood stem cells from his father. Post-transplant period was stormy with mucositis, Candida krusei fungemia, persistent lung nodules and respiratory failure, complicated by septic shock due to Stenotrophomonas maltophilia, and multi-organ dysfunction. He succumbed to the illness on day 17 of transplantation.

Conclusions:

This case highlights the complex interplay of HLH, TMA, and CKD which is very rare in XLP1, the challenges of HSCT in a high-risk patient, and the importance of meticulous multidisciplinary care in managing such complications

Figures, tables:



CC-2

Abstract Title:

When arthritis and anemia become confluent, thinking of Majeed syndrome could be prudent

Abstract no: 18

All authors: Gayathri[1], Deepti Suri[1], Vignesh Pandiarajan[1], Abarna Thangaraj[1], Ahmed Jamal[1], Surjit Singh[1].

Complete details of Institute including city state:

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Abstract:

Background:

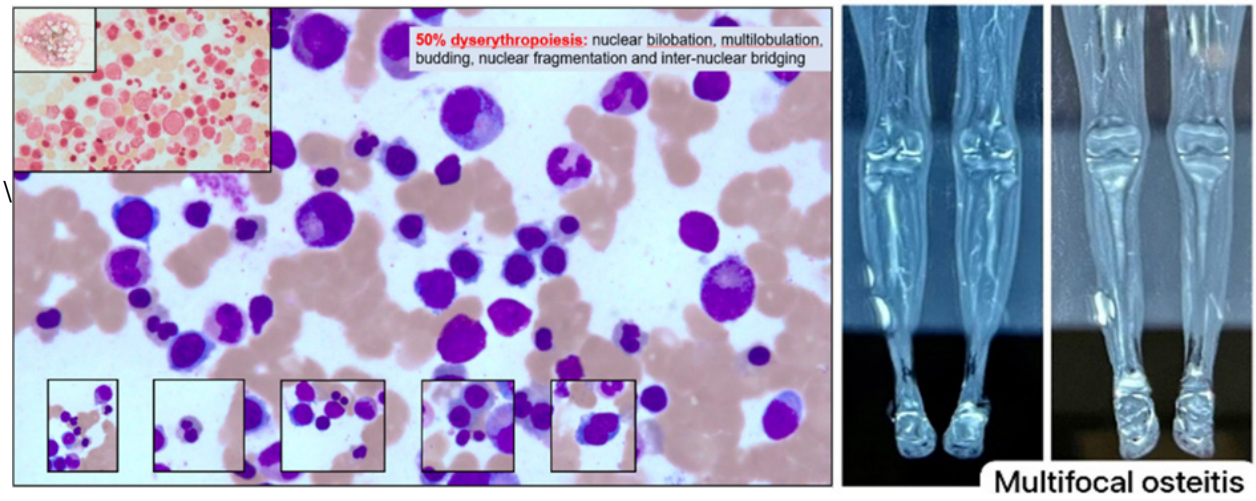
Autoinflammatory diseases are disorders of immune dysfunction where there is hyperinflammation in an antigen-independent manner. They are broadly classified as interferenopathies, inflammasomopathies, and other dysregulation including aberrant activation of NFκB. Majeed syndrome is an autoinflammatory disorder with IL1-mediated inflammation causing sterile osteomyelitis, Sweet syndrome and dyserythropoietic anemia.

Objective: We report an unusual finding of an Majeed syndrome in two children from two different regions of the Indian subcontinent. Case Presentation: P1 is a 14-year-old female, born of 3rd-degree consanguineous marriage, was symptomatic since 4 years of age with recurrent arthritis. Despite the use of 2 DMARDs, she had multiple flares of arthritis with asymmetric involvement of joints of both upper and lower limb . She also had persistent anemia throughout her course and had disproportionately elevated Inflammatory markers like ESR and CRP . She had failure to thrive and splenomegaly at 12 years of age; Bone marrow examination was suggestive of Congenital dyserythropoietic anemia. Whole-exome sequencing revealed a homozygous variant c.2442+3_2442+6del at intron 18 of the LPIN2 gene; Her whole-body Magnetic resonance imaging (MRI) showed carpal effusion, multifocal osteitis; She is currently started on Anakinra, and she is improving, with no flares of arthritis, improved anemia. P2 is a 6.5 year old girl, 1st born of 2nd degree consanguinuity, symptomatic since 5 months of age. She had recurrent episodes of large joint swelling with effusion documented in ultrasonography and partial response to NSAIDs. On evaluation she was found to have severe Anemia (Hemoglobin 72g/L), elevated inflammatory markers (Erythrocyte sedimentation rate of 80mm/hour, C-reactive protein – 169mg/L). MRI at 2 years of age revealed T1 hypointensities and T2 hyperintensities in distal metaphysis, epiphysis of femur, proximal and distal metaphysis of tibia and Left Talus. Genetic analysis was sent with a suspicion of Autoinflammatory syndrome which showed a homozygous pathogenic nonsense variant in Exon 4 c.589C>T in LPIN2 gene. She has now been registered under the national policy of rare disease and is awaiting Government support for IL1 blockade therapy.

Conclusions:

We report Majeed Syndrome in two children, from different families, with Arthritis as the presenting manifestation. Persistent anemia in a child with chronic refractory arthritis could point towards Majeed Syndrome. Interestingly, there was improvement in Anemia in the child started on Anakinra therapy. Early onset arthritis, with unexplained anemia and disproportionately elevated inflammatory markers, with or without organomegaly, failure to thrive may be clues to think beyond Juvenile idiopathic arthritis.

Figures, tables:



CC-3

Abstract Title:

Recurrent enteritis due to CMV- A rare presentation of CTLA4 haploinsufficiency

Abstract no: 24

All authors: Anushka Prabhudesai[1], Rudrarpan Chatterjee[1], Amita Aggarwal[1]

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Abstract:

Introduction: Cytotoxic T lymphocyte antigen 4 (CTLA4) is a negative immune regulator essential for the proper functioning of regulatory T cells, thus maintaining self-tolerance and immune homeostasis. Heterozygous mutations in CTLA4 can lead to immune dysregulation and immunodeficiency.

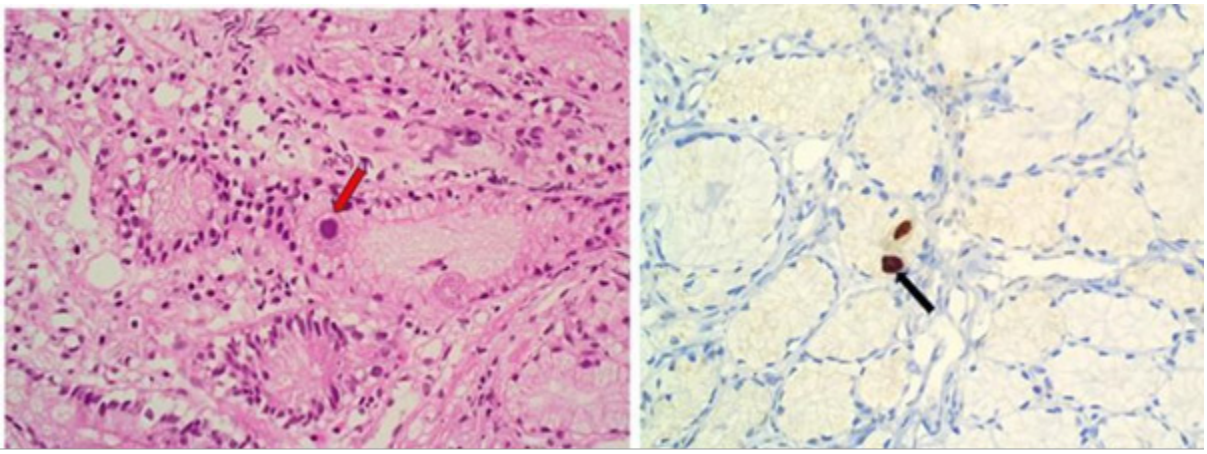
Case: A 17-year-old boy presented with complaints of recurrent watery diarrhoea for 7 years. The episodes lasted for about 3-4 days, not associated with blood in stools or tenesmus and often required hospitalization for fluid resuscitation and intravenous antibiotics. His past investigations were largely unremarkable with normal blood counts, negative TTG IgA and normal upper GI endoscopy and small bowel biopsy with no organisms isolated from blood and stools. For the last 1 year, he had also developed atopic dermatitis responsive to oral steroids. He is the second born child of non-consanguineous parents with no significant family history. His weight was 43kg (between -3 to -2 SD) and height 159cm (between -3 to -2 SD). At his current presentation, blood counts were within normal limits (Hb 12 g/dl, TLC 6400/cumm, ANC 3584/cumm, ALC 2432/cumm, Platelets 2.38 x106/ cumm) with raised acute phase reactants (ESR- 42mm/hr, CRP-7.4 mg/l). Stool showed positivity for occult blood but there was no evidence of opportunistic pathogens and culture was negative. Upper GI endoscopy showed duodenal (D2) scalloping, colonoscopy was normal. On histopathology, duodenal mucosa displayed focal shortening and broadening of villi with moderate mixed inflammatory infiltrates. The crypts and Brunner's

glands showed enlarged cells with intranuclear smudgy viral inclusions. Similar viral inclusions were also seen in the gastric glands. These were suggestive of Cytomegalovirus inclusion bodies on immunohistochemistry (Image). In view of the recurrent diarrhoea with CMV enteritis, a detailed immunological work up was done. He had low IgM levels on 2 occasions (IgM-57mg/dl and 40mg/dl, IgG-1490mg/dl, IgA- 302mg/dl, IgE-266 iU/ml). Lymphocyte subset showed low B cells and CD4/CD8 reversal along with activated naïve T cells predominating and low memory T cells (Table). Suspecting combined immunodeficiency, whole exome sequencing was done which showed a heterozygous missense variant in the CTLA4 gene (exon 2, c.436G>A, p.Gly146Arg) associated with immune dysregulation with autoimmunity, immunodeficiency and lymphoproliferation. He was treated with valganciclovir and his diarrhoea resolved.

Conclusions:

CTLA4 haploinsufficiency may present with combined immunodeficiency without overt autoimmunity. The management dilemma in this case is with regards to future therapy as Abatacept is unavailable in our country and he has isolated IgM deficiency which would not be corrected by IVIG.

Figures, tables:



Lymphocyte subset	Percentage	Absolute counts
CD3	85.6%	1080/cumm
CD 19	0.7%	09/cumm
CD 56	12.1%	156/cumm
CD4	24.3%	245/cumm
CD8	63.6%	642/cumm

CC-4

Abstract Title:

H Syndrome: A Rare Multisystem Challenge – Insights from Two Cases

Abstract no: 31

All authors: Dr Suma Balan[1], Dr Kumar Abhinav[1], Sabin George[1].

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Abstract:

Introduction

H Syndrome is a rare genetic disorder characterized by a range of symptoms, including hyperpigmentation, hypertrichosis, hearing loss, growth retardation, arthritis, and systemic inflammation. First described in 2008, it results from mutations in the SLC29A3 gene, which encodes the human equilibrative nucleoside transporter-3 (hENT3). The clinical presentation is variable, complicating both diagnosis and management. This report presents two pediatric cases with confirmed SLC29A3 mutations, aiming to provide insights into the clinical spectrum and therapeutic strategies for this rare condition.

Case 1- A 12-year-old girl, symptomatic since age 4, presented with arthritis affecting small joints, wrists, ankles, and feet. She later developed bilateral sensorineural hearing loss (SNHL), atopic dermatitis, hypertrichosis, and hyperpigmentation. At age 9, she experienced macrophage activation syndrome (MAS), characterized by high-grade fever, thrombocytopenia, hyperferritinemia, borderline splenomegaly, and elevated inflammatory markers. Autoimmune markers were negative, and echocardiography was normal. Genetic testing revealed a homozygous pathogenic mutation in SLC29A3 (Exon 4, c.400C>T, p.Arg134Cys). Initial management included steroids, methotrexate (MTX), and leflunomide. The patient is currently stable on MTX (20 mg weekly) with folic acid supplementation, demonstrating good control of her joint symptoms.

Case 2- A 12-year-old boy, symptomatic since infancy, presented with recurrent fever and multiple joint pains, initially suspected to have systemic juvenile idiopathic arthritis (SJIA). He later developed hyperpigmentation, hypertrichosis, hirsutism, and bilateral SNHL. At age 6, he was diagnosed with Type 1 diabetes mellitus following an episode of diabetic ketoacidosis (DKA). He also exhibited dysmorphic facial features and growth retardation. Genetic testing confirmed a homozygous pathogenic mutation in SLC29A3 (Exon 4, c.400C>T, p.Arg134Cys). Despite attempts with various immunosuppressive agents, including steroids, methotrexate (MTX), cyclosporine, and others, his disease remains uncontrolled. He also developed anaphylaxis to intravenous treatments and skin ulcers from subcutaneous tocilizumab, presenting a significant treatment challenge.

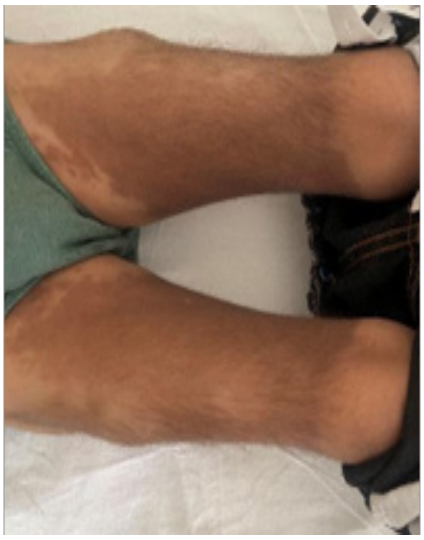
Discussion

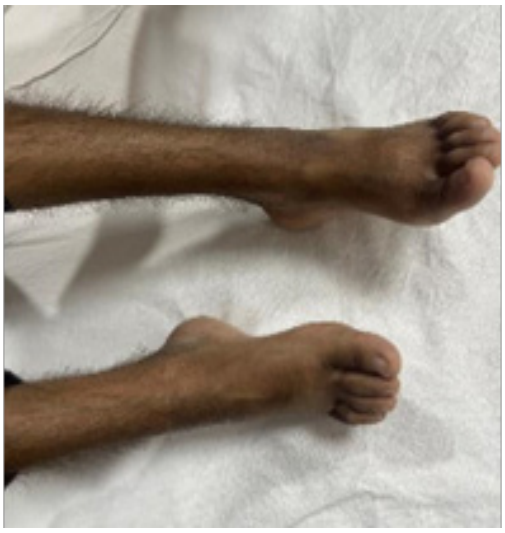
Both cases exemplify the hallmark features of H Syndrome, including bilateral SNHL, hyperpigmentation, hypertrichosis, arthritis, and systemic inflammation. Case 1 displayed MAS, while Case 2 had Type 1 diabetes and growth retardation, highlighting the diverse endocrine involvement in H Syndrome. Genetic testing confirmed a homozygous pathogenic mutation in SLC29A3 (Exon 4, c.400C>T, p.Arg134Cys) in both cases. Treatment remains challenging due to the disease's chronic inflammatory nature and its limited response to standard therapies. Methotrexate provided some control in Case 1, while Case 2 required multiple immunosuppressive agents with limited success.

Conclusions:

This case series underscores the clinical heterogeneity of H Syndrome.

Figures, tables:





CC-5

Abstract Title:

IL12RB1 with ALPS-like phenotype

Abstract no: 34

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Abstract:

INTRODUCTION IL12RB1 is one of the mendelian susceptibility disorders. Here we present a child with homozygous IL12RB1 deficiency presenting with lymphoproliferation and autoimmune cytopenia.

CASE PRESENTATION AND DISCUSSION: A 5-year-old male born of consanguineous marriage presented with persistent cervical lymphadenopathy, hepatosplenomegaly and fever. He had a previous sibling death with suspected disseminated tuberculosis. He was treated with antitubercular therapy in past for left axillary lymphadenopathy at 6 months of age. At 1.5 years fever with cervical lymphadenopathy was treated with ATT. From 2 years of age, he additionally developed recurrent lower limb palpable purpura rash responding to short courses of steroids. Skin biopsy revealed leucocytoclastic vasculitis. In view of past history with possible BCG adenitis and a sibling death with disseminated Tb, MSMD was suspected clinically and exome sequencing was undertaken. It showed a homozygous IL12RB1 defect. Current investigation also revealed normocytic normochromic Coombs positive anemia with Hb 7g/dl. In view of persistent lymphoproliferation with AIHA ALPS-like illness was considered. Literature suggested patients with IL12RB1 defect can have apoptosis error

similar to ALPS. DNT estimation 2% with normal CD4 and CD8 ratio. He was started on 2mg/m2 of sirolimus with levels 10ng/ml. This normalized hemoglobin with DCT turning negative and reduction in lymph node sizes with disappearance of the palpable spleen.

Conclusions:

IL12RB1 may lead to different clinical phenotypes, including ALPS-like disease and Mendelian susceptibility to mycobacterial diseases. Knowledge of the genetic defect underlying an ALPS-like phenotype helps to decide choice of treatment options.

CC-6

Abstract Title:

Twice the Challenge: Decoding the Complexity of Dual Gene Mutations in a case of Combined Immunodeficiency disorder

Abstract no: 73

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Abstract:

A 13-year-old male, the first-born of a third-degree consanguineous marriage, presented with fever and multiple small cervical lymphadenopathies persisting for six months. He had a history of Hodgkin's lymphoma diagnosed at age 7, treated with 6 cycles of ABVD chemotherapy. After two asymptomatic years, he developed recurrent respiratory tract infections requiring multiple hospitalizations. Empirical anti-tubercular therapy provided limited relief.

Examination revealed sub-centimeter cervical lymphadenopathies, mild hepatosplenomegaly, and a significant family history. His younger brother had recurrent infections with panhypogammaglobulinemia. His targeted clinical exome sequencing was done in 2019 suspecting an underlying immunodeficiency which identified a homozygous VUS c.1597A>G in DNAAF2. He succumbed to illness despite intravenous immunoglobulin and antibiotic prophylaxis. Their grandfather died of gastric malignancy.

His imaging showed mild hepatosplenomegaly, peri-pancreatic, mesenteric, and mediastinal lymphadenopathies. Lymph node biopsy indicated reactive lymphadenopathy, and EBV serology was negative.

Immunological evaluation revealed panhypogammaglobulinemia, low Th cells (463 cells/cmm), low naïve Tc and Th cells, poor T cell proliferation to PHA, and an abnormal B cell profile with reduced memory, class-switched, transitional B cells, and plasmablasts and CD21 low B cells. His phospho-Akt and pS6 levels were low compared to controls. Whole exome sequencing identified a homozygous c.1150G>T variant of uncertain significance (VUS) in LCP2 and compound heterozygous c.431A>G and c.3065C>T variants in POLE. Reanalysis confirmed c.1597A>G in DNAAF2 as a BP4 variant, not considered further. His sibling's reanalysis didn't cover the LCP2 gene since it was not a part of the panel as it was described to cause IEI in 2020. Though POLE was covered, the sibling didn't harbour either of the said variants.

The findings are consistent with a combined immunodeficiency disorder, with phenotypic overlap with LCP2 and partial overlap with POLE deficiencies, complicating diagnosis and management.

The patient was started on intravenous immunoglobulin replacement therapy and prophylactic antibiotics. Further studies, including familial segregation of identified variants, Vβ repertoire analysis, NK cell degranulation + IL-2 studies, Dihydrorhodamine assay, platelet aggregation studies, and Polε western blot, are planned to clarify the diagnosis. The patient is started on intravenous immunoglobulin replacement therapy and put on septran prophylaxis.

This case underscores a complex immunological phenotype with diagnostic challenges due to mutations in multiple genes. Definitive management, including hematopoietic stem cell transplantation, remains a difficult decision requiring further diagnostic refinement.

POSTER PRESENTATIONS

P-1

Abstract Title:

Clinical and molecular spectrum of RAG1 and RAG2 deficiency: A 24 years' experience from a tertiary care centre in Northwest India

Abstract no: 6

All Authors: Dev Desai[1], Vignesh Pandiarajan[1], Aditya Dod[1], Rakesh Kumar[1], Manpreet Dhaliwal[1], Saniya Sharma[1], Ankur Jindal[1], Deepti Suri[1], Surjit Singh[1], Amit Rawat[1]

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Abstract:

Background:

The proteins RAG1 and RAG2 play an important role in VD(J) recombination. Mutations in the RAG1 or RAG2 can have presentations ranging from typical severe combined immunodeficiency (SCID) to various degrees of immune dysregulation. (1,2)

Objective:

To review the profile of patients with RAG1/RAG2 defects at our centre.

Methods:

The study was a retrospective observational study carried out by review of records of SCID patients with mutations in RAG1/RAG2 detected by Sanger or Next-Generation Sequencing over a period from 2000-2024 at our centre.

Results:

A total of 25 patients with proven RAG mutations were included in this study; majority had a mutation in RAG1 (16/25). RAG mutations comprise 1/4th of our total cohort of SCID patients. Two-thirds were male (17/25) and had an early onset of symptoms (median age 1.5 months). Median age at diagnosis was 5 months with most patients presenting with pneumonia (21/25) and failure to thrive (17/25), nearly half with diarrhea (12/25) and one-third with a history of rash (8/25). Most of our patients presented with a typical SCID-like phenotype, while 3 presented with combined immunodeficiencies and autoimmunity- 1 girl had recurrent infections with

acrofacial vitiligo, 1 boy had an inflammatory bowel disease like presentation and a third had adult onset combined variable immunodeficiency like phenotype. History of early death among siblings was present in less than half of the patients (11/25), while one-fifth were born of consanguineous marriages. BCG related complications were seen in one-third of the patients (8/25), while the most common microbiologically proven infections were Candida sp., cytomegalovirus, and Enterococcus fecalis, seen in 7, 5 and 2 patients respectively. The median absolute lymphocyte count was 1244 cells/mm3 and there was profound B-cell lymphopenia with median B-cell proportion being 3.04%, whereas median T and NK cell proportions were 24.7% and 57.11%, respectively. A 3/4th of the patients had hypogammaglobulinemia (Table 1). All RAG1/RAG2 mutations in our cohort were exonic and most commonly missense (Table 2). Outcomes were known for 19 patients, out of which the majority succumbed to various infections (14/19), 1 patient underwent a successful hematopoietic stem cell transplantation, and the remaining 4 are currently on antimicrobial prophylaxis and intravenous immunoglobulin replacement.

Conclusions:

Nearly 90% of patients with RAG1/2 defects tend to present at an early age like typical SCID. A relatively low number of CID cases in RAG deficiency suggests these cases are probably missed and an increase in awareness is needed.

Figures, tables:

Table 1: Clinical and immunological characteristics of patients with proven RAG1/RAG2 mutations in our cohort

Characteristic	Number of patients (n=25 unless otherwise specified)
Male gender	17 (68%)
Median age at onset of symptoms (months)	1.5 months
Significant family history present	11 (44%)
Symptoms at presentation • Pneumonia • Failure to thrive • Diarrhea • Rash • Hepatosplenomegaly • Vitiligo • Inflammatory diarrhea	 21 (84%) 17 (68%) 12 (48%) 8 (32%) 9 (36%) 1 (4%) 1 (4%)
Infection profile • BCG-related complications • Candida • Cytomegalovirus • Enterococcus • Pneumocystis jiroveci	 8 (32%) 7 (28%) 5 (20%) 2 (8%) 1 (4%)
Median absolute lymphocyte count	1244 cells/mm^3
Median percentage • CD3+ • CD19+ • CD16/56+	 24.70% 3.04% 57.11%
Immunoglobulin profile (n=15) • Low IgG • Low IgM • Low IgA	 11 (73.33%) 12 (80%) 13 (86.67%)

P-2

Abstract Title:

Infant with autoimmunity, recurrent infections and hypotonia – an interesting case of a PID with channelopathy!

Abstract no: 7

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Abstract:

Background:

Calcium release-activated calcium (CRAC) channels encoded by the ORAI1 gene are essential for the activation of lymphocytes. ORAI1 deficiency patients present in infancy with severe life-threatening infections along with non-immune developmental manifestations.

Objective:

To describe a case of a Syndromic Primary Immune deficiency disease with autoimmunity as the first manifestation.

Methods:

A retrospective review of clinical records was performed. A detailed clinical history, including the age of presentation, symptoms, findings on physical examination, laboratory findings, and details of treatment, was recorded. Whole exome sequencing was performed on a next-generation sequencing (NGS) platform.

Results:

A 6-month-old male, 2nd born to a consanguineously married Indian couple presented with complaints of recurrent hospitalizations since the age of 3 months because of recurrent infections, cytopenias, and seizures. He had not achieved neck holding and had significant motor developmental delay. He would have intermittent fevers and was reported to have poor sweating.

On examination, he was failing to thrive and had petechial spots over the limbs along with hypotonia of all four limbs. His blood counts showed anemia and thrombocytopenia with elevated inflammatory parameters. Workup for bacterial & viral infections was negative. Immature platelet fraction and the retic count were elevated, and the Direct Coombs test (DCT) was positive. Bone marrow biopsy was normal. ANA by IF was positive, ANA profile was negative, and he had hypocomplementemia (Table). He was diagnosed to have Evans syndrome and IVIG (2 gm/kg) was given. Following IVIG his hemoglobin stabilized, and platelet counts improved. Workup for hypotonia included serum creatinine phosphokinase levels, electrolytes, and an MRI brain within normal limits. On evaluation for primary immune deficiency (PID), he had hypergammaglobulinemia, and lymphocyte subsets were normal. However, naïve T cells were low. Chest X-ray showed the absence of thymic shadow. Hence, a provisional diagnosis of Syndromic Combined Immunodeficiency (CID) with hypotonia and immune dysregulation was made. Whole exome sequencing showed a pathogenic homozygous mutation in the ORAI1 gene. He was started on antimicrobial prophylaxis and IVIG replacement therapy and his family was counseled for a bone marrow transplant.

Conclusions:

ORAI1 deficiency being a syndromic PID, the non-immunologic manifestations persist even after undergoing

an HSCT. To the best of our knowledge, this is the first report of autoimmunity as a presenting manifestation of ORAI1 deficiency from the Indian subcontinent

Figures, tables:

Table: Investigations at presentation

Test	Report
CBC	Hb-7.7 g/dl TC- 11,000/cumm (N-14% L-74%) PC-5000/cumm
CRP	183 mg/dl
ESR	135 mm/hr
Blood culture	sterile
Urine routine, culture	15-20 pus cells, *Enterococcus faecalis*
Immature platelet fraction	17.3 (0.7 – 4.3)
Retic count	2.5 % (<2)
Direct Coombs Test	Positive
ANA by IF ANA profile	3+, Nucleolar pattern, 1:100 Negative
Serum complements	C3 – 34 (80-100) C4 – 7.1 (10-40)
Serum Immunoglobulins(mg/dl)	IgG – 1648 (172-1069) IgA - 650 (4.4-84)) IgM - 1767 (33-126) IgE - 2240 (15 IU/ml)
LSSA	T cell - 4047 (1680 - 7754) B cell - 700 (470-4327) NK cell – 112 (167-359) Naïve CD4 – 204 (1092-5337) Naïve CD8 – 107 (330-1841)
Genetic test	ORAI1 Exon 2 c.421del (p. Ser141AlafsTer11) Homozygous Likely pathogenic AR

P-3

Abstract Title:

Silent Inflammation To Fatal Amyloidosis

Abstract no: 8

All authors: Jagan Babu K L[1], Gayathri M.S[1], Edwin Fernando[2], Nived Haridas[2], Anila Kurien[2], Anna C. Das[1], Aishwarya G[1], Chengappa K.G[1], Molly Mary Thabah[1], V.S. Negi[1]

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Abstract:

Background:

Majeed syndrome is a rare autoinflammatory disorder characterized by a triad of chronic recurrent multifocal osteomyelitis(CRMO), dyserythropoietic anaemia, and neutrophilic dermatosis. It is associated with mutations in the LPIN2 gene. Secondary renal amyloidosis is a known complication of chronic inflammatory conditions but has not been previously reported in Majeed syndrome.

Case Details

An 18-year-old female, born of a third-degree consanguineous marriage, presented with anasarca for three months. Her history revealed episodic bilateral knee swelling since the age of three, without fever or joint deformity, along with global developmental delay and poor scholastic performance.

Examination revealed pallor without joint deformities or systemic abnormalities. Laboratory findings revealed anaemia with normocytic indices, and bone marrow examination showed normoblastic erythroid hyperplasia and nuclear budding, confirming dyserythropoietic anaemia. Acute phase reactants were unexpectedly low, while renal function tests revealed elevated creatinine, proteinuria, and hypoalbuminemia(Table 1), indicative of nephrotic syndrome. MRI of the skeletal system(Fig 1 A) revealed multifocal bone lesions with osteitis and sclerosis, characteristic of chronic recurrent multifocal osteomyelitis(CRMO). Infectious osteomyelitis was ruled out. Whole exome sequencing confirmed a homozygous deletion in the LPIN2 gene, with an autosomal recessive inheritance pattern. These findings with clinical history, led to the diagnosis of Majeed syndrome. Renal amyloidosis was confirmed as a secondary complication through biopsy(Fig 1 B,C), highlighting the severe outcomes of untreated autoinflammatory diseases

Despite symptomatic management and treatment with Baricitinib due to the unavailability of IL-1 antagonists, the patient's renal function remained static while proteinuria improved. Unfortunately, she succumbed to complications related to severe anaemia.

Discussion

Majeed syndrome should be considered in children presenting with atypical arthritis, delayed milestones, or unexplained anaemia. Chronic inflammation driven by autoinflammatory diseases like Majeed syndrome predisposes to amyloid deposition in the kidneys, a potentially fatal complication if untreated. Challenges in accessing targeted therapies such as IL-1 antagonists underscore the need for timely recognition and management of such conditions to mitigate severe outcomes.

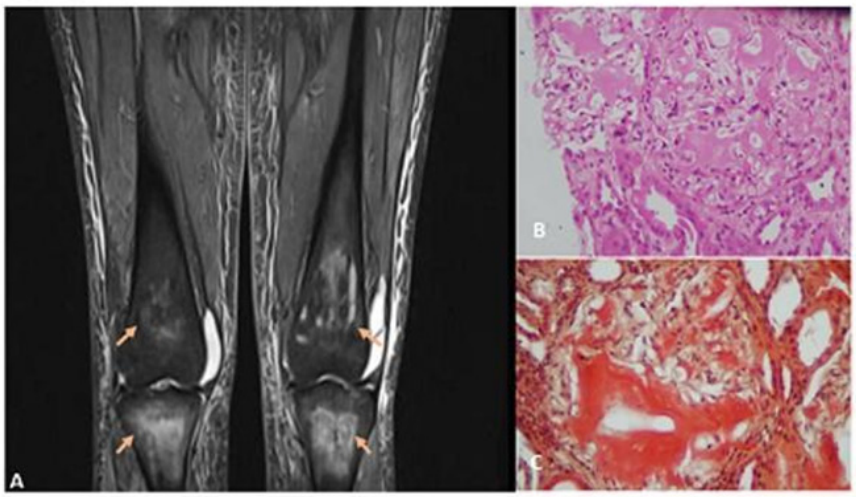
Conclusions:

This case highlights the first reported instance of renal amyloidosis in a proband with Majeed syndrome. Early diagnosis and intervention are critical in preventing complications such as renal amyloidosis, which significantly worsens prognosis

Figures, tables:

Table 1: Baseline Investigations	
Hb (g/dL)	7
MCV (fL)	97
Urea/Cr (mg/dl)	91/2.48
TP/Albumin (g/dL)	5.1/2.1
Urine R/m	Protein 3+
Urine PCR	26.2
S. Ferritin ng/ml	405
Hs-CRP (mg/L)	<2.98
Bone Marrow	Normoblastic erythroid hyperplasia and erythroid cells showing nuclear budding s/o dyserythropoiesis

Figure 1



A. MRI Knee T2 TRIM image showing high signal changes in the metaphyseal regions of distal femur and proximal tibia

B. Renal biopsy specimen with Hematoxylin eosin staining showing acellular amorphous material deposits in mesangium, interstitium, tubular basement membrane and blood vessels

C. Congo red staining of amorphous material

P-4

Abstract Title:

Griscelli Syndrome type 2: A Tragic Tale of Two Siblings

Abstract no: 9

All authors: Muppalla Mowlika[1], Dr. Vijaya Prasanna Parimi[1], Dr. Tejaswini Ramineni[1]

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Abstract:

Griscelli syndrome is a rare autosomal recessive disorder characterized by pigmentary dilution affecting the skin and hair, recurrent skin and pulmonary infections, neurologic complications, hypogammaglobulinemia, and immunodeficiency, all associated with a high mortality rate. The most lethal manifestations include Hemophagocytic lymphohistiocytosis and progressive central nervous system involvement, typically observed in the first and second offspring of affected parents, respectively.

We report a case involving a 5-year-old male child, the second in birth order to a third-degree consanguinous parents. He experienced seizures at 8 months of age, followed by recurrent upper and lower respiratory and gastrointestinal infections starting at 2 years. Notably, there was a familial history of silvery white hair observed in his sister, along with pancytopenia and subsequently died at the age of 3.5 years.

Upon examination, the patient exhibited silvery gray hair, including eyebrows and eyelashes, without any signs of organomegaly or focal neurological deficits. Routine laboratory investigations, including complete blood count, liver function tests, creatinine levels, and erythrocyte sedimentation rate, yielded normal results. Imaging studies indicated bilateral cerebellitis, nodular leptomeningeal enhancement, and obstructive hydrocephalus, necessitating a ventriculo-peritoneal shunt procedure at the age of four. His T, B, and NK cell counts, as well as immunoglobulin subsets, were within normal ranges.

In suspicion of inborn errors of immunity, particularly Griscelli syndrome type 2, further investigations revealed clumps of melanin pigment within the hair shafts upon microscopic examination. Genetic testing subsequently identified a missense variant of the RAB27A gene, confirming the diagnosis of Griscelli syndrome. Although planned for allogeneic hematopoietic stem cell transplantation(HSCT), he ultimately succumbed to refractory status epilepticus further complicated by pneumonia.

The long-term prognosis for Griscelli syndrome remains poor, with most patients not surviving beyond the first decade of life. The identification of cases through thorough family history assessments and genetic screening may pave the way for pre-emptive HSCT, providing a potential avenue for improving outcomes in affected individuals.

P-5

Abstract Title:

Exploring LPIN2 Mutations in Majeed Syndrome: Clinical and Therapeutic Observations from Four Cases.

Abstract no: 10

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Abstract:

Background:

Majeed syndrome (MJS) is a rare autosomal recessive auto inflammatory disorder caused by biallelic pathogenic variants in the LPIN2 gene. It is characterized by chronic recurrent multifocal osteomyelitis (CRMO), congenital dyserythropoietic anemia (CDA), and neutrophilic dermatosis. Data on MJS outside the Middle East, particularly in South Asia, are limited.

Objective:

This study aims to analyse the clinical, radiological, genetic, and therapeutic profiles of four MJS patients to broaden understanding of its clinical spectrum and treatment outcomes.

Methods:

Four patients clinically diagnosed with MJS underwent genetic confirmation using next-generation sequencing (NGS) or whole-exome sequencing (WES) to identify LPIN2 mutations and blended genome exome sequencing (BGES). Data on demographics, presenting symptoms, imaging, laboratory findings, and treatment responses were collected.

Results:

The cohort included three females and one male, with ages at presentation ranging from 8 months to 1 year. CRMO primarily affected the femur and tibia in three cases, with two patients also showing involvement of the feet and one of the upper extremities (humerus and radius). All patients exhibited anemia, and three had dysplastic features consistent with CDA. Neutrophilic dermatosis was observed in two cases. Two patients were initially misdiagnosed with systemic juvenile idiopathic arthritis (SJIA). Genetic testing confirmed homozygous pathogenic LPIN2 variants, including a missense mutation (c.1157C>G, p. Ser386Ter), a splice-site mutation in intron 2, and a pathogenic mutation (589C>T). In one case, an 85 kb LPIN2 deletion identified by BGES was refined to 53 kb using low-pass WES, confirming the diagnosis. All patients were treated with NSAIDs. Pamidronate and colchicine were used in two cases each. Methotrexate and tofacitinib (DMARDs) were administered in two cases with prominent systemic features. Anakinra was planned for two refractory cases, showing good outcomes.

Conclusions:

Majeed syndrome underscores the importance of early genetic testing for accurate diagnosis and targeted therapy. While NSAIDs and corticosteroids provide partial relief, IL-1 inhibitors are essential for long-term disease control. These findings offer valuable insights into the clinical and therapeutic aspects of this rare disorder.

P-6

Abstract Title:

Expression of Immune checkpoints (CTLA-4, PD-1, PD-L1), cytokines and T-reg cells in Lupus Nephritis (LN).

Abstract no: 11

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Abstract:

Background:

Systemic lupus erythematosus (SLE) is multisystem autoimmune disorder of which Lupus Nephritis (LN) remains an important complication affecting both short-term and long-term outcomes. Abnormalities in regulatory T cells (T-reg) and immune checkpoints (CTLA-4, PD-1 and PD-L1) have been recognized to play important role in pathogenesis of SLE. However, they have not been correalted with severity, response to therapy and risk of relapse in LN.

Objective:

To look in SLE patients with LN

1. Expression of immune checkpoints in lymphocytes and proportion of T-reg cells
2. Co relation of above parameters with clinical and/or histological profile of LN

Methods:

Total of 56 Lupus patients (18 with Active and 38 with Inactive disease) and 44 Healthy Control were included in the study. All demographic and Biochemical analysis were done for all patient included in the study.

Samples collection:

Total of 5ml of Blood was drawn from the patient as well as healthy control used for PBMCs separation to quantify the T-regulatory cell and immune checkpoints.

PBMCs were isolated using Ficoll density gradient. The isolated PBMCs were analysed by Flow cytometry to see immune cells expression.

Ethics:

The study was approved by the Institute Ethics Committee (Ref No. 480/05.06.2020)

Results:

There was no changes in the total percent of T-cells between healthy controls and diseased patients, however significant change was observed in percent of CD25+ T-regulatory cells and FOXP3+ cells. In patients with LN the number of FOXP3+ cells were significantly lower in patients with as compared to inactive disease.

Conclusions:

Better understanding of these pathogenic processes will not only help to understand the pathogenesis of this complex disease but also aid in identification of patients likely to develop severe for of the disease. We till now have markedly lower CD25 (T-regulatory cells) and FoxP3 cells in patients having LN. These findings need to be further validated in remaining sample specially in active versus inactive LN.

Figures, tables:

Table 1: Comparison of immune cells and FoxP3 expression in healthy controls and lupus nephritis patients

	Healthy control	Lupus Nephritis patient	Ratio Healthy Vs Disease	p-value
CD3+	59.65 ± 0.40	57.73 ± 0.424	1:0.96	0.59
CD4+	14.26 ± 9.32	14.55 ± 0.250	1:1.02	0.9
CD8+	36.53 ± 0.40	40.047 ± 0.53	1:1.09	0.4
CD25+	45.65 ± 0.70	12.48 ± 0.63	1:0.273	<0.001
FoxP3+	23.86 ± 0.787	0.787 ± 0.05	1:0.03	<0.001

Table 2: Comparison of immune cells and FoxP3 expression in active and inactive lupus nephritis patients

	Healthy control	Lupus Nephritis patient	Ratio Healthy Vs Disease	p-value
CD3+	58.19 ± 0.81	57.65 ± 0.40	1:0.99	0.755
CD4+	12.59 ± 0.354	15.54 ± 0.44	1:23	0.5
CD8+	36.622 ± 1.07	42.54 ± 0.432	1:1.16	0.8
CD25+	17.025 ± 1.00	13.11 ± 0.595	1:1.29	0.7
FoxP3+	0.372 ± 0.066	1.04 ± 0.11	1:2.79	0.3

P-7

Abstract Title:

Assessment of cytokine profile in children with primary hemophagocytic lymphohistiocytosis and macrophage activation syndrome

Abstract no: 12

All authors: Rashmi Arun[1], Saniya Sharma[1], Amit Rawat[1], Manpreet Dhaliwal[1], Vignesh P[1], Pulkit Rastogi[1]

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Abstract:

Background:

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening condition associated with the hyperactivation of lymphocytes and histiocytes, eliciting a hyperinflammatory response as a result of hypersecretion of cytokines. The estimated incidence of HLH in children below 18 years old is approximately 1 in 100,000. Primary HLH (pHLH) is associated with T/NK cell cytolytic function or degranulation in response to an antigenic stimulus (familial HLH [FHLH]) or defects in primary immunodeficiency diseases like XLP1 and XLP2.

Objective:

This study aims to assess cytokine levels in pediatric patients with primary HLH and macrophage activation syndrome (MAS). It also seeks to correlate serum cytokine levels in HLH patients with hematological and other laboratory parameters.

Methods:

This observational study, conducted at an Advanced Pediatric Center in North India from January 2023 to June 2024, enrolled newly diagnosed and follow-up cases of pHLH and MAS. A total of 20 cases were included in the study. IL-6 and IFN-γ levels were measured using the Bioplex assay, while IL-18 and IL-1β levels were measured using ELISA. Data were entered in Microsoft Excel and analyzed using SPSS version 29 (IBM Corp). Quantitative data were compared using the Student's t-test. The Mann-Whitney U test was performed for comparing nonparametric quantitative data.

Results:

IL-1β, IL-6, and IFN-γ levels were higher in pHLH cases compared to controls, though not statistically significant (p-values: 0.27, 0.22, and 0.208, respectively). IL-18 levels were significantly higher in cases compared to controls ($p < 0.001$). Similarly, in MAS cases, IL-1β, IL-6, and IFN-γ levels were higher compared to controls, though not statistically significant (p-values: 0.18, 0.028, and 0.367, respectively). However, IL-18 levels were significantly higher in MAS cases compared to controls ($p < 0.002$).

Conclusions:

IL-18 was a statistically significant cytokine in both pHLH and MAS cases. ROC analysis showed the highest sensitivity (93.8%) and specificity (93.7%) for IL-18. IL-18 levels were negatively and significantly correlated with Hb and platelet counts in pHLH patients and positively correlated with ferritin levels in both pHLH and MAS cases. IL-6 levels were negatively correlated with platelet counts, while IFN-γ levels were positively correlated with ferritin and triglyceride levels in MAS cases.

Keywords:

Hemophagocytic lymphohistiocytosis, Macrophage activation syndrome, Interferon gamma

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P-8

Abstract Title:

"Immune Cytopenia As The Sole Presentation Of Digeorge Syndrome: A Diagnostic Challenge"

Abstract no: 13(A)

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Abstract:

INTRODUCTION:

DiGeorge Syndrome is a T cell disorder occurring due to microdeletion of Chromosome 22q11 commonly presenting with hypoplasia of thymus and parathyroid glands along with cono-truncal anomalies. Immune-cytopenia as an initial presentation of DiGeorge Syndrome is rarely reported.

CASE DESCRIPTION:

1st admission: 20 months old girl child, born to unrelated parents, immunized up-to date, with no significant dysmorphisms, was hospitalized for febrile illness during which labs showed pancytopenia (anemia, neutropenia and thrombocytopenia) with positive Direct antiglobulin Test (DAT – 1+) and low reticulocyte count. Abdominal Ultrasonography showed Hepatosplenomegaly. She had gum bleeds necessitating platelet transfusion. Bone marrow aspiration revealed normocellular marrow. Given the suspicion of post-infective pancytopenia, the child was treated with intravenous immunoglobulin (IVIG) and subsequently discharged in stable condition.

2nd admission: Within a week, she presented with high grade fever, periorbital cellulitis and Methicillin-resistant Staphylococcus aureus (MRSA) bacteremia. Investigations revealed persistent pancytopenia with DAT 3+. Echocardiogram and serum electrolytes were normal. Immunoglobulin profile, T, B & NK cell subset analysis were normal. Hemophagocytic Lymphohistiocytosis (HLH) markers (ferritin, fibrinogen, triglycerides, coagulation profile) were within normal range. Child was treated with MRSA coverage along with high dose IVIG. Genetic analysis was sent suspecting immune-cytopenia. She was discharged on

steroid and fluconazole prophylaxis awaiting genetic results.
3rd admission: One week after discharge, child presented with septic shock due to submandibular and submental cellulitis with abscess, requiring PICU admission. Child had persistent neutropenia, anemia with low reticulocyte count. Platelet count was normal. DAT and Anti-Nuclear Antibodies (ANA) were positive. MRI neck showed extensive cellulitis. Surgical exploration was done. Lymph node culture grew MRSA. Bone marrow aspiration showed normocellular marrow with few hemophagocytes. Methylprednisolone and IVIG were given along with antibiotics. Whole exome sequencing reported as likely pathogenic copy number variant of chromosome 22 deletion. MLPA revealed Microdeletion in the 22q11.21 region confirming DiGeorge Syndrome.
She was started on Sirolimus and Co trimoxazole prophylaxis along with regular IVIG replacement therapy. On follow up, steroids were tapered and stopped, pancytopenia improved. She is doing well on above mentioned treatment with no further hospitalizations.

Conclusions:

This case highlights that the possibility of DiGeorge syndrome should be considered in persistent immune-cytopenia even in the absence of phenotypic features.

P-9

Abstract Title:

Estimation Of Anticytokine Antibodies In Patients With Recurrent, Severe Or Atypical Infections

Abstract no: 14

All authors: Gayathri[1], Amit Rawat[1], Rakesh Pilania[1], Vignesh Pandiarajan[1], Saniya Sharma[1], Surjit Singh[1]

Complete detail of Institute including city state:

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Abstract:

Background:

Patients with anti-cytokine autoantibodies may present with a clinical profile that mimic inborn error of immunity that affect the cytokine or its downstream pathway as these antibodies inhibit the cytokine's biological action. Though a few genetic variants have been implicated, they are predominantly considered adult-onset disease.

Objective:

We aimed to identify and quantify anti-cytokine antibodies in symptomatic patients with recurrent/severe / disseminated infections and to study and analyze the clinical profile of patients with anti-cytokine antibodies in pediatric population in south east Asian country, India.

Methods:

Patients with recurrent, atypical or severe infection attending the Out patient department or admitted in the wards of Allergy Immunology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India were enrolled between July 2023 to Dec 2024.

Results:

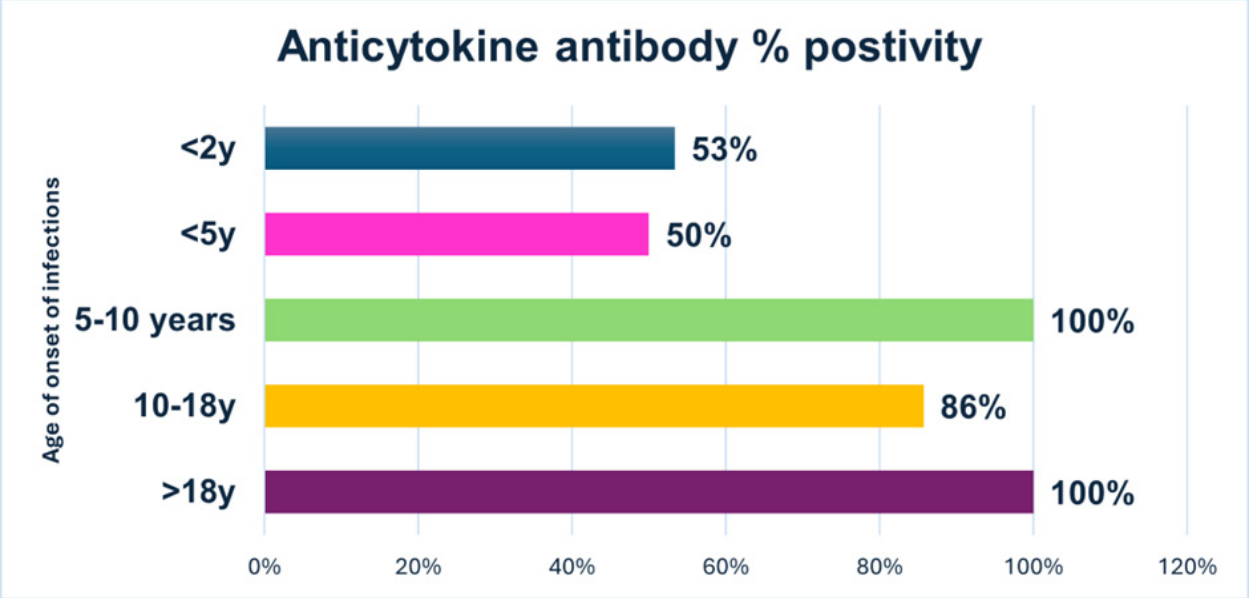
11 female patients and 25 male patients (36 patients) and 30 controls were enrolled. All the patients were excluded of human immunodeficiency viral infection through serology. Median age at the time of collection of sample was 5 years (range 6months – 66 years). Anti IL 6 antibody was associated with staphylococcal infection and low CRP. Anti IFN ω,β,α2 antibodies were associated with viral infections. Anti IFNγ antibodies

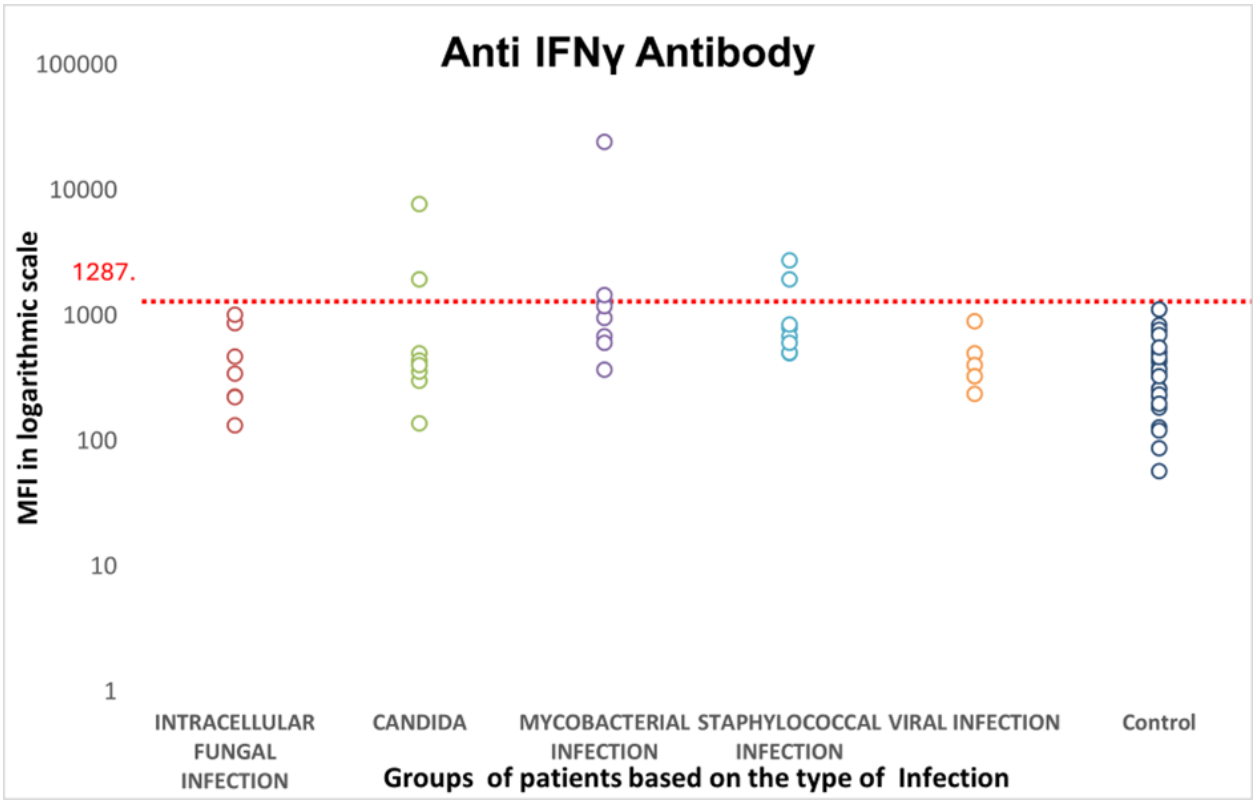
were associated with tuberculosis and NTM infection. Anti IL12p40 was associated with intracellular fungal infections. Anti IL17A/Anti IL17F and anti IL22 antibodies were associated with candidal infection. In addition, Anti IL 22/17 antibodies and Anti IL12p40 antibodies were associated with Staphylococcal infection with high CRP. Anti IL1, Anti IL8, Anti IL18 were associated with prolonged disease duration and increased inflammation. Apart from RAG1 defect, FOXN1, IL12RB1, STAT3 were associated with formation of anticytokine antibodies with possible predisposition to infection.

Conclusions:

We report the first study from the Indian subcontinent on anti-cytokine antibodies predisposing to infection. We found that apart from RAG1 defect, STAT3, FOXN1, IL12RB1, ZNFX1 can be associated with Anti cytokine antibodies. We observed that children can develop anticytokine antibodies without an underlying inborn error of Immunity. A high index of suspicion may help in diagnosis, initiation of appropriate treatment including immunosuppression and targeted therapy, and prevention of infection in predisposed individual by appropriate use of vaccines, antimicrobial prophylaxis.

Figures, tables:





P-10

Abstract Title:

Screening for Inborn Errors of Immunity (IEI) in a tertiary healthcare centre of Eastern India: Our experience with the immunoglobulin deficiencies

Abstract no: 17

All authors: Gautom Kumar Saharia[1], Dr. Amit Kumar Satapathy[1], Dr. Rashmi Ranjan Das[1], Dr. Tapas Kumar Som[1], Dr. C Preetam[1], Dr. Anupam Dey[1], Dr. Manaswini Mangaraj[1].

Complete detail of Institute including city state:

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Presenting Author email: gsaharia@yahoo.com

Abstract:

Background:

Recently announced National Policy for Rare Diseases (NPRD) 2021 has put IEIs like SCID, CGD, WAS in Group 1a and XLA & CVID in Group 2b. Because of inadequate medical awareness, a significant number of patients with IEI goes unrecognized or are diagnosed late. There is a severe dearth of data in terms of incidence or prevalence of IEIs in the eastern part of India. Hence, we are carrying out this study with objectives of determining the prevalence of the selected IEI in our population and to evaluate the causes and pattern of IEI along with creating awareness amongst parents and health care workers.

Methods:

The study is a prospective, observational hospital-based study. All children up to 18 years of age satisfying the inclusion criteria by Jeffrey Modell Foundation are enrolled. Sample collected after approval from Institutional

Ethics Committee. Venous blood samples were taken in plain and EDTA vials. Serum concentration of Immunoglobulins and Complements were estimated from plain vial using photometric analyser. The analysis of T-B-NK-cell immunophenotypes and DHR assay in EDTA blood were carried out by flow cytometry.

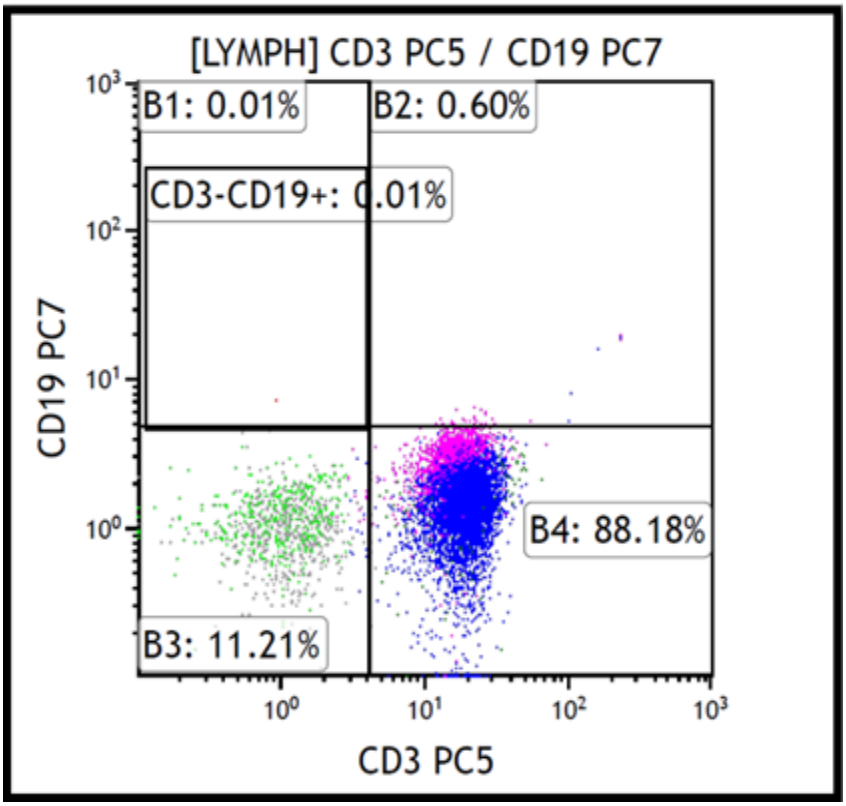
Results:

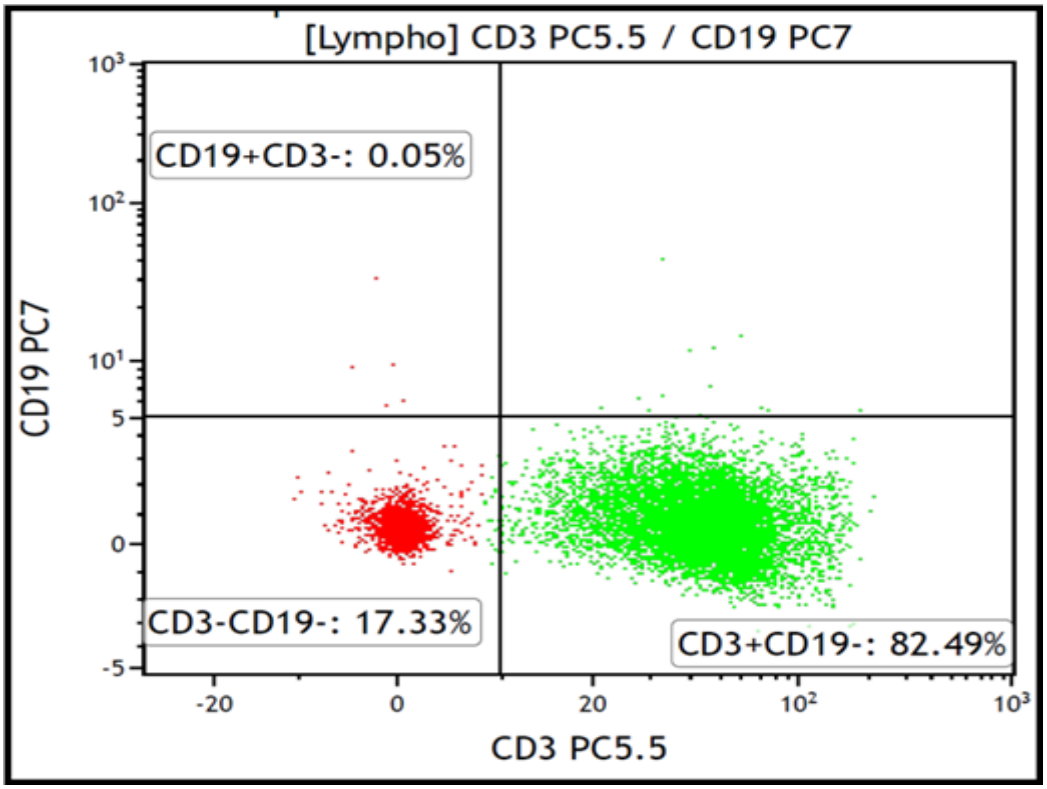
We screened 140 suspected cases of IEI till date and age of participants 4 weeks to 12 years. Multiple consultations done before visiting us. Most common presentation: repeated sepsis, pneumonia, abscess formation, failure to thrive the preliminary data analysis of the immunophenotyping revealed 1 case of SCID, 4 cases of CVID, 4 cases of CGD, 2 cases each of XLA and ALPS and 1 of C1q deficiency. So, the predominant pattern of IEI is the Immunoglobulin deficiency type. Our findings also correlate with the available literature from other centres in India where predominant pattern is Ig deficiency.

Conclusions:

We expect to know the prevalence of IEIs from this region after completion of the study along with the dominant pattern of disease in the region. We also expect to raise the awareness about IEIs amongst parents and health care workers while carrying out the study resulting in strengthening the healthcare delivery system.

Figures, tables:





P-11

Abstract Title:

Intracranial granulomas in a patient with Chronic Granulomatous Disease: An unusual entity

Abstract no: 20

All authors: Madhusudan S[1], Mounika Reddy[1], Taallapalli Ashok Vardhan Reddy[1], Niraj Kumar[1], Abhishek Jagdishchander Arora[1], Vignesh Pandiarajan[2], Amit Rawat[2]

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[2]PGIMER, Chandigarh, India

Presenting Author email: madhu_1511@yahoo.com

Abstract:

Background:

Mycobacterial infections are well known in patients with chronic granulomatous disease (CGD); intracranial tuberculomas are rare.

Case details:

A 13 years-old-boy presented with recurrent pneumonia from infancy. ELISA for human immunodeficiency virus was non-reactive. Immunoglobulin profile showed normal IgM, elevated IgG and IgE, and reduced IgA levels. Nitroblue tetrazolium test and dihydrorhodamine test were suggestive of CGD. Next generation sequencing did not identify any pathogenic variant in CGD genes. Screening for NCF1 GT deletion by genescan showed a homozygous variant in the NCF1 gene, c.75_76delGT, p.(Tyr26Hisfs*26), known to result in a p47phox deficient form of CGD. Trimethoprim-sulfamethoxazole and itraconazole prophylaxis were started.

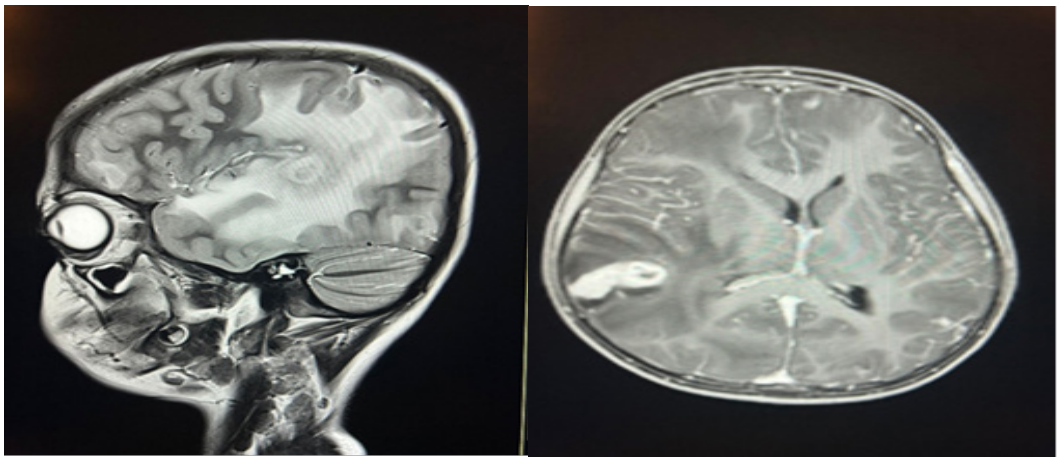
Four months later, he presented with intermittent fronto-temporal headaches, initially transient, and self-limited, and subsequently severe. Examination was unremarkable. Magnetic resonance imaging (MRI) of the brain revealed multiple, conglomerate ring enhancing lesions with perilesional edema in bilateral parietal, frontal and cerebellar lobes causing midline shift; magnetic resonance spectroscopy (MRS) showed decreased NAA and lipid peak with lactate reversal – suggestive of infective etiology, likely tuberculoma. As multiple hemorrhagic lesions were noted in the SWI sequence fungal etiology was also suspected. Review of literature showed aspergilloma to be more common than tuberculoma in CGD. As immediate laboratory confirmation was not possible, both empirical ATT and voriconazole were started, with intravenous dexamethasone. Serum aspergillus galactomannan was negative. Histopathology examination of the brain biopsy sample showed multiple granulomas with aggregates of epithelioid histiocytes with dense inflammatory infiltrate of lymphocytes and plasma cells and areas of necrosis, suggesting necrotizing granulomatous inflammation. No bacterial or fungal elements or acid-fast bacilli were seen; culture was sterile. As no evidence of fungal etiology was found, antifungals were stopped, ATT and steroids were continued. Symptomatic resolution and radiological improvement were noted.Discussion:

The brain is an uncommon but well-known site of infection; brain abscesses in CGD are of bacterial or fungal etiology [1-4]. Mycobacterial infections are well-known but CNS tuberculosis is rare [1-5]. In a series of 236 patients, mycobacterial disease was seen in 44; only one had CNS tuberculosis [4]. Granulomatous infections in the brain have a wide etiology [6]. A combination of clinical, laboratory, imaging and histopathological features is usually diagnostic but may remain inconclusive [6, 7].

Conclusions:

Our patient highlights the persisting lack of awareness of CGD, the need for urgent neuroimaging when patients have intractable neurological symptoms, the diagnostic dilemma in intracranial granulomas, and intracranial tuberculomas, a rare manifestation in CGD.

Figures, tables:



P-12

Abstract Title:

Clinical and Histopathological features of Gastrointestinal involvement in Common variable immunodeficiency (CVID): A single center experience from South India.

Abstract no: 21

All authors: Harikrishnan Gangadharan[1], Sankar Sundaram[1], Letha V[1], Manisha Madkaikar[2], Umair Bargir[2], Lavina Temkar[2]

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Abstract:

Background:

Gastrointestinal involvement is an important but underdiagnosed complication of CVID. We aim to describe the clinical, microbiological, and histopathological findings in five adult patients with CVID-related gastrointestinal involvement.

Methods:

Among a prospective cohort of patients with inborn errors of immunity (IEI) who attended the Rheumatology clinic of our hospital between October 2020- April 2024, the case records of patients diagnosed with CVID were screened for gastrointestinal involvement. The diagnosis of CIVD was made as per the ESID 2014 criteria and gastrointestinal involvement was diagnosed based on clinical symptoms, gastrointestinal imaging, stool microbiology, upper and lower gastrointestinal biopsy.

Results:

Among 32 patients with IEI who attended our clinic during the study period, 8 patients were diagnosed with CVID. Among the 8 CVID patients, 5 patients were found to have gastrointestinal involvement. The demographic, clinical, microbiological and histopathological features of these five patients are summarized in table 1. Among the five patients, 3 were female. The mean age of patients was 29.8 ± 7.25 years and median disease duration was 15 years (IQR, 13.5-27.5). The median diagnostic delay was 15 years (IQR, 7.5-27). The most common symptom was chronic diarrhea (80%) followed by weight loss (60%). Autoimmune features were seen in 80% of patients and splenomegaly was seen in 60%. The most common upper gastrointestinal biopsy finding was antral gastritis and most common lower GI biopsy finding was cryptitis. Two patients had biopsy findings compatible with CVID related enteropathy. Infection related complications were seen in only 2 patients.

Conclusions:

We found a high incidence of gastrointestinal involvement in our CVID patients (62.5 %) and a significant diagnostic delay was seen in CVID patients with gastrointestinal involvement. Autoimmune manifestations are frequent in CVID patients with gastrointestinal involvement, which adds to the challenges in the management of these patients.

Figures, tables:

Table 1: Clinical, microbiological and molecular characteristics of gastrointestinal involvement in patients with CVID

	P1	P2	P3	P4	P5
Age (years)	34	31	37	29	18
Gender	Male	Female	Male	Female	Female
Disease duration (years)	15	30	25	12	15
Diagnostic delay (years)	3	29	25	12	15
Diarrhea	+	+	+	-	+
Abdominal pain	-	+	-	-	+
Weight loss	+	+	+	-	-
Autoimmune features	Colitis CVID related enteropathy	-	CVID related enteropathy	Autoimmune cytopenia, vitiligo	Autoimmune hemolytic anemia, autoimmune thyroiditis
Liver disease	-	-	-	Chronic liver disease- liver biopsy suggestive of non-alcoholic steatohepatitis, Portal hypertension	Non-alcoholic fatty liver disease
Splenomegaly	absent	absent	present	present	present
Infectious complication	bronchiectasis	bronchiectasis	none	none	none
Immunological features	Pan hypogammaglobulinemia, low class switched memory B cells	Pan hypogammaglobulinemia, low class switched memory B cells	Pan hypogammaglobulinemia, low class switched memory B cells	Pan hypogammaglobulinemia, low class switched memory B cells	Pan hypogammaglobulinemia, low class switched memory B cells
Pathogen identified	None	Clostridium Difficile	Helicobacter Pylori	None	None
Whole exome sequencing	No variant identified	No variant identified	No variant identified	Novel heterozygous missense variant in exon 2 of SBDS gene (c.257A>G) **(p.Gln86Arg)** Reported as a variant of uncertain significance	Homozygous silent variant in exon 51 of NBAS gene. (c.6840G>A) **(p.Thr2280=)** Reported as a variant of uncertain significance
Outcome	Alive, on monthly IVIG, cotrimoxazole prophylaxis.	Death from severe malabsorption, sepsis. Was treated with monthly IVIG, cotrimoxazole prophylaxis and mesalamine	Lost to follow up	Alive, on monthly IVIG, cotrimoxazole prophylaxis, tapering dose of oral prednisolone	Alive on monthly IVIG, cotrimoxazole prophylaxis, tapering dose of oral prednisolone and mycophenolate mofetil

P-13

Abstract Title:

A unique and interesting phenotypic presentation of a 10 year old child with IL-2RA deficiency.

Abstract no: 23

All authors: Gaurang Deshpande[1], Liza Rajasekhar[2], D Phani Kumar[2]

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Abstract:

A 10-year-old adolescent boy was referred with manifestations of recurrent eczema, recurrent infections, cytopenia and organomegaly. He was born to a non-consanguineously married couple, first in birth order with uneventful birth history and development normal for age. Symptomatic since 1st week of life, when noticed to have fever and papular rashes over the whole body including face. Prominent dysmorphic features e.g. depressed nasal bridge, low set ears, retained teeth, mild kyphosis were noted as a child grew up. His mother denies any history of antenatal exposure to toxic agents, substance abuse or any infections during her pregnancy. Breastfeed till 6-8 months of age and received vaccination as per followed protocol. 4-5 years from birth patient persisted to have erythematous skin rash, recurrent rhinitis, mucositis, ocular congestion. At 2 years of age cervical and inguinal lymphadenopathy associated with purulent discharge along with hepato-splenomegaly was observed and skin biopsy done was suggestive of spongiotic dermatitis with dermal peri vascular lymphocytic infiltrates. At the age of 6 years he developed polyarthralgia and multiple episodes of loose stools requiring admission with ongoing mucocutaneous manifestations. Importantly, patient also had recurrent episodes of multiple infection including, URTI's, recurrent pneumonia, mucocutaneous candidiasis, skin abscesses, seborrheic dermatitis. Patient was admitted 4-5 times for ongoing complaints in the pediatric hospital and was known to have one admission with febrile neutropenia and oral candidiasis and pneumonia. 1 year back, at first visit to our hospital,weight was 20 kg i.e. less than 3rd centile(underweight), Height 124 cm i.e. between 3rd to 10th centile (stunting) and dysmorphic features as mentioned above were seen. Hyperpigmented scaly rash over periorbital and peri oral area, hyperpigmented macules over thighs,PIPs, Interphalangeal area, Seborrheic scales over Scalp and Left external ear candidiasis was observed. Multiple Discrete lymph nodes 1-3cm size in cervical, axillary and inguinal area were noted. Sr. IgE levels repeated were very high, 2879(2.1-48.5), anemia and leukopenia were persistent. To rule out causes of cytopenia, repeat BM biopsy was done which revealed normal cellularity with lymphocytosis, IHC for lymphoma was negative. EBV serology was negative, ANA was was strongly positive and probability of autoimmune cytopenia was considered.. Lymphocyte subset enumeration analysis showed the normal proportion of T cell, B cell and their subtypes(CD3,CD4,CD8 T Cells, CD19 B Cells).Genetic exome sequencing was done, to our surprise it was suggestive of CD25RA deficiency with a background of highly suggestive clinical clinical suspicion of AD-HIES (NIH Score-48).

Figures, tables:

Haemoglobin	4.2
TLC	3800
N,L)	7/88
Platelet	2.7 Lacs
ESR	130

IgA(70-400)	731
IgM(40-230)	223
IgE(2.1-48.5)	206
IgG(700-1600)	2060

I. Bone Scan/ Hb Electrophoresis/ Sickling test :	○ NORMAL
II. Bone Marrow (2017):	○ Few *epitheloid granuloma* and langerhens cell. ○ AFB negative Myeloid series depleted ○ 40% cellularity ○ Few foci of fibroblastic cells

Important Labs:
ANC-1053
CD8:332(490-1300)
CD19,CD3,CD4 normal
CD4/CD8: 2.6%

Further Work Up at our institute

CBP: 5.7/1600/1.2lacs

ANA: 4+(S)

Bone Marrow:
1. Marrow Lymphocytosis
2. Normal M:E ratio
3. IHC Negative for lymphoma

Sr. IgE:2815

EBV Serology: IgG 1.4 (+), IgM negative

Lymphocyte Subset Enumeration :**Normal values** of
- CD3+/CD4+/CD8+/CD19+(B Cells)/CD16+ & CD56+
- CD4/CD8 : 1.1

ALPS (Flow Cytometry): **Borderline**

P-14

Abstract Title:

Outcomes of hematopoietic stem cell transplant in children with Mendelian susceptibility to Mycobacterial disease from a tertiary care centre from Southern India

Abstract no: 27

All authors: Kavitha Ganesan[1], Anupama N[1], Vijayashree M[1], Nithya S[1], Minakshi B[1], Anurag NR[1], Ramya U[1], Revathi R[1]

Complete detail of Institute including city state:

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Presenting Author email: kavitha5293dr@gmail.com

Abstract:

Introduction:

The IL-2 and IFN pathway mediated immunity is essential for host defense against mycobacterium tuberculosis. Mendelian susceptibility to mycobacterial disease (MSMD) can be associated with significant morbidity and hematopoietic stem cell transplantation (HSCT) is a curative option.

Methods:

We describe the outcome of children with MSMD due to IFN-receptor and IL12 defect who underwent HSCT in our unit from December 2015 to December 2023. In view of graft rejection in a child who received reduced intensity conditioning for a haploidentical HSCT with IFN-levels, pre-transplant immune suppression(PTIS) with 2 cycles of Fludarabine(40mg/m2 for 5 days) and dexamethasone(25mg/m2) followed by double volume plasma exchange, a myeloablative conditioning and a high stem cell dose of 10 million cells per kg of recipient was performed in children with IFN-receptor.

Results:

Seven children underwent eight HSCT in our cohort. Four children had genetic mutation with IFN gamma defect while the remaining three had IL12 defect. The male: female ratio was 1.6:1 and median age was 4.5 years in the cohort (range 6 months to 10 years). Haplo-identical HSCT was performed in five children while the remaining had a matched family donor HSCT. Majority of the children received Peripheral blood stem cell (PBSC) as the stem cell source (75%). The children with IL12 defect tolerated and engrafted well with reduced intensity conditioning while children with high levels of IFN gamma defect performed better with myeloablative conditioning due to high risk of graft rejection. Acute GVHD was seen in two children with grade 1-2 involving the skin and gut. Chronic GVHD of liver was seen in one child following donor lymphocyte infusion for his mixed chimerism. Cytomegalovirus reactivation was seen in four children with maximum copies of 1,90,000 and all of them responded well to Ganciclovir and cidofovir therapy. One child had primary graft failure that was managed with a second HSCT and the child is doing well while another child had secondary graft failure leading to death due to invasive fungal infection. The overall survival in the cohort is 87%. All the children are on long term follow-up ranging from 2 years to 8 years post HSCT.

Conclusions:

HSCT can be potentially curative, however is fraught with challenges in MSMD. PTIS with fludarabine and dexamethasone followed by plasma exchange, use of myeloablative conditioning and providing a high stem cell dose are needed for durable engraftment and to prevent graft rejection in children especially with IFN-receptor

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P-15

Abstract Title:

"Chronic Recurrent Infections and Gingivitis in a Young Male: A Case of Cyclic Neutropenia with ELANE Mutation"

Abstract no : 29

All authors: Lovely Kumari[1], Dr. Jagan Babu[1], Dr. Aishwarya G[1], Dr. Molly Mary Thabah[1], Dr. Chengappa Kavadichanda[1]

Complete details of Institute including city state:

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Presenting Author email: lovely.4821@gmail.com

Abstract:

Introduction:

Severe congenital neutropenia (SCN) is characterized by a severe reduction in neutrophil counts (absolute neutrophil count [ANC] <500/µL), typically presenting in infancy. It is marked by recurrent bacterial infections due to neutropenia and risk of progression to myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). We report one such case of a 19 year male with recurrent infections and gingivitis to highlight importance of early diagnosis, response to Granulocyte Colony Stimulating Factor (G-CSF)and monitoring for risk of leukemogenesis.

Case Presentation: A 19 year-old male born full term with normal development out of non consanguineous marriage presented with history of recurrent otitis media and externa (leading to right ear conductive hearing loss) since age five, rhinosinusitis, painful oral ulcers, recurrent diarrheal episodes. Over the years there were recurrent pustular skin lesions over back, gluteal region, legs and forearm, that ruptured and formed ulcers and healed with scars and atrophy. Examination revealed generalised lymphadenopathy, gingival hyperplasia, and multiple healed scars and ulcers(Figure 1). He also had episode of abdominal pain with a left iliac fossa collection; CT scan revealed a lung cavity and necrotic nodal masses. Tuberculosis work up was negative. Each episode was treated with antibiotics.

Investigations: Investigations revealed neutropenia on several occasions suggesting underlying immunodeficiency due to neutrophil defects along with compensatory monocytosis. Immunoglobulin profile showed elevated IgG and IgE with normal IgA and IgM (Table 1). Whole Exome sequencing showed heterozygous pathogenic variant in the ELANE(Exon2, c.137C>T) gene linked to cyclic neutropenia and two variants(one pathogenic and one of uncertain significance) in the CFTR(Exon9,c.1210-11T>G) gene associated with cystic fibrosis. Bone marrow aspiration indicated myeloid maturation arrest and marginal blast prominence, suggesting risk for MDS but cytogenetic analysis was negative. The patient was started with G-CSF (filgrastim)300 mcg daily resulting in improved neutrophil counts and ulcer healing.

Conclusions:

ELANE mutation can be seen in spectrum of both severe congenital neutropenia and cyclic neutropenia. This case highlights the importance of considering cyclic neutropenia in young adults presenting with recurrent infections and gingivitis. The identification of an ELANE mutation helped establish the diagnosis, and treatment with G-CSF led to clinical improvement. Regular monitoring is crucial for early detection of potential leukemic transformation, ensuring timely intervention and optimal patient management.

Figures, tables:

Parameters		22.1.20	11.7.22	26.4.23		1.6.23	27.9.23	6.10.23	24.1.24	12.05.24
		Before G-CSF				After G-CSF				
Haemoglobin(gm/dL)		9.9	10.9	11.9		9.4	11.8	10.8	12.4	12.6
Total Leukocyte Count		4090	4550	4910		3350	4040	4950	5510	6980
Absolute Neutrophil Count		0	1000	1060		150	40	1250	1680	1500
Neutrophils(%)		0	21.9	21.6		4.5	1.1	25.3	30.4	21.6
Lymphocytes (%)		40.8	47.7	42.4		31.6	43.8	53.5	40.5	34.8
Monocytes(%)		50.6	24.0	30.5		56.7	43.3	9.7	19.6	27.2

Immunoglobulin profile		
Isotype	Levels (g/L)	Normal Range
IgG	32.9	7-16
IgA	7.51	0.7 - 4
IgM	1.64	0.4 – 2.3
IgE	2340	< 100

TBNK-analysis by Flow Cytometry		
Cells	Percentage	Cells/uL
Lymphocytes	%Lymphocytes	4701.0
CD3+	74.3	3492.1
CD3+CD4+CD8-	39.8	1870.5
CD3+CD4-CD8+	27.2	1278.4
CD3-CD19+	12.7	595.2
CD3-(CD16+CD56+)	12.5	589.0

P-16

Abstract Title:

Novel gene causing Severe Congenital Neutropenia

Abstract no: 30

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Abstract:

Introduction:

Severe congenital neutropenia (SCN) comprises a heterogeneous group of genetically determined disorders characterized by decreased neutrophils in the peripheral blood and severe skin and deep bacterial infections.

CASE REPORT:

A 4 year old male child, born of nonconsanguineous marriage; presented with recurrent sinopulmonary infections starting from 5 months age. He was admitted at 15 months with bronchopneumonia, pyoderma gangrenosum and sepsis. He subsequently also suffered multiple episodes of impetigo and abscess. Immunological tests including lymphocyte enumeration, nitroblue tetrazolium test and immunoglobin levels were normal. Neutrophil count persisted at <500 cells/cumm. Bone marrow examination revealed hypocellular marrow with sequential maturation of neutrophils. He was started on GCSF to maintain ANC>1500/cumm along with antibiotic and antifungal prophylaxis. We performed exome sequencing which did not reveal any pathogenic or likely pathogenic variants in any known genes associated with neutropenia. On follow up he developed acquired microcephaly with delayed speech development and was diagnosed with autism spectrum disorder. Neurological evaluation revealed subclinical epileptic discharges and cerebellar atrophy suggestive of possible neurodegenerative disorder. On re-analysing the data we found a novel homozygous variant in VPS52 gene which was confirmed by Sanger sequencing in index patient. The variant is a splice variant in intron 10 and likely pathogenic according to ACMG guidelines with a CADD score of 29. Both parents are heterozygous for this variant. RNA sequencing showed an aberrant transcript with loss of intervening exons. Golgi-associated retrograde protein (GARP) and endosome-associated recycling protein (EARP) are related heterotetrameric complexes that associate with the cytosolic face of the trans-Golgi network and recycling endosomes, respectively. VPS52 is a vacoular transporting protein existing as a complex with VPS51 and VPS53. GARP and EARP share three subunits, VPS51, VPS52 and VPS53. Defects in VPS51 and VPS53 also have neurodegenerative phenotype and mild neutropenia.

Conclusions:

We present a novel genetic cause of SCN, which combines features of a neurodegenerative disorder with heightened susceptibility to severe infections. In today's era, clinical immunologists must equip themselves with the skills for raw data analysis to uncover novel genes underlying complex phenotypes.

P-17

Abstract Title:

PID And Nocardia: An Ignored Association.

Abstract no: 32

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Abstract:

Background:

Nocardiosis is caused by the gram-positive bacterium Nocardia spp. The most common PID associated with nocardiosis is CGD. This case series highlights three cases of nocardiosis with a diagnosis of PID other than CGD.

Methods:

Three patients with Nocardia spp isolated from different sites were included.

Results: P1, 9 year old male child, diagnosed case of IL12RB1 deficiency, presented with seizures. MRI brain was suggestive of multiple ring enhancing lesions. As he had multiple episodes of TB in past, he was empirically treated with AKT and steroids for tuberculomas although CSF GeneXpert and AFB were negative. Persistent signs of raised ICT & newer lesions on MRI brain prompted us to undertake biopsy that showed gram positive and acid fast filaments on modified ZN stain. Culture grew Nocardia spp on culture. Initiation of ceftriaxone, linezolid and amikacin arrested the disease with complete resolution after 3 months of therapy.

P2, 10 year old male presented with cachexia, deep jaundice, abdominal distension with right pyopneumothorax and large splenic abscess. Splenic aspirate and pleural tap revealed presence of Nocardia spp on culture and Nocardia cyriacigeorgica on MALDI-TOF. In view of disseminated nocardiosis, NBT/DHR test was advised which was normal, WES revealed homozygous IL12RB1 pathogenic variant. He received high dose co-trimoxazole and linezolid according to sensitivity. The child gained 9kg weight with resolution of chest lesions and reduction in size of splenic lesions after 6 months of therapy.

P3, 9 year male with refractory atopic dermatitis since 3 months of age. He had eosinophilia (10,000 cells/cumm) and hyper IgE (2360 IU/ml). He was diagnosed with DOCK8 deficiency on NGS. While being evaluated for BMT he had focal seizure with ataxia, MRI brain revealed presence of cerebellar abscess. Biopsy revealed Nocardia spp. He was treated with cotrimoxazole, ceftriaxone and linezolid for 6 weeks followed by BMT.

Conclusions:

Isolation of Nocardia at any age must prompt one to look for underlying PID other than CGD as well. Extensive and invasive tests along with radiological tests need to be undertaken in patients with PID to isolate and appropriately treat.

P-18

Abstract Title:

Infantile Monogenic IBD: A Case Series

Abstract no: 33

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Abstract:

Background:

Patients with a varied spectrum of rare genetic disorders can present with inflammatory bowel disease like phenotype.

Methods:

Retrospective study of all children referred to us with infantile onset of chronic diarrhoea with a monogenic error.

Results:

12 children (6females:6males). All children had failure to thrive. The mean age of presentation was 3.5

months with an average delay in diagnosis of ~3 years. 6 were born of consanguineous unions. 7 children had enteropathy like presentation with chronic diarrhoea, 5 had enterocolitis like presentation with bloody diarrhoea and abdominal pain. Additional features included global developmental delay in 4, seizures in 1 among these 4, 5 had recurrent sinopulmonary infections. 3 had low birthweight, 3 children had facial dysmorphism. Hypothyroidism, IDDM and AIHA were also seen. Among the monogenic defects identified, 3 children had pathogenic variants in TTC37, 2 each with CARMIL2 and FERMT1 defect, 1 each with FOXP3defect, CD25deficiency, ARPC1B, Wiskott-Aldrich and LRBA defect. 2 children were initiated on sirolimus and 1 on abatacept. However, in majority the diarrhoea remained refractory to therapy. Currently 4 are alive, including all children with TTC37 who had self-limiting diarrhoea, 4 have died and 4 have lost to follow up.

Conclusions:

Majority of children with monogenic IBD in this cohort had onset within 6 months of life. Extra-intestinal manifestations were common. There exist limited treatment options as majority remained refractory to therapy. HSCT can be performed for some of the defects hence early identification can be curative in some.

P-19

Abstract Title:

Good Syndrome: Not So Good After All

Abstract no: 35

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Abstract:

Background:

Good syndrome is a rare adult-onset immunodeficiency characterized by thymoma, immunodeficiency and autoimmunity. Here we present a case series of 6 cases diagnosed with Good syndrome.

Methods:

6 patients with Good syndrome were included and their clinical and laboratory data evaluated.

Results:

The median age of diagnosis was 49 years. 4 males and 2 females were included. Two had Type AB thymoma, three had type B2 and in one the type was not available. In all except two, thymoma was the primary presentation while two patients had recurrent RTI and thymoma was detected while being investigated for it. Only one patient had myasthenia gravis. All patients had panhypogammaglobinemia with a median IgG of 500mg/dl (260-681mg/dl). 5/6 had recurrent RTI. Organisms detected in sputum included PCP, pseudomonas, histoplasma, nocardia, & mycobacterium tuberculosis. Two patients had severe COVID infection requiring remdesivir. 3/4 had B cell lymphopenia, 2/4 had reduced CD4 naïve and central memory cells and 1/4 had reversal of CD4/8 ratio. Two patients have been lost to follow up, 4 patients are on monthly IVIG and antibiotic/antifungal prophylaxis with significant reduction in RTI episodes. One has undergone radical thymectomy with persistent hypogammaglobinemia, in one it's unresectable due to encasement of aorta and two have been posted for thymectomy.

Conclusions:

Patients with Good syndrome have diverse organisms including organisms usually found in phagocytic/innate immune defects. All patients had hypogammaglobinaemia including the patient without clinical RTI hence baseline IgG levels may not have prognostic value. Hypogammaglobinaemia may not improve even with thymectomy.

P-20

Abstract Title:

Severe congenital neutropenia with ELANE gene mutation presenting with necrotizing fasciitis: A case report.

Abstract no: 36

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Abstract:

Background:

Severe congenital neutropenia (SCN) is a rare genetically heterogeneous disorder of granulopoiesis, characterized by arrest in the myeloid maturation at the promyelocyte stage, resulting in consistently low absolute neutrophil counts (ANCs). We report the case of a 1 – year – old female child with a mutation in the ELANE gene who presented with necrotizing soft tissue infection of the perineal and perianal region.

Clinical Case:

1 – year – old girl child, the first child of non-consanguineous parentage, with uneventful antenatal, natal and postnatal period presented with history of fever and pustular lesions over the perineal and perianal region. The lesions were initially erythematous, pruritic and associated with local rise of temperature. By the fifth day, the lesions developed a blackish discoloration and became extensive, because of which the baby had difficulty in passing urine and stools. The baby also developed poor activity. There was a significant past history of infections in the form of omphalitis, recurrent skin infections, scalp abscess, and otitis media since early infancy.

Examination showed extensive necrotic lesions involving the perineum and perianal region.

Intravenous antibiotics (cefotaxime and amikacin) were started at presentation, which were hiked to meropenem and vancomycin, when the lesions progressed. A diagnosis of necrotizing fasciitis of the perineal and perianal soft tissues was made and surgical debridement with divided colostomy was done. Pus from the lesion yielded MDR Klebsiella sp.

In view of the significant past history and unusually severe course of the illness, a detailed workup for an underlying inborn error of immunity was done. The baby was found to have persistent neutropenia, which was

present even in the previous hospitalizations which went undetected. On exome sequencing, a heterozygous missense variant in exon 3 of ELANE gene (chr19: g.853290 G>A, p. Gly85Arg) was identified. The baby was started on G – CSF therapy. The child had good response to G – CSF in the form of better wound healing and improving neutrophil counts. The colostomy site was later closed and currently the child is doing well on G – CSF and antibiotic prophylaxis.

Conclusions:

This case highlights the importance of suspecting an underlying phagocytic disorder in necrotising soft tissue infections. Severe Congenital Neutropenia is rare in children and the diagnosis can be missed if importance is not given to the absolute neutrophil counts in a child presenting with recurrent infection

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P-21

Abstract Title:

A Novel Pathogenic BTK Variant in X – linked Agammaglobulinemia: Implications for Point of Care Genetic Diagnosis and Precision Therapies in Immune Deficiency

Abstract no: 37

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Abstract:

Introduction:

X-linked agammaglobulinemia (XLA) is a primary immunodeficiency disorder resulting from pathogenic mutations in the Bruton tyrosine kinase (BTK) gene. This condition results in the impaired development and maturation of B lymphocytes. The global prevalence of XLA is estimated to be 1 in 1,90,000 male births. Recurrent respiratory infections in children can be a manifestation of primary immunodeficiency disorders. Despite the availability of immunoglobulin replacement therapy the genetic basis of many immunodeficiencies remains underexplored. This case describes a 3 year 6 months – old child with recurrent infections and severe immune dysfunction ultimately diagnosed with a novel mutation.

Case:

A three and a half – year – old boy with a past history of 3 admissions for bronchopneumonia, presented with a large gluteal abscess. He underwent incision and drainage and pus culture drained Pseudomonas aeruginosa. On examination, he had absent tonsils. Laboratory tests showed low levels of immunoglobulin G and M and a very low CD19 count indicating impaired B cell function. Imaging studies, including CECT and USG abdomen confirmed appendicular perforation, while clinical signs of hand, foot, and mouth disease (HFMD) were also observed.

Sanger sequencing identified a novel pathogenic variant in the X chromosome (chrX:100626686-100626691:TCTCT>-, NP_000052.1:p.Arg82Ter) resulting in a truncated protein that disrupts B cell

development consistent with XLA. The patient's immune dysfunction was confirmed by severely reduced immunoglobulin levels and B cell count further supporting the diagnosis.

Conclusions:

This case highlights the critical role of point of care genetic diagnosis of primary immunodeficiencies like XLA in shaping the future of precision medicine. These findings offer valuable insights into the genetic underpinnings of immune deficiencies and provide a foundation for developing targeted therapies to improve patient outcomes.

P-22

Abstract Title:

Biological Therapies in Hyper IgD Syndrome: The Promise of Etanercept as an Alternative to Anakinra in Paediatric Management

Abstract no: 38

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Abstract:

Background:

Hyper IgD Syndrome (HIDS) is a rare autoinflammatory disorder caused by mutations in the MVK gene, manifesting as recurrent febrile episodes, rash, arthralgia, organomegaly, abdominal pain, and elevated serum IgD levels. Effective management of HIDS is often challenging, particularly in paediatric patients, due to the limited availability of targeted biological therapies like Anakinra in resource constrained settings. This study presents a case series of six paediatric patients with genetically confirmed HIDS, aged 3 months to 17 years, highlighting the significant role of Etanercept as an alternative biologic therapy. These patients experienced recurrent inflammatory episodes resistant to traditional treatments, including NSAIDs, steroids, and colchicine. Misdiagnosis was a notable hurdle, with three cases initially labelled as Crohn's disease or systemic juvenile idiopathic arthritis.

Objective:

To evaluate the clinical outcomes, treatment responses, and challenges of managing paediatric HIDS with Etanercept, particularly in cases where Anakinra is inaccessible, and to discuss the long term management needs of HIDS.

Methods:

Five paediatric patients clinically diagnosed with HIDS were included in the study. Following genetic confirmation of MVK mutations, treatment strategies were revised, and biologics were initiated. Due to accessibility issues with Anakinra, Etanercept was introduced in four patients, resulting in marked symptom control, including resolution of fever, abdominal pain, and arthralgia.

Results:

Over six months of Etanercept therapy, no significant disease flares were reported, and all four patients demonstrated improved quality of life. This underscores the efficacy of Etanercept in controlling inflammatory

episodes and managing long term disease activity when the preferred agent, Anakinra, is unavailable.

Conclusions:

This study highlights the critical role of biologics in managing HIDS, particularly in the paediatric population, where early intervention is vital to prevent complications and improve outcomes. While Anakinra remains the first line biologic therapy due to its targeted mechanism of action, Etanercept provides a viable and effective alternative in cases where access is limited. The findings emphasize the importance of early genetic diagnosis and tailored therapy, advocating for increased awareness and accessibility of biologic treatments. Long term biologic therapy is essential for disease control, as HIDS symptoms persist throughout life, underscoring the need for a comprehensive and adaptable management approach.

P-23

Abstract Title:

Gene expression profile in patients of interleukin-1βeta (IL-1β) activation disorder.

Abstract no: 39

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Abstract:

Background:

Diagnosis of systemic autoinflammatory diseases (SAIDs) is essentially based on next-generation sequencing (NGS). Gene expression studies have shown promise in aiding diagnosis and monitoring treatment response in patients with interferonopathies; however, similar studies for inflammasomopathies are lacking. This study aimed to investigate the gene expression of inflammasomes (NLRP3, AIM2, NLRC4, NLRP12 and CASPASE-1) in patients with interleukin-1βeta (IL-1β) activation disorder.

Objective:

To examine the gene expression profiles of inflammasomes (NLRP3, AIM2, NLRC4, NLRP12 and CASPASE-1) in patients with IL-1β activation disorder, including those with NLRP3-related disorders and MVK deficiency, and to compare these profiles with healthy controls.

Methods:

Patients with NLRP3-related disorders, MVK deficiency, and healthy controls were enrolled in this study. mRNA expression levels of inflammasomes (NLRP3, AIM2, NLRC4, NLRP12 and CASPASE-1) were analyzed using SyBr green chemistry, and expression levels were quantified using the delta Ct method with GAPDH as a housekeeping gene. Relative gene expression was calculated as fold change compared to healthy controls.

Results:

Patients with MVK deficiency (n=3), NLRP3-related disorders (n=4), and healthy controls (n=10) were analyzed. Among the NLRP3-related disorder patients, 3/4 patients showed high NLRP3 gene expression, whereas only 1/3 MVK deficiency patients exhibited elevated NLRP3 expression. AIM2 gene expression was variable in NLRP3-related disorders, with 1 patient showing increased expression and 2 showing decreased expression, while 2 out

of 3 MVK deficiency patients had high AIM2 expression. NLRP12 expression was decreased in three patients with NLRP3-related disorder but was found to be increased in one patient with MVK deficiency. Notably, 2 MVK deficiency patients had elevated NLRC4 gene expression (377.95; 15.49), a finding not observed in NLRP3-related disorders. These results suggest that while NLRP3-related disorders primarily involve upregulation of NLRP3, MVK deficiency is associated with more diverse inflammasome pathway activation, highlighting distinct molecular mechanisms in the two conditions.

Mean fold change in all ten healthy controls for NLRP3, AIM2, NLRP12, CASPASE-1 and NLRC4 was 1.36, 1.02, 1.14, 1.00 and 1.00 respectively.

Conclusions:

This study highlights the distinct gene expression profiles of inflammasomes in patients with IL-1β activation disorder which could serve as a potential tool for distinguishing it from other genetic etiologies. Further validation with larger sample size is needed to validate these findings and develop gene expression-based diagnostic assays for inflammasomopathies

Figures, tables:

Table: Fold change of *NLRP3*, *AIM2* and *NLRC4* in patients with NLRP3 related AIDs and MVK deficiency.

Fold Change	NLRP3 related AIDs (n=4)	MVK deficiency (n=3)	Controls (n=10) Mean Fold Change
NLRP3	53.37	38.75	1.36
	140.45	9.44	
	6.5	1.52	
	129.24		
AIM2	0.06	273	1.02
	28.06	15.02	
	2.3	6.28	
	0.02		
NLRP12	0	20.47	1.14
	4.2	6.81	
	0.41	0.52	
	0.01		
CASPASE-1	1.22	59.14	1
	3.36	11.89	
	2.2	3.67	
	0.31		
NLRC4		377.95	1
		15.49	
		2.97	

P-24

Abstract Title:

A Clinico-Molecular Profile Of Patients With X-Linked Chronic Granulomatous Disease: Our Experience At Chandigarh, North India

Abstract no: 40

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Abstract:

Background:

Chronic Granulomatous Disease (CGD) is an inborn error of immunity due defect in NADPH oxidase complex that results in increased susceptibility to infections and hyperinflammation. Reports of genotype-phenotype correlation in X-linked Chronic Granulomatous disease (XL-CGD), X-linked carriers of CYBB defect, and G6PD-deficient forms of CGD are scarce from developing countries.

Methods:

Records of XL-CGD were reviewed for the period August 1993- December 2024. Diagnosis was based on nitroblue tetrazolium, dihydrorhodamine (DHR) assays, flow cytometry for gp91phox expression, and variant confirmation by Next-Generation or Sanger sequencing. Patients were categorized into null variants (DHR Stimulation index (SI) <2) and residual NADPH oxidase activity (DHR SI ≥2) and their clinical characteristics were compared.

Results:

Of the 54 patients with XL-CGD, 49 had hemizygous pathogenic variants in CYBB, 3 were X-linked CYBB carriers with skewed lyonization, and 2 had G6PD defects. 35 patients were categorized in null variant group and 14 in residual NADPH oxidase group. Age at diagnosis (p=0.002), and median delay (p< 0.001) in diagnosis were high in residual NADPH oxidase group. Spearman correlation coefficient suggests that higher the DHR SI, older the age at diagnosis (p<0.001) and higher the delay in diagnosis (p<0.001). Residual NADPH oxidase group had increased rates of pneumonia (p=0.02) and lymphadenitis (p=0.03). Mortality was higher in null group (82.8%, p=0.001) compared to residual NADPH oxidase group (35.7%). Kaplan Meir analysis revealed better survival in residual NADPH oxidase group (p=0.0034). There were 44 CYBB variants (12 novel), predominantly missense variants in residual NADPH group. Three patients of skewed lyonization and 2 G6PD variants had severe manifestations, and 1 patient with G6PD defect succumbed to pulmonary complications. Five XL-CGD carriers were symptomatic, of which 1 patient had severe lupus-like manifestation.

Conclusions:

XL-CGD patients with residual NADPH oxidase activity exhibit better survival with increased morbidity than null variants. G6PD-associated CGD-like manifestations and severe presentations in skewed lyonization in X-linked CYBB female carriers emphasize the need for awareness and timely diagnosis in these sub-groups. Genetic heterogeneity in CYBB mutations highlights the necessity for molecular diagnosis and tailored management strategies.

Figures, tables:

Table 1: Demographics details, clinical features and infectious profile of null variants and patients with residual NADPH oxidase of X-linked CGD

Clinical features	XL CGD- Null variant (DHR SI<2) (n=35)	XL CGD- Residual NADPH activity (DHR SI >2) (n=14)	P value
Age at symptom onset	1.5 (IQR-0.6-5 months)	6 months (IQR-2.5-9.75 months)	p= 0.062
Age at diagnosis	9 (IQR-4 -24 months)	44 months (IQR-12.25-109 months)	p= 0.001
Delay in diagnosis	7 months (IQR1-12months)	36 months (IQR-9.97-81.5months)	P <0.001
Number of admissions	3 (IQR-1-5)	5 (IQR-3.75-8.5)	P= 0.016
Pneumonia	30 (85.7%)	13 (92.85%)	P= 0.5
	65 episodes (8 patients had more than/ equal to 3 episodes)	47 episodes (8 patients had more than/ equal to 3 episodes)	P=0.026
Lymphadenitis	16 (45.7%) with 32 episodes	11 (78.5%) with 19 episodes	P= 0.039
Abscess	15 (42.8%) with 33 episodes	7 (50%) with 17 episodes	P= 0.714
Liver abscess	2 (5.7%)	2 (14.2%)	-
Osteomyelitis	3 (8.5%)	1 (7.1%)	-
Hyperinflammatory complications	17(48.5%)	9 (64%)	p= 0.330
B558 Stain index	Median stain index -1.19 IQR- 1-1.3	Median stain index -3 IQR- 1.06-3.5	P=0.135
Mortality	29 (82.8%)	5 (35.7%)	P= 0.001
Follow up months	1 (IQR-0.55-22) Total – 473.5 patient months	22.5 (IQR-1-70) Total- 514 patient months	P= 0.006

P-25

Abstract Title:

Need for Extended Family Screening in Inborn Errors of Immunity – A classic family pedigree

Abstract no: 42

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Abstract:

Introduction

X-linked A gammaglobulinemia (XLA), is one of the common forms of primary immune deficiency disorders where there is mutation in the Bruton tyrosine kinase gene (BTK). There is failure of development and maturation of B lymphocytes. Here we present a family suffering from XLA.

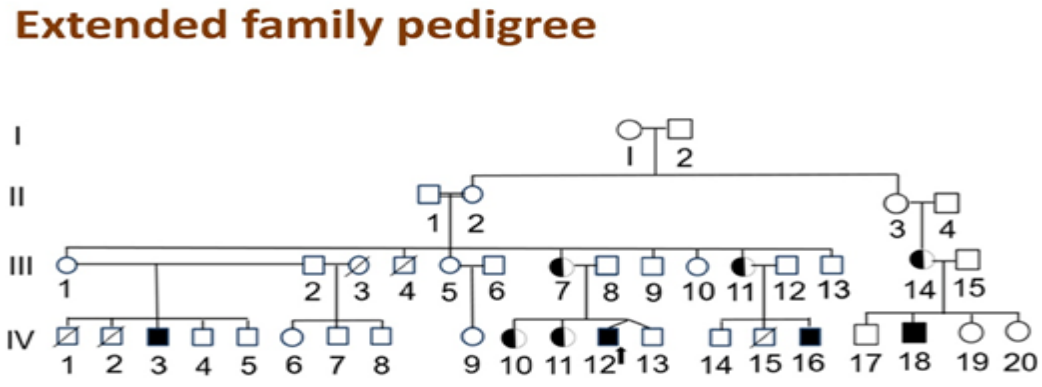
Case

A 2.5 years old boy suffering from recurrent oral thrush, recurrent diarrhoea and acute suppurative otitis media with onset from 5 months of age. He is 4th child born to parents of non-consanguineous marriage. The family history is notable for the death of four male cousins within the family. Additionally, four male cousins are also believed to have been affected by the same disease. Two female siblings and three female cousins have been identified as carriers of the condition. Investigations revealed pan hypogammaglobulinemia. The flow cytometry (lymphocyte subset analysis) revealed absent B lymphocytes. Whole genome sequencing revealed a hemizygous deletion spanning chrX:100,624,323-100,629,618 loci encompassing BTK exon 3-5 deletion. He underwent bone marrow transplantation from a matched sibling donor and is healthy after transplantation. Fragment analysis of the test DNA of other affected children was performed using standard multiplex ligation—dependent probe amplification method.

Conclusions:

A detailed pedigree analysis is a valuable tool in genetic counselling, diagnosis and early detection of disease ultimately leading to better management and more informed healthcare decision. The possibility of XLA should be kept in mind when considering the differential diagnosis of low Ig levels. High degree of penetrance is characteristic. Initiating prophylactic treatment as soon as the diagnosis of XLA is established is important. Here we are focussing on the importance of extended family screening.

Figures, tables:



P-26

Abstract Title:

Combined immunodeficiency as a predominant feature of RMRP defect: Our experience from North India

Abstract no : 43

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Abstract:

Background:

RMRP (RNA component of Mitochondrial RNA Processing endoribonuclease) is a non-coding nuclear RNA gene, mutations in which cause Cartilage Hair Hypoplasia (CHH)- an autosomal recessive metaphyseal dysplasia associated with growth failure, immunodeficiency and malignancies.

Objective:

To describe the clinical profile of 3 patients with RMRP mutations who primarily presented with combined immunodeficiency without obvious skeletal or hair abnormalities.

Methods:

Retrospective observational study carried out by review of records of patients with pathogenic mutations in RMRP detected by Next-Generation Sequencing over a period from 2018-2024 at our centre.

Results:

Male female ratio was 2:1, and, the onset of symptoms was in early infancy in all three patients. In the first case, there was a diagnostic delay of more than 5 years, while in the third the diagnosis of CHH was posthumous. Patient 1 and 3 had recurrent infections while autoimmune hemolytic anemia (AIHA) was the predominant presenting feature in patient 2. Patient 3 also had erythroderma. None of the three cases had skeletal dysplasia. Clinical details of the patients are elaborated in table 1.

All three cases had lymphopenia with low CD-19+ B cells and low naïve T cells (Table 2). Only 1 case had hypogammaglobulinemia. Lymphocyte proliferation study was done for patient 1 and found to be reduced. HLA-DR expression was normal in 2 cases and increased in the third. In conventional whole exome sequencing by the Next-Generation Sequencing performed from commercial laboratories in India that generally do not cover non-coding RNA, none of them were noted to have any pathogenic variants related to SCID or CID. A subsequent targeted PID exome panel performed identified pathogenic RMRP variants in patients 1 and 2. A repeat whole exome sequencing that also included coverage for non-coding RNA identified the pathogenic RMRP variant in patient 3.

Patient 1 underwent haplo-matched related hematopoietic stem cell transplant (HSCT) at the age of seven years but unfortunately succumbed to infective complications and grade 4 graft versus host disease (GVHD). Patient 2 is currently 23 months old and doing well on anti-microbial prophylaxis and intravenous immunoglobulin replacement. Patient 3 expired due to polymicrobial infections at the age of 5 months.

Conclusions:

RMRP defects may present with a SCID or CID without obvious skeletal or dermatological abnormalities. It is important to remember RMRP defect as a cause of combined immunodeficiency because sequencing techniques that exclude coverage for non-coding RNAs may miss this gene in analysis.

Figures, tables:

Characteristic	Case 1	Case 2	Case 3
Gender	Male	Female	Male
Age at onset	9 months	15 months	1.5 months
Age at diagnosis	6 years	18 months	Posthumous diagnosis
Infection profile	• Recurrent pneumonia • Otitis media • Recurrent diarrhea • CMV retinitis • Sinusitis	• Pneumonia	• Recurrent diarrhea • Pneumonia • Otitis media • BCG site complication • Generalised lymphadenopathy
Organisms isolated	• Blood- CMV, Weissella confusa • Stool- Giardia lamblia, Bocavirus • Sputum- Enterobacter cloaceae, Pseudomonas aeruginosa • Nasopharyngeal swab- Adenovirus • Nasal scraping- Exserohilum species • Esophageal biopsy- Candida • Colon biopsy- CMV, Cryptosporidium	• Blood- Escherichia coli	• Blood- Enterococcus • Left axillary swelling FNAC- BCG
Autoimmune manifestations	• IBD • AIHA	• Pancytopenia with positive DCT	• Erythroderma
Skeletal manifestations	No skeletal dysplasia	No skeletal dysplasia	No skeletal dysplasia
Outcome	Succumbed post haplo-matched HSCT at	On replacement IVIg, antimicrobial	Succumbed to infective complications at

Characteristic	Case 1	Case 2	Case 3
Immunoglobulin profile	• IgG= 1350 mg/dL • IgA= 347 mg/dL • IgM= 103 mg/dL	• IgG= 1790 mg/dL • IgA= 130 mg/dL • IgM= 354 mg/dL	• IgG < 205 mg/dL • IgA – • IgM= 34 mg/dL • IgE= 3.69 kU/L
Absolute lymphocyte count	670 cells/mm³	1101 cells/mm³	2498 cells/mm³
Lymphocyte subset	• CD3+ = 72.3% • CD19+ = 11.14% • CD16/56+ = 13.75%	• CD3+ = 91.04% • CD19+ = 4.74% • CD16/56+ = 3.68%	• CD3+ = 78% • CD19+ = 4.44% • CD16/56+ = 13.12%
T-cell subset	CD4:CD8 reversal; markedly reduced absolute counts of CD3+, CD4+ and CD8+ T-cells; markedly reduced naïve T-cells and normal memory T-cells	CD4:CD8 reversal; markedly reduced absolute counts of CD3+, CD4+ and CD8+ T-cells; markedly reduced naïve T-cells and normal memory T-cells	Decreased naïve T-cells and increased memory T-cells
T-cell proliferation	Reduced as compared to control after stimulation by PHA and CD3/CD28	-	-
HLA-DR expression	Comparable to control	Comparable to control	Increased proportions of activated T-lymphocytes
Whole exome sequencing	*RMRP* compound heterozygous mutations • *RMRP*(NR_003051.3):n. 147 G>A, heterozygous, pathogenic (inherited from father) • *RMRP*(NR_003051.3):n. 82A>G, heterozygous, variant of uncertain significance (inherited from mother)	*RMRP*(NR_003051.3):n.6C>T, homozygous, pathogenic (parents were heterozygous carriers)	*RMRP*(NR_003051.3):n.37C>A, homozygous, pathogenic (parents were heterozygous carriers)

P-27

Abstract Title:

Periodic Fever Unveiled: A Rare Case of STAT3 Gain-of-Function Mutation.

Abstract no: 44

All authors: Maya Gupta[1], Pallavi Gaikwad[1], Disha Vedpathak[1], Tiphanie P. Vogel[2], Harikrishnan Gangadharan[3], Umair A. Bargir[1], Nidhi Desa[1], Neha Jodhawat[1], Parag Tamhankar[4], Vandana Pradhan[1], Manisha Madkaika[1]

Complete detail of Institute including city state-

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Presenting Author email: maya_rk@rediffmail.com

Abstract:

Introduction:

STAT3 gain-of-function (GOF) syndrome is a rare autosomal dominant immune disorder presenting with autoimmunity, immune dysregulation, recurrent infections, and potential malignancies. We report a novel STAT3:c.199C>A mutation (p.Gln67Lys) in a patient with periodic fever, mild autoimmunity, and BCG adenitis. Elevated pSTAT3 levels and in-vitro luciferase assays confirmed GOF activity. This is the first reported case of STAT3 GOF syndrome presenting with periodic fever.

Case Report:

A 16-year-old South Indian female presented with a history of BCG adenitis at five months, recurrent high-grade fevers since infancy, herpes zoster at age eight, recurrent pneumonitis, and lymphadenopathy with hepatosplenomegaly. She underwent adenoidectomy and tonsillectomy at 15 years for recurrent infections.

Investigations revealed elevated CD19+ B cells, increased double-negative T cells (7.73%), low memory B cells (3.09%), and markedly elevated IFN-γ levels (134.4 pg/mL). Autoimmune serology showed ANA and weak ANCA positivity. Whole exome sequencing identified a novel heterozygous STAT3:c.199C>A mutation, inherited from her asymptomatic father.

Functional studies showed elevated baseline and IL-21-stimulated pSTAT3 expression, consistent with GOF activity. Luciferase assays confirmed a 3.1x increase in transcriptional activity of the p.Gln67Lys variant, establishing its pathogenicity.

Conclusion:

We report a novel STAT3:c.199C>A (p.Gln67Lys) mutation in STAT3 GOF syndrome, with periodic fever as a unique feature. Functional assays confirmed its pathogenicity, highlighting the need for genetic and functional studies in rare immune disorders and further research into the variable clinical expression of STAT3 GOF mutations.

P-28

Abstract Title:

Unraveling the mystery of abdominal fistulas and scars : Exploring the genetic underpinnings !

Abstract no : 45

All authors: Anjani Gummadi[1],Parijat Ram Tripathi[1], Dr Narendra Kumar[2]

Complete detail of Institute including city state-

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Abstract:

Introduction:

Recurrent abdominal fistulas are rare and have significant morbidity. We are presenting here a rare case with

combination of two genetic disorders.

Case report:

8 year boy, presented with a spontaneous entero (colo)-cutaneous fistula for last 6 months. Patient had past history of colonic peroration at 1 year age, twice spontaneous gastric perforations at 1.5 year age, entero-cutaneous fistula at 2.5 years age, colonic perforation and reopening of anastomosis at 6 year age. For these complaints he underwent total of 7 abdominal surgeries. Child also had recurrent fever, skin infections and oral ulcers. Revision of all his records showed neutropenia along with mild anemia, very high CRP and ESR. A bone marrow aspiration and biopsy were done and was normal. Upper gastrointestinal endoscopy was normal; colonoscopy showed patchy erythema, whitish scar areas and no ulcers except for hepatic flexure where a large fistula was communicating to the skin. Colonic biopsies showed features of chronic inflammation.

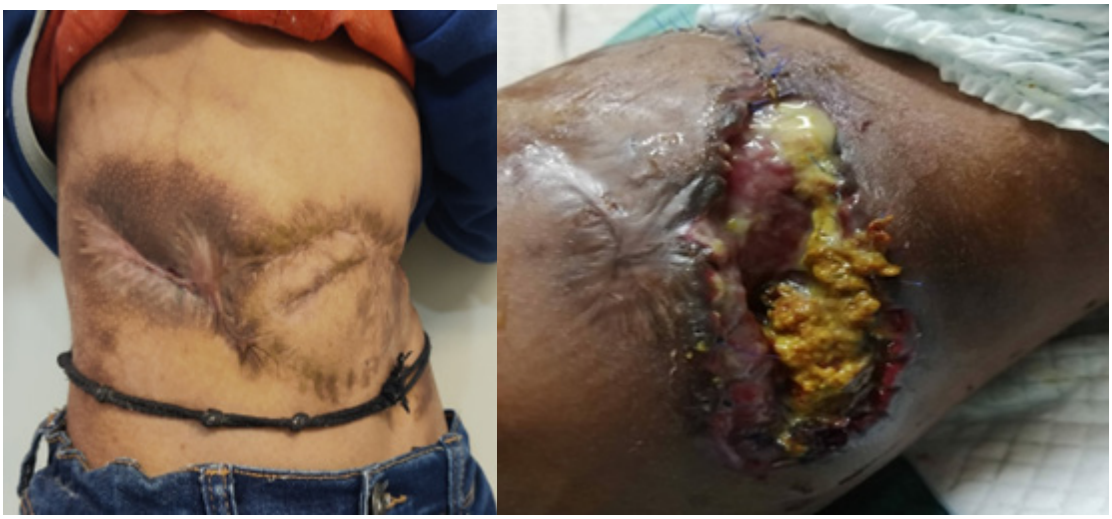
Whole exome sequencing showed two mutations: 1.Heterozygous in TNF AIP3 gene suggestive of Autoinflammatory syndrome, familial, Behcet-like 1 (autosomal dominant). 2. Homozygous in HAX1 gene suggestive of severe congenital neutropenia (autosomal recessive).

Clinically patient had features of both the disorders. After literature search and consent from parents, patient was started on cotrimoxazole prophylaxis and infliximab (IFX) which resulted in complete fistula closure in 6 months, with gain in 10 cm height and child restarted going to school and participation in sports. After 9 months, fistula recurred although very small. Investigations showed low IFX levels with very high antibodies to IFX. Now patient is started on Adalimumab for which response is still awaited. As the absolute neutrophil count also showed a decreasing trend with nadir of 790 cells/mm3, he was also given G-CSF subcutaneous injections.

Conclusion:

There is need to do early genetic analysis in unusual cases. Both the above mentioned diseases are very rare and unfortunately our index patient suffered from both which made our choice of treatment difficult and challenging

Figures, tables:



P-29

Abstract Title:

Measuring the disease activity of patients with Inborn errors of immunity using the Immune deficiency and dysregulation score (IDDA2.1)

Abstract no : 47

All authors: Jyothi Janardhanan[1],Dr. Sagar Bhattad[1]

Complete detail of Institute including city state-

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Presenting Author email: jyothi428@hotmail.com

Abstract:

Background:

Inborn errors of Immunity (IEI) are a diverse group of disorders characterized by increased susceptibility to infections, autoimmunity, autoinflammatory diseases, allergy, bone marrow failure, and malignancy. Assessing phenotypic features aids in the diagnosis, classification, and evaluation of disease severity.

Objective:

Measure disease activity in patients with IEI.

Methods:

A prospective study at a tertiary care center in South India from May 2023 to December 2024 included patients with IEI followed for one year, excluding those with secondary immune deficiencies or prior hematopoietic stem cell transplants (HSCT). The Immune deficiency and dysregulation score (IDDA2.1) was utilized, with statistical analysis performed using SPSS version 22.

Results:

During the study period, 112 patients were enrolled, with 81 completing the study. Mean age at presentation was 6.5 years, and mean age at diagnosis was 12.3 years. Male-to-female ratio was 2.5:1. The most prevalent immune deficiency was Common Variable Immune Deficiency (17%, n=14). The IDDA 2.1 score was applied to each patient individually and was categorized according to the IUIS 2022 classification. The overall mean score was 9.47, with the maximum mean score (11.43 ± 7.67) observed in patients with diseases of immune dysregulation. As illustrated in the graph 1, most patients exhibited a reduction in the IDDA 2.1 score at subsequent visits, attributed to the therapies provided. A plateau in the graph was noted for those with diseases of immune dysregulation, indicating ongoing disease activity. This scoring system is a valuable tool for assessing disease activity and monitoring therapeutic effects. For instance, among 20 patients with primary antibody deficiency, significant improvement was observed with antibiotic prophylaxis and regular immunoglobulin replacement ($p=0.02$). Within this cohort, 16 patients with various immune deficiencies underwent HSCT, resulting in a significant difference in scores ($p=0.02$). Additionally, this scoring approach assists in evaluating disease severity among patients with the same genetic variant. In one comparison between two patients with the XLPS-2 variant, Patient 1 had a mean score of 19.75, while Patient 2 had a mean score of 2.07 (Graph 2). However, a limitation of the scoring system is that, while infections are weighted significantly, individual infections cannot be assessed in detail. Furthermore, malignancies are not included in the scoring, which may downplay the overall score.

Conclusions:

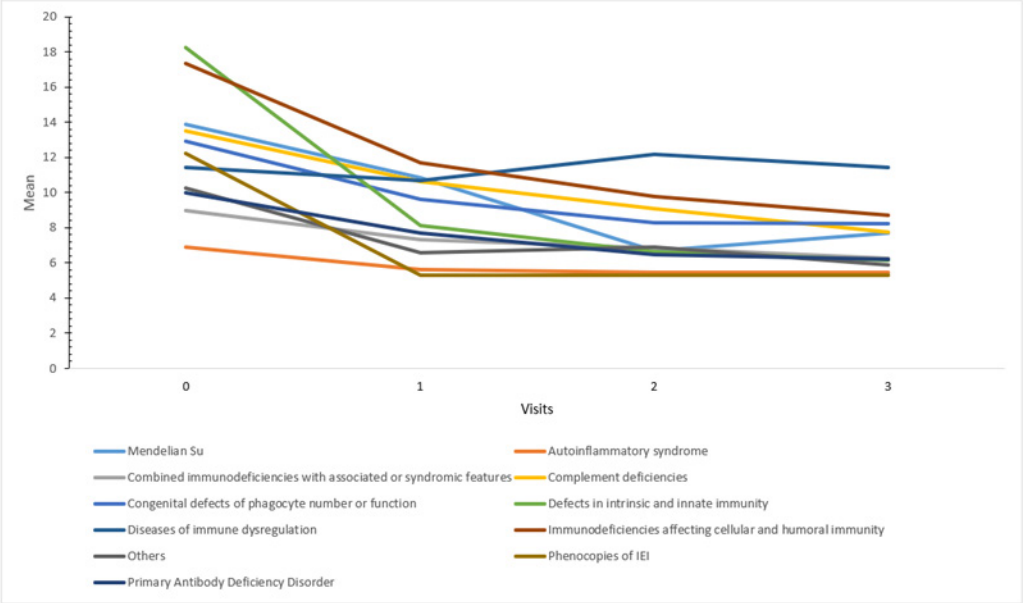
The IDDA score is a promising tool to assess disease activity and burden in the setting of IEIs. It allows for

longitudinal monitoring by using a number of relevant clinical parameters.

Figures, tables:

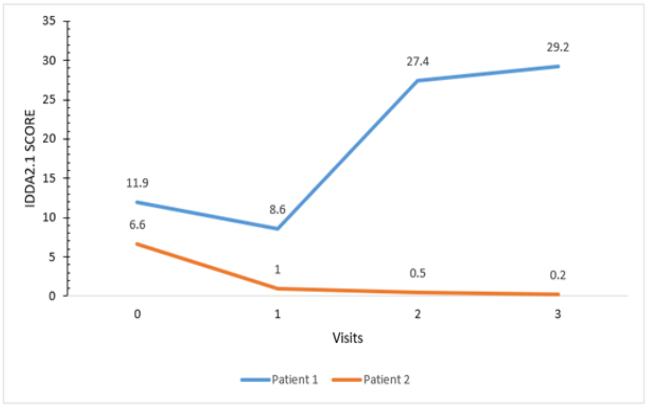
Graph 1

Line chart of Mean IDDA2.1 SCORE in IEI Category



Graph 2

Line chart of IDDA2.1 SCORE of two Patients having X-linked lymphoproliferative disease Type 2



P-30

Abstract Title:

Clinical profile and follow-up data of patients suspected with Hyper IgE syndrome (HIES) from a tertiary care center.

Abstract no: 48

All authors: Challa Madhuri[1],Dr. Yerram Keerthi Vardhan[1], Dr.Liza Rajasekhar[1]

Complete details of Institute including city state-

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Abstract:

Background:

Inborn errors of immunity (IEI) marked by the triad of eczema, recurrent skin and pulmonary infections, and high IgE levels (usually >2000 IU/ml) have been called hyper-IgE syndromes. Reports from India include AD STAT3 and prolidase deficiency.

Objectives:

To study the clinical, immunological, and genetic variations among patients with the hyper-IgE syndrome phenotype.

Methods:

Data of all patients screened for IEI in the pediatric immunology clinic (2015-2024) were reviewed. Clinical, immunological, genetic, and follow-up data of cases with HIES phenotype were collected in a structured proforma.

Results:

26 cases (18 males) had HIES phenotype of eczema and recurrent skin/sinopulmonary infections along with IgE levels >1000 (except in four cases). The median age at the onset of symptoms was 7.5 months (0-84 months). The median age at the first visit to our center was 48 months (1-180 months). The median duration of follow-up was 39 months (1-130 months).

The frequency of eczema-38.5%, skin abscess/furuncles- 50%, and recurrent pneumonia- 58% (PTB in 1 patient). Facial dysmorphism was observed in 8 patients, and skeletal abnormalities in 1 patient. The mean NIH score was 29.5. IgE levels >2000 IU/ml were observed in 18 and>1000 IU/ml in 3 patients. One patient had low IgG and IgM, and another had low IgA levels. Four patients had CD3 lymphopenia,6 CD4 lymphopenia, 2 CD8 lymphopenia, and 2 low CD19 (<1% in one).

Whole Exome sequencing (WES) was performed in 15. WES of 2 patients did not show any pathogenic variants. One has persistent eczema, the other is asymptomatic, and neither has recurrent infections. Table 1 lists 8 cases with pheno-geno concordance. Four patients from 3 families had DOCK8 deletion, listed now as combined immunodeficiency in the IUIS 2022 classification. Prolidase deficiency is classified as an immunoregulatory disorder with autoimmunity without Treg defects. The genetic variants in 5 cases (Table 2) are not listed under HIES.

Eight patients were lost to follow-up, 6 expired, 5 remained asymptomatic, and 6 were symptomatic with eczema or recurrent infections (1 developing bronchiectasis). One patient is planned for IVIG therapy and BMT at another center.

Conclusion:

In this cohort, DOCK8 AR-HIES was more often seen than STAT3 AD-HIES.We also report a case of Netherton syndrome and CARD11-related HIES. We need to further follow up on the patients with phenotype-genotype discordance and ascertain the functional significance of these variants

Figures, tables:

Table 1: Cases with HyperIgE syndrome with phenotype-genotype concordance (DOCK8 deficiency and prolidase deficiency are now reclassified under other categories according to IUIS 2022 classification)

S.No	Gender	Age at presentation	Age at onset of symptoms	Eczema	Skin infection	Systemic infections/site/Others	Facial dysmorphism/skeletal abnormalities	IgE levels	NIH score	WES report
1	F	3 years	2 years	Yes	Yes	Pneumonia	Yes (broad nasal bridge)	>3000	25	STAT3 deletion/Heterozygous variant/AD/Likely pathogenic
2	M	12 years	5 months	No	No	Recurrent Pneumonia	No	889	14	DOCK8/Compound Heterozygous/AR/Likely pathogenic
3	F	9 years	7 years	Yes	Yes (nail candidiasis)	Recurrent pneumonia (Streptococcus pneumoniae) Non-specific colitis	Depressed nasal bridge and high-arched palate	>3000	37	DOCK8 Homozygous deletion (Exons 9-28)/AR/Pathogenic Confirmed by MLPA
4	M	6 years (younger brother of patient 3)	5 years	No	No	Pneumonia (PTB) Father heterozygous carrier (spinal TB)	No	126	18	DOCK8 Homozygous deletion (Exons 9-28)/AR/Pathogenic/Confirmed by MLPA (younger sib of patient 3)
5	M	12 years	12 months	Yes	Yes	Recurrent URTIs, Pneumonia, and diarrhea, low Ig	Broad nasal bridge, anteverted ears, and hypertelorism	>3000	46	DOCK8 Homozygous deletion/Pathogenic Not confirmed by MLPA
6	M	15 years	Birth	Yes (scaly erythroderma and brittle bamboo hair)	No	None (Recurrent allergic rhinitis)	Classic Ichthyosis linearis circumflexa and stiff spiky hair over scalp, mustache, and eyebrows	2555	14	SPINK5 Homozygous deletion/AR/Pathogenic Netherton Syndrome
7.	M	5 years	1 year	Yes	Yes	Recurrent pneumonia	Broad and depressed nasal bridge, low-set ears, Hyperextensibility of joints	>3000	41	PEPD Homozygous Intronic splice site variant/AR/Pathogenic/Prolidase deficiency
8.	F	4 months	3 months	Yes	Yes	Recurrent pneumonia diarrhea, UTI, rash, lymphopenia, low Igs	None	NA	50	CARD 11/ c.1493G>A/Heterozygous, PM2, PP2

TABLE 2: Cases with suspected Hyper IgE syndrome with genotype discordance (1 case reclassified as IL2RA deficiency- T Regulatory cell defects)

S.No	Gender	Age at presentation	Age at onset of symptoms	Eczema	Skin infection	Systemic infections/site/Others	Facial dysmorphism/ skeletal abnormalities	IgE levels	Variant in gene/Franklin review/ /IUIS 2022 Classification	Follow up
1.	F	4 years	2 years	Yes	No	Recurrent pneumonia	Depressed nasal bridge frontal bossing	>3000	SAMD9(-):c.1031G>A, C.4666G>T,both Heterozygous//VUS PM2, PP2/ Bone marrow failure syndromes	Expired after 1 year of visit
2.	M	1 year	2 months	Yes	Yes	Recurrent URTI/ASD	No	1188	ABCA3:c.5042G>C,Homozygous/PM2,PP 3/ not mentioned PLCG2/Heterozygous/ VUS PM2 / APLAID	Asymptomatic
3.	M	5 years	18 months	No	Yes	Perianal abscess	No	1631	CYBB/Hemizygous/VUS/ PP3, BS1,BS2,BP6/ Phagocyte defect with abnormal DHR	Lost to follow-up (DHR assay normal)
4.	M	1 year	3 months	No	No	Recurrent pneumonia NIH score 18 WBC/Neutrophil count-normal	Deep-set eyes and a broad nose	316	LAMTOR2:c330T>A,Heterozygous/VUS PP2, BP7 (likely benign) Congenital neutropeniia	Asymptomatic
5.	M	10 years	1 month	No	Yes	Recurrent pneumonia CSOM/autoimmune cytopenias, ANA 4S NIH score 48	Coarse facies, retained primary teeth	2815	IL2RA,c.368-2A>G, Intronic splice variant, Homozygous PVS1,PP2(likely pathogenic) Immunoregulatory disorder with autoimmunity and Treg defects	Asymptomatic (doing well on Low dose steroids)

P-31

Abstract Title:

Arrested maturation, reduced motility or abnormal function- study of patients with Neutrophil Defects from a center in Western India

Abstract no: 49

All authors: Akshaya Chougule[1], Prasad Taur[1], Vaishnavi Iyengar[1], Vijaya Gowri[1], Manisha Madkaikar[1], Mukesh Desai[1].

Complete details of Institute including city state -

[1]B.J. Wadia Hospital For Children Mumbai, Maharashtra, India.
Presenting Author email- akshaya.chougule@gmail.com

Abstract:

Background and aims:

Phagocytic or neutrophil defects fall under class V, IUIS classification and are further grouped as IEI with neutropenia or functional defects. We present a retrospective analysis of patients with laboratory or genetically proven cases with neutrophil defects

Methods:

Clinical and laboratory findings were analyzed retrospectively. Of the 110 children included, 71 had chronic granulomatous disease (CGD), 22 had leukocyte adhesion deficiency (LAD) and 17 had severe congenital neutropenia (SCN). Of the 22 patients with LAD, 19 had LAD-1 of which 15 had complete LAD-1 and 4 had partial LAD-1, and 3 patients had LAD-3.

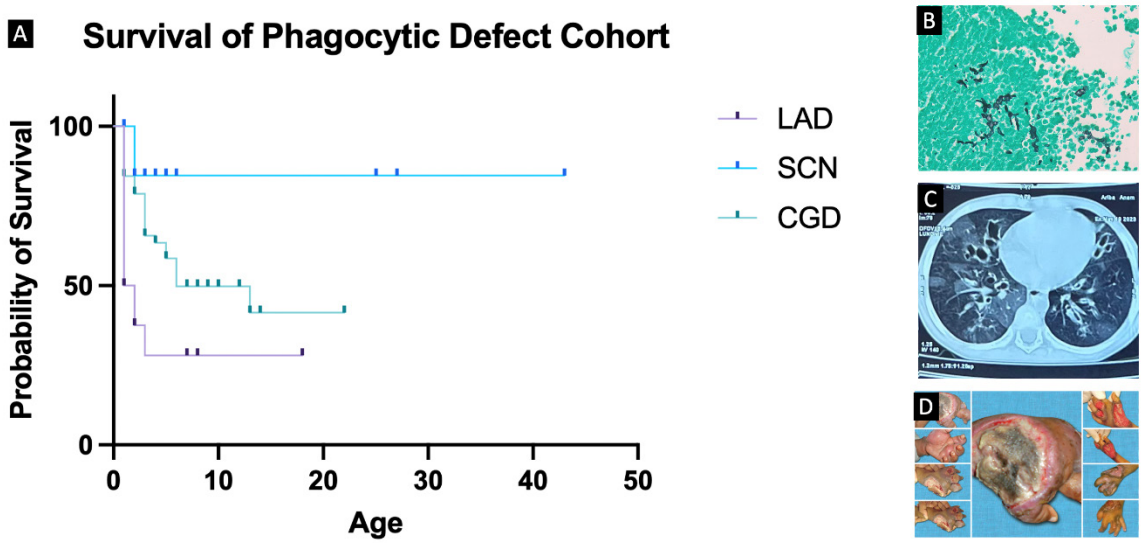
Results:

Median age of onset was 6 months. Lungs were the most common infection site, 73% had at least one pneumonia. Persistent pneumonia (39%) was more common with CGD. Recurrent pneumonia, pleural effusion/ empyema, and bronchiectasis were noted in all three groups. Subcutaneous abscesses were seen in all three groups. Deep-seated abscesses, osteomyelitis, and septic arthritis were more common with CGD. CNS infections, including bacterial and tuberculous meningitis, tuberculoma, and aspergilloma were more common with CGD. Omphalitis, neonatal sepsis were seen with SCN and LAD. BCG adenitis and BCGosis were seen only with CGD. Bacterial organisms isolated predominantly were Mycobacteria tuberculosis, Staphylococcus aureus, gram-negative organisms like Pseudomonas aeruginosa and klebsiella pneumonia. Uncommon organisms like Pasturella canis, Citrobacter freundi, Chromobacterium violaceum and non-typhi salmonella were seen with CGD. Fungal infections, including invasive aspergillus infections, were seen in all three groups. Immune dysregulation included pyoderma gangrenosum (LAD-1), HLH (CGD, LAD-3, SCN), and recurrent oral ulcers (CGD, LAD-1, SCN). Mortality was higher and earlier for un-transplanted complete LAD-1, LAD-3 as compared to CGD, SCN. Initiation of Inj.GCSF reduced infections in patients with SCN. Longest duration on Inj.GCSF was 4.5 years, dose range was 2.5mcg/kg/day to 12mcg/kg/day. None of the SCN patients developed MDS/ AML. G6PC3 responded to empagliflozin. 3/71 GCD and 3/19 LAD1 underwent successful HSCT.

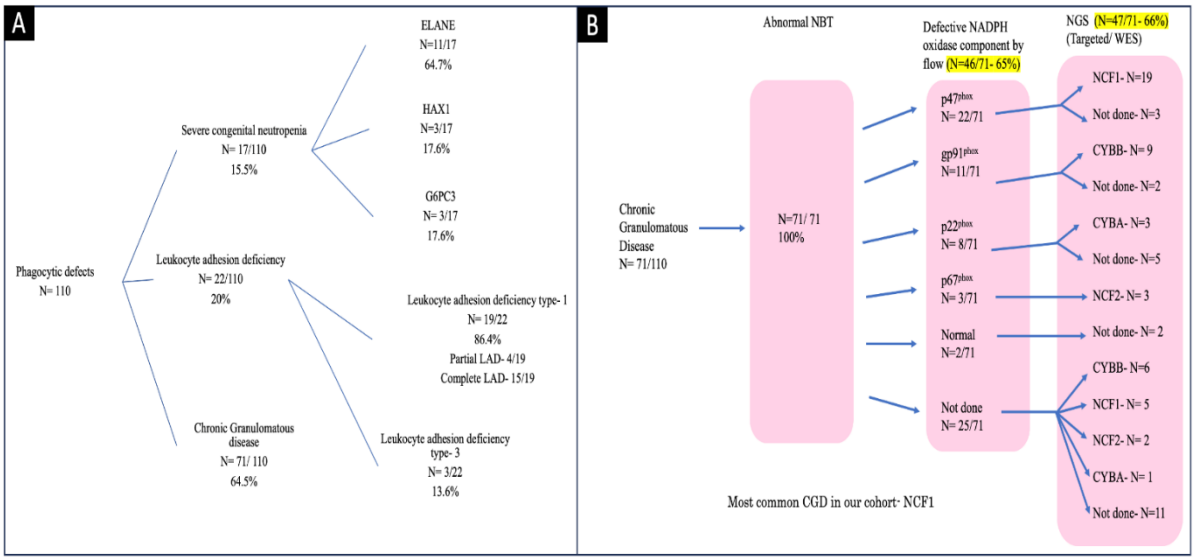
Conclusions:

Phagocytic defects have considerable morbidity and mortality, early diagnosis is essential. Patients with SCN on GCSF/ empagliflozin have better survival than un-transplanted CGD/ LAD.

Figures, tables:



A- Survival curve analysis showing early and higher mortality in patients with LAD1 and LAD3 as compared to CGD and SCN
B- Brain biopsy of P108 with CGD showing Aspergillus hyphae
C- HRCT chest of of P34 with cyclic neutropenia showing severe bronchiectasis
D- Picture of P43 with CGD with Basidiobolus infection of hand



A- Spectrum of the neutrophil defects seen at our center
B- Diagnostic algorithm of the patients with Chronic granulomatous disease diagnosed at our center

P-32

Abstract Title:

Ataxia, Infections, Autoimmunity, Neoplasms- varied clinical manifestations of patients with Ataxia Telangiectasia

Abstract no: 50

All authors: Akshaya Chougule[1],Prasad Taur[1], Vaishnavi Iyengar[1], Vijaya Gowri[1], Mukesh Desai[1]

Complete detail of Institute including city state -

[1] B.J. Wadia Hospital For Children Mumbai, Maharashtra, India.

Presenting Author email- akshaya.chougule@gmail.com

Abstract:

Background and aims:

Ataxia Telangiectasia (AT) is characterized by progressive cerebellar ataxia, variable immunodeficiency, malignancies and radiation sensitivity. We present clinical details of seven children with AT.

Methods:

The clinical details and laboratory findings of seven children, with pathogenic/ likely pathogenic homozygous mutations in ATM gene and fulfilling the ESID criteria for AT, were analyzed retrospectively.

Results:

Four were born of consanguineous marriage; P3 and P4 are brothers, P6 had two older sibling losses due to AT. Male: female ratio was 4:3. Median age at diagnosis was 5 years (Range- 1 year to 8 years). Onset of infections preceded onset of neurological manifestations in 4/7 (median age of onset of infections-1year, range- day 6 of life to 5 years). Infections included recurrent URTI (6/7), ear infections (3/7), mastoiditis (1/7), chronic sinusitis (1/7), UTI (2/7) and sepsis (2/7). Four had at least one pneumonia, 1/7 had recurrent pneumonias, 2/7 had persistent pneumonia, 1/7 had empyema. Organisms isolated were MRSA, Mycobacteria tuberculosis, CMV, Parvovirus B19. Median age of documentation of ataxia was 3 years (range- 2 years to 6 years). P5 had global developmental delay with hypotonia, gross motor milestones were affected more than social milestones. Others had normal social and mental milestones. Cutaneous manifestations included Café-au-lait spots (3/7), generalized hyperpigmentation (1/7), 4/7 had conjunctival telangiectasia. P5 had anterior mediastinal mass (T lymphoblastic lymphoma). P1 had autoimmune hemolytic anemia and autoimmune hypothyroidism. 7/7 had elevated AFP. All had T and B lymphopenia. P1 had low IgA, P5 and P7 had hyper IgM and 4/7 had normal immunoglobulin levels. Five had diffuse cerebellar atrophy on MRI. In addition, P3 had a left periventricular white matter lesion favoring low grade neoplasm and P1 had cystic changes with diffuse cerebral atrophy and hyperintensities in multiple areas with multiple micro hemorrhages suggestive of atypical PRES (Posterior reversible encephalopathy syndrome). Two had normal MRI. All were started on IVIG and prophylaxis. P1 succumbed to pneumonia.

Conclusions:

Patients with AT show variability in clinical features with respect to onset of ataxia, infections and can present with varied manifestations ranging from immunodeficiency to malignancy and autoimmunity

Figures, tables:

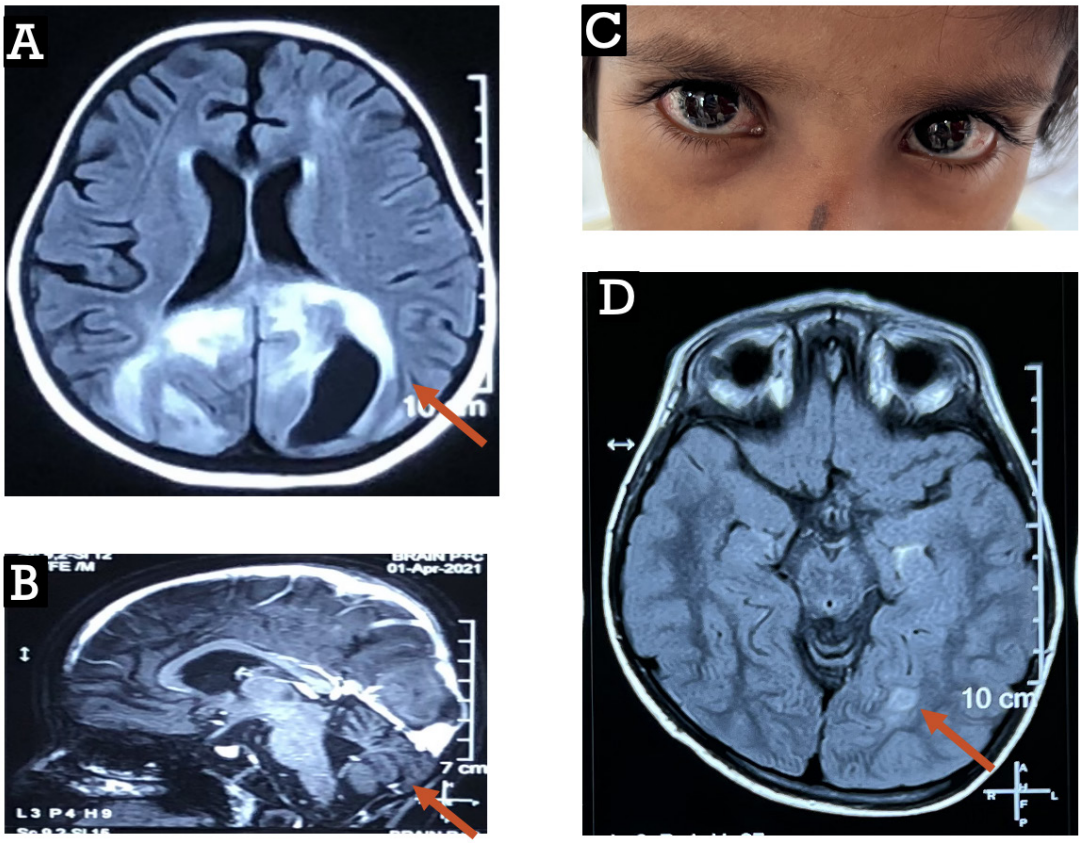


Figure:1- A- MRI brain of P1 showing features of atypical PRES
B- MRI brain of P1 showing diffuse cerebellar atrophy
C- Clinical picture of P2 showing conjunctival telangiectasia
D- MRI brain of P3 showing features of low grade neoplasm

P-33

Abstract Title:

Bronchiectasis in Inborn Errors of Immunity

Abstract no: 51

All authors: Akshaya Chougule[1], Prasad Taur[1], Vaishnavi Iyengar[1], Vijaya Gowri[1], Mukesh Desai[1]

Complete detail of Institute including city state -

[1] B.J. Wadia Hospital For Children Mumbai, Maharashtra, India.

Presenting Author email: akshaya.chougule@gmail.com

Abstract:

Background:

Bronchiectasis is caused by progressive injury of airway walls as a result of chronic/ repeated airway inflammation causing irreversible bronchodilation. Here we present a cohort of patients with IEI with bronchiectasis.

Methods:
Clinical, laboratory information of 31 patients with genetic/ laboratory evidence of IEI were analyzed retrospectively.

Results:
Male: female ratio was 21:10. Median age at onset of symptoms was 1.5 years, onset was earliest at 1 month for P8 (ARPC1b deficiency) and latest at 12 years for P9, P22 (CVID). P9 (CVID), P21 (CVID), P26 (XLA), P30 (APDS2) had only one episode of documented pneumonia. P29 had only hyperreactive airway disease but no documented pneumonia. Rest of the cohort has had multiple pneumonias, with P5 (STAT1 GOF) and P11 (APDS1) having maximum number of documented pneumonias (seven). Ear infections were common, followed by CMC, meningitis, recurrent infective diarrhea, viral infections, sepsis. 19/31 had immune dysregulation (autoimmunity, HSP, allergies, oral ulcers, lymphoproliferation, EBV LPD). P23 (CVID) had B-ALL and P30 (APDS2) had Hodgkin's lymphoma. Organisms isolated were predominantly Pseudomonas aeruginosa, Streptococcus pneumoniae, MRSA, Mycobacterium tuberculosis. Four had normal lymphocyte subsets, 6/31 had low B cells, 6/31 had isolated CD4 lymphopenia, 3/31 had low CD4 and B cells, 3/21 had low class switch and memory B cells, 3/31 had low T cells, 5/31 had pan-lymphopenia. Fourteen had pan-hypogammaglobulinemia, 6/31 had normal immunoglobulins, 3/31 had hyper IgM, 3/31 had hypergammaglobulinemia, 1/31 had low IgA, 1/31 had low IgA and IgM. Genetic diagnosis were STAT1 GOF (5/31), BTK (3/31), ARPC1b deficiency (2/31), DOCK8 (2/31), LRBA (2/31), PI3K (2/31), PI3KR1 (1/31), TACI (1/31), TCF3 (1/31), AICDA (1/31), CD40LG (1/31), ELANE (cyclic neutropenia) (1/31), P19 (CVID) has heterozygous mutations in RAG1, RAG2. Five did not have mutations but had laboratory evidence for CVID or XLA.

Conclusions:
Apart from patients with B cells defects, patients with diseases of immune dysregulation (STAT1 GOF, LRBA deficiency and APDS) and those with combined immunodeficiencies (ARPC1b deficiency) can also have debilitating bronchiectasis.

P-34

Abstract Title:
Unravelling the immunological and molecular landscape of BCG complications: A national referral centre experience

Abstract no: 52

All authors: Aparna Dalvi,Dr[1]. Umair Barfir, Dr[1]. Reetika Yadav[1]

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Abstract:

Background:
The Bacille Calmette-Guérin (BCG) vaccine is crucial for preventing severe tuberculosis, but it can cause severe complications in individuals with inborn errors of immunity (IEIs). This study investigates the demographics, clinical presentation, and laboratory findings in patients referred for adverse effects following BCG vaccination.

Methods:
We conducted a retrospective analysis of 74 patients referred for advanced immunological work-up at our centre

between 2020 and 2024 due to BCG complications.

Results:

Of the 74 patients, 20 (27%) were diagnosed with probable BCG-osis, and 54 (73%) had BCG-adenitis, with 50 cases of localized disease and 4 presenting with BCG reactivation, site swelling, or abscess. The median age at presentation was 3 months (IQR: 2–5 months), and at diagnosis, it was 7 months (IQR: 5–18 months). Consanguinity was noted in 17 families (23%), with 2 families (2.7%) having a history of inherited immunodeficiencies (IEIs). Four families (5.4%) had a history of sibling deaths, and 3 patients (4%) had TB exposure. Mycobacterial infection was confirmed in 34 patients, including 27 with Mycobacterium tuberculosis complex and 7 with acid-fast bacilli. Whole exome sequencing (WES) on 62 patients revealed pathogenic variants in 22 (35.5%), with 17 (27.4%) diagnosed with Mendelian susceptibility to mycobacterial disease (MSMD). Functional testing revealed defects in IFNγ and IL12 production in several patients.

Conclusion:

BCG complications can serve as an early indicator of underlying IEIs. MSMD was the most common disorder, highlighting the critical role of IFNγ in mycobacterial defense. Families with a history of IEIs or sibling deaths should undergo IEI screening before BCG vaccination.

P-35

Abstract Title:

Primary Immunodeficiency in Adults: One-Year Experience from a Tertiary Care Centre in North India

Abstract no: 54

All authors: Siddharth Jain[1],Baidhnath Kumar Gupta[1], Md Tariq Maula[1], Rakesh Kumar Deepak[1], Neeraj Nischal[1], Manish Soneja[1], Naveet Wig[1]

Complete detail of Institute including city state-

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Abstract:

Background:

Primary immunodeficiencies (PIDs) are a heterogeneous group of disorders caused due to defects in the immune system, which present variably with recurrent infections, autoimmune disorders, lymphoproliferation/ malignancy, and/or bone marrow failure. Traditionally believed to be a pediatric problem, PIDs are probably under-recognized and underdiagnosed in adults. Published data on adult PID is scarce, and much remains unknown about PID in adults.

Objectives:

To characterize the clinico-laboratory profile and treatment outcomes of adults diagnosed with primary immunodeficiency.

Methods:

This single-centre prospective cohort study done at the Department of Medicine, AIIMS (Delhi) included adult (>14 years) patients diagnosed with PID (immunologically and/or through genetic testing) between December 2023- December 2024. Data pertaining to demographics, clinical presentation, laboratory findings including

functional immunological workup, genetic testing (where available), treatment, and outcomes were collected and reported.

Results:

In the one year time period specified, a total of 30 patients (21 males, 70%) were confirmed to have a diagnosis of adult PID. Patients with "unclassified immunodeficiency" or those who were suspected to have PID but whose diagnostic evaluation was incomplete at the time of abstract submission were excluded from the current analysis (n=52). The distribution of study patients in various categories as per the IUIS 2022 classification is shown in Table 1. The median age at diagnosis was 30.5 (range 14-48) years with an average delay in diagnosis of 7.3 (range 0.5-38) years. The presenting manifestations included recurrent infections [n=28 (93%), 20 bacterial/ mycobacterial, 12 fungal, 7 viral, 3 parasitic] and/or auto-immune manifestations [n=11 (37%), including coeliac disease, autoimmune hemolytic anemia, immune enteropathy, Type 1 diabetes mellitus, hypothyroidism]. One (3.3%) patient also had a hematological malignancy (myelodysplastic syndrome). Diagnosis of 12 (40%) patients was confirmed with genetic testing (genetic reports awaited for other patients). Six (20%) patients died, remaining 24 (80%) are currently on treatment and under regular follow-up. Cause of death was life-threatening infections in ⅚ (83%) and HLH in ⅙ (17%).

Conclusion:

PIDs in adults are not uncommon, can have varied clinical presentations, and are genetically heterogeneous. There is often a significant delay in diagnosis. A high index of suspicion, early diagnosis and personalized

treatment strategies, including antimicrobial therapy/prophylaxis, immunoglobulin replacement therapy, immunosuppression (for autoimmune manifestations), and/or HSCT, are crucial for improving patient outcomes

Figures ,tables:

Table 1: Distribution of the adult PID cohort as per IUIS 2022 classification

IEI Category		Total cases (n=30)	Diagnosis
I	Immunodeficiencies affecting cellular and humoral immunity	3	I. SCID (DCLRE1C/ARTEMIS) (n=1) II. SCID (JAK3) (n=1) III. CID (TAPBP) (n=1)
II	Combined immunodeficiencies with associated or syndromic features	3	I. Calcium Channel Defects: STIM-1 deficiency (n=1) II. Hyper IgE (STAT3 HI) (n=1) III. WAS (n=1)
III	Predominantly antibody deficiencies	6	I. CVID (n=5) II. Hyper IgM (n=1)
IV	Diseases of immune dysregulation	4	I. ALPS (n=3) II. CTLA4 haploinsufficiency (n=1)
V	Congenital defects of phagocyte number, function, or both	2	I. CGD (n=2)
VI	Defects in intrinsic and innate immunity	7	I. MSMD (n=5) II. CARD9 deficiency (n=2)
--	Others	5	Idiopathic CD4 lymphopenia

P-36

Abstract Title:

Inborn Errors of Immunity in Adult Patients: Experience from a Tertiary Care Center in South India

Abstract no: 55

All authors: Jyothi Janardhanan[1],Dr. Sagar Bhattad[1]

Complete details of Institute including city state -

[1]Aster CMI Hospital, Hebbal, Bengaluru,Karnataka, India

Presenting Author email- jyothi428@hotmail.com

Abstract:

Background:

Inborn Errors of Immunity (IEI) are a heterogeneous group of disorders predisposing affected individuals to infections, autoimmunity, autoinflammation, and malignancies.

Objectives:

This study examined the profile of IEIs in adults at a tertiary care center in South India.

Methods:

Conducted at a Southern Indian tertiary care center from February 2017 to December 2024, the study involved data collection on IEIs using a pre-designed Excel sheet and detailed analysis of adults diagnosed with IEIs.

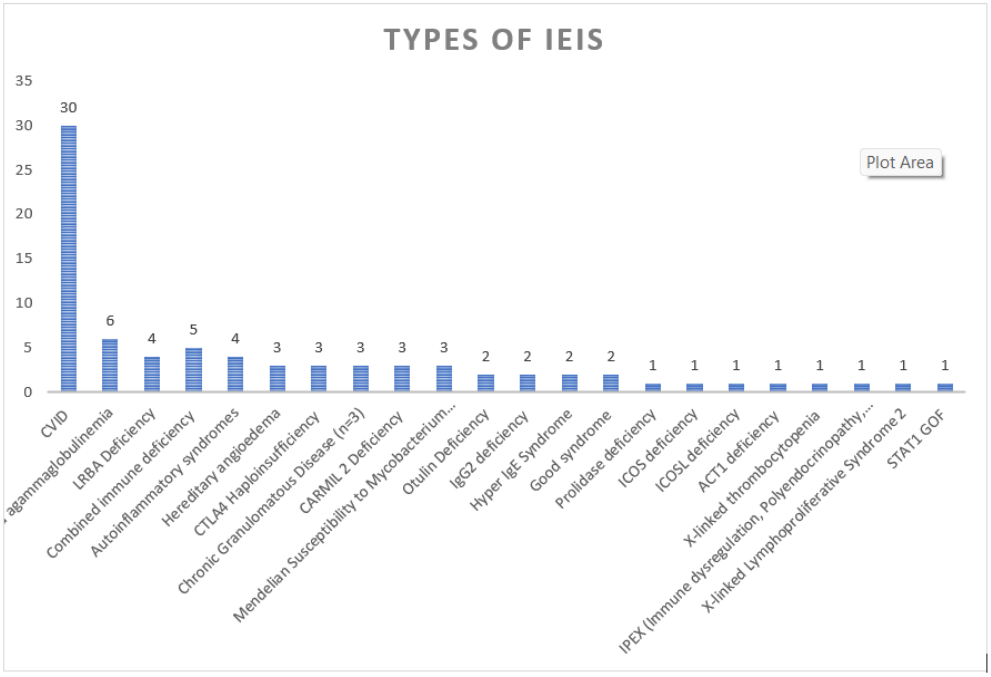
Results:

Among 500 patients diagnosed with various IEIs during the study duration, 80 adults were included in this cohort, with male-to-female ratio of 2:1. Mean age at the onset of the first clinical presentation was 12.7 years (range: 7 months – 45 years), and mean age at diagnosis was 30.43 years (range: 2-62 years). Among those patients with an adult onset of illness (n=25), mean age of presentation was 31.52 years, and mean age of diagnosis was 43.2 years. Overall, the commonest IEI was the Common Variable Immunodeficiency (CVID) observed in 30 patients Adult-onset IEIs predominantly included CVID (n=24). Most of the referrals in adult-onset IEI came from gastroenterologists (n=11) and pulmonologists (n=10). During the study period, 59 patients (73%) were noted to have infections, amongst which pneumonia (n=29) and diarrhea (n=22) were the most common. Bronchiectasis was noted in 10 patients. Autoimmunity was evident in a subset of patients (n=35) (43%), with notable manifestations such as inflammatory colitis (n=12), autoimmune cytopenia (n=10), and arthritis (n=9). Autoimmune skin conditions included pyoderma gangrenosum (n=2) and pemphigus vulgaris (n=1). Genetic testing was conducted in 56 patients, resulting in positive findings for 40 individuals. Those with autoimmunity received steroids (n=19), methotrexate (n=10), colchicine (n=6), cyclosporine (n=3), sirolimus (n=3), mesalamine (n=5), tofacitinib (n=2), mycophenolate mofetil (n=3), and azathioprine (n=6). Biologics such as rituximab (n=3), tocilizumab (n=1), adalimumab (n=1), and infliximab (n=1) were also administered. 54 patients are on Immunoglobulin replacement therapy and 60 patients are on antibiotic prophylaxis. One patient with CARMIL-2 Deficiency with severe inflammatory colitis underwent a successful hematopoietic stem cell transplant (HSCT)from a matched unrelated donor. Another patient with LRBA deficiency underwent an unmatched unrelated HSCT, however, succumbed to sepsis. The overall survival of this cohort is 97.5% (n=78).

Conclusion:

We present an overview of Inborn Errors of Immunity (IEIs) in adults, emphasizing a significant delay in diagnosis within our cohort. This emphasizes the importance of increasing awareness among physicians, particularly gastroenterologists and pulmonologists, about the referrals

Figures, tables:



P-37

Abstract Title:

Spectrum of Systemic Autoinflammatory Diseases at a Tertiary Care Center in South India

Abstract no: 56

All authors: Jyothi Janardhanan[1],Dr. Sagar Bhattad[1]

Complete details of Institute including city state -

[1]Aster CMI Hospital, Hebbal, Bengaluru, Karnataka, India.

Presenting Author email- jyothi428@hotmail.com

Abstract:

Introduction

Systemic autoinflammatory diseases (SAIDs) are a growing group of disorders caused by a dysregulation of the innate immune system leading to episodes of systemic inflammation. They often present with recurrent episodes of fever, skin lesions, oral ulcers, and arthritis. Molecular genetics and next-generation sequencing technologies have increased our understanding of these diseases.

Objective

To study the profile of autoinflammatory diseases in patients at a tertiary care center in Bangalore, India.

Methods

A retrospective review of clinical records was performed and patients with Inborn Errors of Immunity (IEI) were categorized according to the International Union of Immunological Societies (IUIS), Primary Immunodeficiency Diseases Committee Report on Inborn Errors of Immunity (2022). Patients with underlying IEI who were diagnosed to have autoinflammatory disease were included in the study. A detailed analysis was performed to understand the types of autoinflammatory diseases.

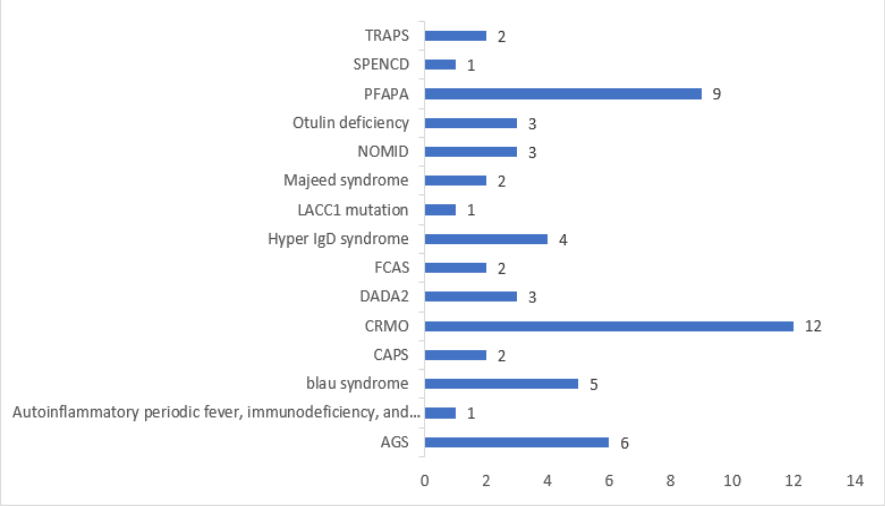
Results

A total of 500 patients with various IEIs were diagnosed during the study period (February 2017 to December 2024). Of these, 56 patients were diagnosed to have systemic autoinflammatory diseases (SAID). The male-to-female ratio was 1.2:1. The mean age at onset of symptoms was 4.8 years and the mean age at diagnosis was 10.6 years. As per the International Union of Immunological Societies (IUIS) 2022 classification, 24 out of 56 patients had non-inflammasome-related diseases (43 %), eleven had diseases affecting inflammasome (19.6 %), ten had Type I interferonopathies (17.8 %), nine patients had PFAPA (16 %) and two were unclassified (3.5 %). The most common types of NSAIDs were Chronic recurrent multifocal osteomyelitis (CRMO) (n=12), and PFAPA (n=9). The most common manifestations were recurrent or periodic fevers (n=22, 44%), rash (n=17, 34%), arthritis/arthralgia (n=15,30%), and recurrent oral ulcers (n=10,20%). Whole exome sequencing was performed in 42 patients, and mutations were identified in 35 patients. Treatment included corticosteroids (n=20), NSAIDS (n=10), methotrexate (n=11), colchicine (n=8), leflunomide (n=3), thalidomide (n=2), and cyclosporine (n=1). Five CRMO patients were treated with Pamidronate, however, two of them failed to respond warranting adalimumab. Eight patients (TRAPS, Otulin deficiency, DADA2, NOMID, CRMO, SPENCD) were treated with biologics (Infliximab n=1, Tocilizumab n=1, Adalimumab n=4, Tofacitinib=1, Anakinra n=2) and showed a brisk response. Thirty-two patients remain on close follow-up.

Conclusion:

We hereby present one of the largest single-center cohort of SAIDs with a genetic confirmation in the majority. Significant delays in the diagnosis continue to remain a challenge in our set-up.

Figures ,tables:



P-38

Abstract Title:

Experiences from Inborn errors of immunity registry of India – a preliminary report

Abstract no: 58

All authors: Reetika Malik Yadav[3],Deepti Suri[1], Satheesh C[4], Prajnya Ranganath[2], Reena Gulati[5], Umair Bargir[3], Lavina Temkar[3], Persis Khalon[1], Manpreet Dhaliwal[1], Saniya Sharma[1], Rakesh Pilania[1], Ankur Jindal[1], Vignesh

Pandiyarajan[1], Amit Rawat[1], Surjit Singh[1], Manisha Madkaikar[3]

Complete details of Institute including city state-

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Abstract:

Introduction:

PID registry was developed by ICMR as part of a comprehensive multi-centric registry for rare inherited diseases in 2019. This paper represents an analysis of the PID registry data.

Methods:

The registry sought to collect data on diagnosed cases from centres who expressed interest in contributing to the national database. ICMR-NIIH and PGI Chandigarh, the designated nodal centres for PID by ICMR, developed a data collection form, and Qc criteria for validation of data entered by the contributing centres. Data was collected after ethics approval from the participating centres. Data was collected in a structured format comprising of demographic, clinical, laboratory, diagnosis including IUIS category of disease, genetics, and treatment details. The data was compiled in excel format and analysed using Epi Info v7.2.5.0.

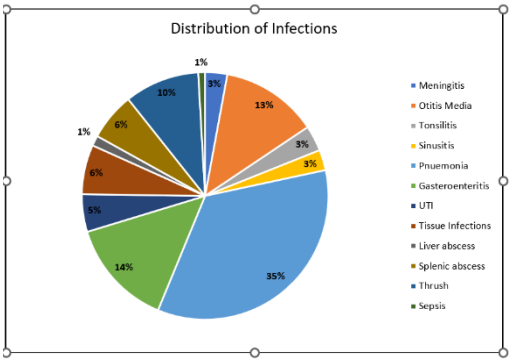
Results:

Six participating centres including ICMR-NIIH Mumbai, PGI Chandigarh, Apollo Chennai, JIPMER Pondicherry, Nizams Institute Hyderabad, and Sir Gangaram Hospital Delhi together contributed data for 708 PID patients. After exclusion of incomplete entries, data of 676 patients enrolled between January 2019- October 2024 was analysed. Immunodeficiencies affecting cellular and humoral immunity (CID) and CID with associated or syndromic features taken together were the most frequent PID (27.65%) with 94 (13.90%) and 93 (13.75%) patients respectively. Predominantly Antibody deficiency was the next frequent with 146 (21.59%) diagnosed patients, followed by 117 (17.30%) patients diagnosed with Congenital phagocytic defects. The median age of presentation and diagnosis were 16 (IQR 4,63) and 53 (IQR 13,128) months respectively, with diagnostic delay of 16 (IQR 3,55) months. 453(67.71%) patients were males. Consanguinity was observed in 155 (22.98%) families. A previous history of sibling death was present in 94(13.90%) and death of male member in 27(3.99%) families. The presenting clinical manifestations comprised of recurrent infections in 459 (67.89%) patients, autoimmune or autoinflammatory in 292 (43.19%) patients, complications to live vaccines in 38(5.62%), and malignancy in (n=5) 0.73%. The spectrum of infections which is the commonest presentation is depicted in Figure 1Regarding treatment, 166 (24.55%) patients are on IVIG therapy and 90 (13.31%) patients underwent HSCT. On follow up of these patients in 2024, 118 (17.45%) patients had succumbed to infections.

Conclusion:

The PID registry developed by ICMR as an attempt to maintain a patient database gives us insights on the demographic, clinical presentation, diagnostic delay and treatment outcomes of PID. This registry will help further in patient management and care by emphasising the importance of timely diagnosis and treatment.

Figures, tables:



P-39

Abstract Title:

Autoimmunity and Immune Dysregulation in Inborn Errors of Immunity: Experience from a Tertiary Care Center in South India

Abstract no: 59

All authors: Jyothi Janardhanan[1],Dr. Sagar Bhattad[1]

Complete detail of Institute including city state -

[1]Aster CMI Hospital, Hebbal, Bangalore, Karnataka, India

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Abstract:

Introduction:

Inborn Errors of Immunity (IEI) are a heterogeneous group of disorders causing infections, autoimmunity, autoinflammation, and malignancies. The literature on autoimmunity in IEI in the Indian subcontinent is limited hence, highlighting the clinical presentation and management of these patients.

Objectives:

To study the profile of autoimmune manifestations and immune dysregulation in patients with IEIs at presentation or during follow-up.

Methods:

This study was conducted at a tertiary care center in Southern India from February 2017 to December 2024. Data was entered in a pre-designed Excel sheet. Patients of IEI with autoimmune manifestations and immune dysregulation were analyzed.

Results:

500 patients with various IEIs were diagnosed during the study period. The male-to-female ratio was 2:1. In children, the mean age at the onset of the first clinical presentation was 1.5 years, while in adults, it was 19.8 years. The most common IEI was Severe Combined Immunodeficiency (SCID) (n=49,10 %) in children and

Common Variable Immune Deficiency (CVID) (n=36,7.6 %) in adults.
Autoimmunity was observed in 130 (26 %) patients. The 'autoimmune cohort' experienced a mean delay in diagnosis of 8.5 years, significantly higher than the rest of the study population ($p < 0.002$). The most prevalent autoimmune manifestations included inflammatory colitis (n=34), autoimmune cytopenia (n=30), autoimmune endocrinopathy (n=10), and arthritis (n=9). Skin manifestations included pyoderma gangrenosum (n=7), alopecia areata (n=4), vitiligo (n=3), bullous pemphigoid (n=1), dermatitis herpetiformis (n=1), and cutaneous vasculitis (n=1). Others included systemic lupus erythematosus (n=7), Kawasaki disease (n=4), lymphoproliferation (n=15), autoimmune hepatitis (n=3), CNS vasculitis (n=2), systemic vasculitis (n=1), nephritis (n=1), nephrotic syndrome (n=2), oral aphthosis (n=1), sarcoidosis (n=1), and uveitis (n=1).
Patients were treated with various immunomodulatory agents, including steroids (n=40), methotrexate (n=12), colchicine (n=6), cyclosporine (n=3), sirolimus (n=6), mesalamine (n=3), leflunomide (n=2), thalidomide (n=2), tofacitinib (n=2), mycophenolate mofetil (n=3), azathioprine (n=6), and dapsone (n=1). Biologics used were rituximab (n=3), anakinra (n=2), tocilizumab (n=1), adalimumab (n=1), and infliximab (n=1). 38 patients received immunoglobulin replacement therapy. Five patients with C1q deficiency were given fresh frozen plasma infusions. 22 underwent Hematopoietic stem cell transplant. The overall survival rate in the 'autoimmune' cohort was 89 %.

Conclusion:

Autoimmunity is a common yet often overlooked manifestation of IEI. The intrinsic susceptibility to infections complicates the management of autoimmunity, making immunomodulation with vigilant monitoring the imperative approach for these patients

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P-40

Abstract Title:

Adult onset monogenic IEI: missed opportunity

Abstract no: 60

All authors: Vijaya Gowri[1],Prasad Taur[1], Vaishnavi Iyengar[1], Akshaya Chougule[1], Mukesh Desai[1]

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Abstract:

Introduction:

Inborn errors of immunity (IEI) are heterogenous disorders due to defects in genes that functionally impact the innate or adaptive immune system. These genetically driven disorders usually have childhood onset, however diagnosis of monogenic IEI in adults is documented as well. Delayed diagnosis can be secondary to lack of awareness or late onset of symptoms.

Material and Methods:

We retrospectively analyzed the data of 48 adult patients referred between 2018-2024 and subsequently diagnosed with monogenic IEI. History of early onset of symptoms was identified in 52%. The age range at

referral was 18- 61 years, with 37 males and 11 females. The majority (56%) were aged 18-24 years. Patients were stratified according to IUIS classification. 35% of the patients were from Immune dysregulation group, 20% from Antibody deficiency group, 10% each were from SCID/CID, Phagocytic and Intrinsic/Innate immune defects group, 7% had Autoinflammatory disease and 4% each from TLR signaling pathway and Bone-marrow failure syndrome group. The presenting features were Malignancy in 33%, EBV-LPD in 16%, HLH in 10% and infections. Autoimmunity was prevalent in 54% of the cohort. Lymphopenia and hypogammaglobulinemia was seen in 52% and 31% respectively. Bacterial infections with gram-positive and negative organisms were the cause of morbidity in 44% while MTB was isolated in 12% patients. Fungal infections, particularly CMCC, were seen in 14% of patients, with a positive galactomannan test in 2%. The overall mortality rate was 23%.

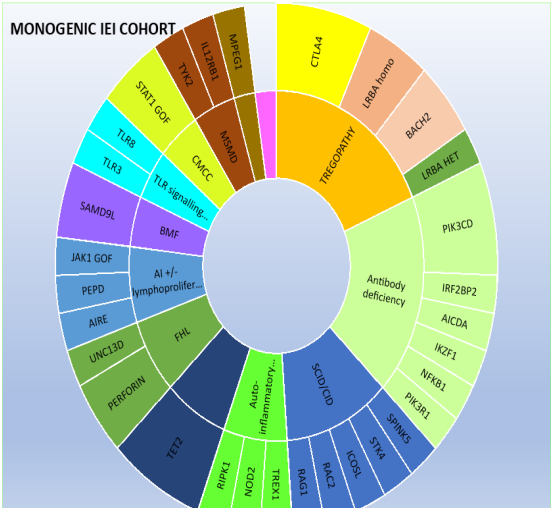
Management:

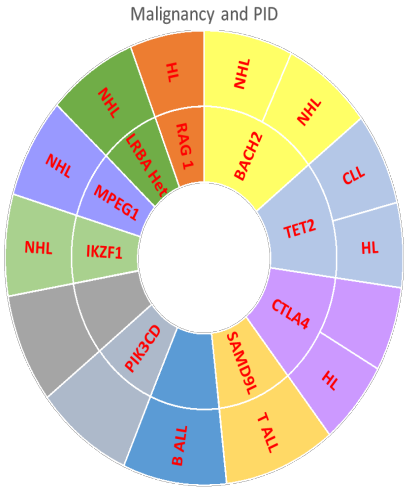
Only 23% patients with hypogammaglobulinemia received IVIG. Autoimmunity was managed with Sirolimus, MMF, Baricitinib and Mesalamine tailored to monogenic defect driving pathological systemic manifestations. Rituximab was used in EBV associated disease (malignant and non-malignant) in 19%, either alone or as an adjunct to chemotherapy. Infections were managed with antibiotic, antifungal and antiviral prophylaxis. Disease specific management included Empagliflozin for G6PC3 mutation. Modified AKT for longer duration was given to patients with monogenic error driving the infection.

Conclusion:

In >50% patients there was retrospective indication of childhood onset of disease (fever, recurrent infections). Delayed identification was responsible for escalation of symptoms and morbidity. Immune dysregulation and malignancy were major presentations. EBV signature in 42% patients underscoring the oncogenic potential of the virus. Infection control in antibody deficiency group was challenging despite treatment due to structural abnormalities like bronchiectasis. Early diagnosis of IEI could prevent significant mortality and morbidity

Figure, Tables:





P-41

Abstract Title:

Hyper IgM syndrome with NK cell deficiency: And MSH6 a Denovo mutation

Abstract no: 63

All authors: Mahesh Gaikwad[1]

Complete details of Institute including city state -

[1]Nizam's Institute of Medical Sciences, Panjagutta ,Hyderabad, Telangana, India.

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Abstract:

Case details

A 6 years old boy born out of 2nd degree consanguineous marriage , symptomatic since 3-4 months presented to us with recurrent pulmonary infections, requiring Oxygen requirement and Failure to thrive , treated elsewhere with antibiotics now came to Nizam's Institute of Medical Sciences for 2nd opinion with a proxy visit.

Birth history was normal, No hospitalization at birth. Birth weight was 2.6kg. Vaccination completed till date with no history Of any adverse events ,and there was no history of any developmental milestones delay.

Documentation showing the following results.

Hemogram 12.6/15600/4.8al

ESR 58

SGOT/PT 30/18

Serum creatinine 0.9

Serum Immunoglobulins

IgG <75(700-1600)

IgA<10(70-400)

IgM 957 (40-230)

Subset analysis

Subset cells Percentage

CD3 85% (60-76)

CD4 36.4 %(31-41)

CD8 43.5% (18-35)

CD4/CD8 0.8

CD19 10.9% (13-27)

CD16/CD56 1.8%(4-17)

Whole exome sequencing:MSH6 Homozygous mutation, Autosomal recessive , pathogenic variant

Discussion: Here we present a rare case of Hyper IgM syndrome with NK cell deficiency. There very few case reports of this condition. We found a Denovo mutation in MSH6 gene which is DNA repair gene and is a pathogenic variant. MSH6 gene mutation associated with LYNCH syndrome,Colorectal cancers,Small intestine,Endometrial cancers, Kidney cancers. MSH6 is one of the important gene responsible for class switch reaction , Defect of which lead to IgA deficiency. Till date, there are 8 case reported with MSH6 mutation having hyperIgM syndrome most of them were Autosomal recessive.

P-42

Abstract Title:

Phenotype-Genotype Discordance in Patients with Inborn Errors of Immunity: A Roadmap to Diagnostic Clinching

Abstract no: 64

All authors: Keerthi Vardhan Yerram[1], Pothina Amarnath[1], Dr.Prajnya Ranganath[1], Dr.Kunal Agarwal[1],

Dr.Kavitha S[1], Dr.Madhuri Challa[1], Dr.Liza Rajasekhar[1]
Complete detail of Institute including city state:
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Presenting Author email- k.undefined5@gmail.com
Abstract:
Background:
Inborn errors of immunity (IEI) are genetic disorders causing recurrent infections, autoimmunity, and malignancies. This dataset highlights clinical and genetic profiles of patients, emphasizing the evolving phenotypic spectrum of genetic variants.
Objectives:
1 . To characterize clinical and genetic profiles of IEI patients, emphasizing novel variants and phenotype correlations.
2. To investigate genotype-phenotype discordances and pathways to concordance.
Methods:
Data was collected on patients presenting for evaluation of IEI, in the year 2024 including. Demographics: Age at presentation, consanguinity, family history, Types and frequency of infections, autoimmune manifestations, and physical findings, immune cell counts ,whole exome sequencing (WES) was done where possible.
Results:
In the year 2024, 90 patients were evaluated at our center for IEI. The cohort included individuals presenting with recurrent infections, autoimmunity, recurrent fever. The mean age of the cohort was 5.94 years (SD: 7.91 years), comprising 49 males (65.33%).
WES was done in 22 patients with a high index of suspicion for IEI. Among these, 11 had recurrent infections, 11 exhibited early-onset autoimmune diseases, some with atypical clinical features. The mean age at presentation for this subset was 5.6 years (SD: 5.0 years), and mean age at diagnosis was 10.2 years (SD: 7.93 years), with a diagnostic lag of approximately 4.6 years. Consanguinity observed in 5 / 21 patients.
Genetic variants correlated with the clinical phenotype in 9 patients (Table 1). These included 2 variants in BTK gene in 3 patients with X-linked agammaglobulinemia and variants in ATM gene, DOCK8, MSH6, ELANE, PRG4 , and C1QB in one patient each.
In 12 patients (Table 2), discordance between genetic variants and clinical phenotypes was observed. A patient with a SOCS1 heterozygous variant had arthritis, pancreatitis, panniculitis, fever, hepatic steatosis, hypothalamic amenorrhea, hypocomplementemia and dsDNA antibody positivity, leading to a diagnosis of systemic lupus erythematosus (SLE). Since the variant is classified as VUS functional analysis will be considered. In the 15-year old patient with arthritis, myositis, recurrent parotid swelling, and severe varicella infection, and a denovo PRF1 compound heterozygous variant was identified. Whole genome sequencing is planned to explore potential novel genetic variants.
Conclusion:
We report a novel variant, (BTK c.974+5G>A) in XLA. In patients presenting with early onset multi system autoimmune disease, segregation analysis, in silico prediction, and functional studies, are needed to classify variants as pathogenic. Enhancing resources, and multidisciplinary genetic research will improve diagnosis, patient care, and outcomes in IEI with autoimmunity.

Figures, Tables:

Table 1 Phenotype-Genotype Concordance: Variant analysis

Sno	Provisional diagnosis	Gene	Variant	protein alteration	ACMG classification	Further diagnostic work-up required
1	Ataxia telangiectasia	ATM	c.6998 del	p.Thr2333AsnfsTer6	Likely Pathogenic	None
2	HyperIgE syndrome	Dock8 del	9p24.3(214508-340321)X0	NA	Pathogenic	None
3	Agammaglobulinemia	BTK	974+5 G>A Splice variant	NA	Likely pathogenic	Insilico splice variant prediction
4	Agammaglobulinemia	BTK	974+5 G>A Splice variant	NA	Likely pathogenic	In Silico splice variant prediction
5	Agammaglobulinemia	BTK	C.215 del	p.Asn72ilefsTer49	Pathogenic	None
6	HyperIgM syndrome (Recurrent Lower Respiratory tract infection,leucopenia,Nk cell deficiency)	MSH6	C.3261 dup	p.Phe1088LeufsTer5	Pathogenic	Segregation analysis to be done
7	Congenital neutropenia	ELANE	c.567C>G	p.Leu189	Likely pathogenic	None
8	Blau/**CACP syndrome**/ inflammatory arthritis	PRG4	c.619del	p.Arg207GlufsTer13	Likely pathogenic	None
9	Probable lupus	C1QB	C.227G>T	p.Ala663Thr	Likely pathogenic	None

Table legends-VUS-Variant of unknown significance, NA-Not Applicable, CACP-Camptodactyly-Arthropathy-Coxa Vara-Pericarditis

Table 2 Phenotype-Genotype discordance: Variant analysis

SNO	Age at onset/age at diagnosis (years)	Phenotype	Predicted phenotype	Gene	Variant	Zygosity	Protein alteration	ACMG classification	Predicted Phenotype/ Additional details/ Further work up planned
1	0.25/0.6	Possible SCID	SCID	ADA	C.1028 T>C	Homozygous	p.Leu343 pro	VUS	Segregation analysis
2	0.25/8	Agammaglobulinemia	SCID	NHEJ1	C.139G >A	Homozygous	p.Glu47Lys	VUS	Segregation analysis CADD Phred 27.6
3	0.25/2	Possible storage disorder, normal Ig	CVID	PIK3CD	c.3061G >A	Heterozygous	p.Glu1021 Lys	Likely pathogenic	Segregation analysis
4	21/24	Possible PRAAS	CVID	NFKB2	c.1987G >A	Heterozygous	pAla669Thr	VUS	Segregation analysis ATM : p.Glu1009LeufsTer14 PD:PM2, FD:PP2,ISP: BP4
5	9/13	Arthritis/nodular rash	Susceptibility to Rheumatoid arthritis	CIITA	c.778G>C c.1849G >Cc.719 T>G	Heterozygous	p.Val260Leu	VUS	Segregation analysis,in silico analysis
6	14/35	Disseminated granulomatosis	Immunodeficiency 17, CD3 gamma deficien	CD3G	C.391delG	Homozygous	pVal131fs	Likely pathogenic	Insilico analysis and Functional analyis
7	14/20	SLE with pancreatitis, hepatic steatosis	Possible Type 1 interferonopathy	SOCS1	c.56c>G	Heterozygous	p.Pro19Arg	VUS	Segregation negative, denovo variant , Functional analysis Planned
8	10/11	Sjogrens's with varicella with parotid calcification	Familial Hemophagocytic lymphohistiocytosis-2	PRF 1	c.1A>G	Heterozygous	p.Met1?	Likely pathogenic	Segregation analysis negative, Whole genome sequencing initiated
9	11/12	Incomplete SLE	Keratosis palmoplantaris striata II	DSP	c.6077A >C	Heterozygous	p.Lys2026 Thr	VUS	Bioinformatics analysis
10	7/14	SLE, cytopenias, pancreatitis, ACLE	Wiskott-Aldrich syndrome	WAS	c.1130G >A	Heterozygous	p.Arg377 His	VUS	Segregation analysis
11	9/14	Lupus with infections	APS type 1	AIRE	871C>T	Heterozygous	p.Leu291 Phe	VUS	Segregation analysis
12	12/15	Lupus with infections	CVID	TNFSRF13B	C.565A >G	Homozygous	p.Arg189 Gly	VUS	Segregation analysis

Table legends-VUS-Variant of unknown significance, PRASS: Proteasome associated autoinflammatory syndrome.APS type 1-Auto polyendocrine syndrome type 1

P-43

Abstract Title:

Autoimmune Manifestations in Patients with Inborn Errors of Immunity: A Retrospective Analysis from a Tertiary Care Center

Abstract no: 65

All authors: Kavitha Shanigaram[1], Keerthivardhan Yerram[1], Devarasetti Phani Kumar[1], Liza Rajasekhar[1]

Complete details of Institute including city state -

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Abstract:

Introduction

Inborn errors of immunity (IEI), also known as primary immunodeficiency disorders (PID), are a group of genetically heterogeneous diseases that lead to increased susceptibility to infections, autoimmunity, auto

inflammation, and malignancies. The intersection of IEI and autoimmune manifestations is of particular interest, as the immune dysregulation inherent in IEI often predisposes individuals to autoimmune diseases. This study investigates the prevalence and types of autoimmune manifestations in patients with IEI.

Methods

We conducted a retrospective analysis of data from the Primary Immunodeficiency Registry at Nizam's Institute of Medical Sciences Hospital, Hyderabad, from 2021-2024, encompassing a total of 100 patients with IEI. The data included demographic details, genetic diagnoses from Whole Exome Sequencing (WES), autoimmune manifestations, other clinical features, and treatment regimens. We identified patients with confirmed IEI who also exhibited autoimmune phenomena. Data were extracted and analyzed to determine the various autoimmune conditions among different IEI subtypes.

Results

The study cohort consisted of 15 patients with IEI and autoimmunity, including 6 females and 9 males. The mean age of presentation was 4.2 ± 2 years. The autoimmune manifestations observed included cytopenia (2), oligoarthritis (12), polyarthritis (2), and autoimmune hemolytic anemia (AIHA) (2). The gap between the diagnosis of IEI and autoimmune manifestations varied, with a mean of 2 ± 0.5 years. The prevalence of autoimmunity in IEI in our cohort was 15%. Key findings are as follows:

Common Variable Immunodeficiency (CVID): 5 patients with autoimmune manifestations such as oligoarthritis and polyarthritis, treated with methotrexate.

X-Linked Agammaglobulinemia (XLA): 4 patients with oligoarthritis and polyarthritis, treated with methotrexate.

Wiskott-Aldrich Syndrome (WAS): 1 patient with arthritis and AIHA, treated with azathioprine.

Hyper IgE Syndrome (STAT3 mutation): 2 patients, both presenting with arthritis, treated with methotrexate.

Ataxia Telangiectasia (ATM mutation): 1 patient with polyarthritis.

C1Q deficiency: 1 patient presenting with cytopenia and arthritis, treated with azathioprine.

Conclusion

Autoimmune manifestations are prevalent among patients with inborn errors of immunity. The diversity of autoimmune conditions in these patients illustrates the complexity of immune dysregulation in IEI. Early identification and targeted treatment of autoimmune manifestations are crucial for improving clinical outcomes. Our findings highlight the need for heightened awareness and comprehensive care strategies for patients with IEI to manage both infectious and autoimmune complications effectively.

P-44

Abstract Title:

Recurrent Fevers And Arthralgia Associated With A Novel Heterozygous Mutation in TREX1

Abstract no: 67

All authors: Nidhi Desai[1],Asma Shaikh[1], Pallavi Gaikwad[1], Disha Vedpathak[1], Janhavi Shirke[1], Umair Bargir[1], Manisha Madkaikar[1]

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Abstract:

Background and Aims

Mutations in TREX1 cause neonatal onset autoinflammatory disorders. Here we describe the immunological consequences of a novel

TREX1 mutation in three patients from two unrelated families.

Methods

WES was performed for index patients and Sanger sequencing was performed on patients and families. Lymphocyte and myeloid subsets were studied on whole blood. ISG score was calculated as the median fold change in expression of 7 interferon-response genes (IFIT1, IFI27, MX1, SIGLEC1, RSAD2, ISG15, IFI44L). STAT1 phosphorylation was measured in response to IFN-α and IFN-γ. DNA damage was measured as a function of γH2AX at 2 and 24 hours post-irradiation (2Gy).

Results

The index cases (P1 and P2, 15 and 19 years, respectively), both males, presented with recurrent fevers with arthralgia occurring once a month, lasting 4-7 days, since adolescence. A heterozygous mutation in TREX1 (p.Ser27Phe) was identified on WES. The father and sibling (12 years, female) of P1 also had recurrent fevers. P2 inherited the mutation from his asymptomatic mother. All patients had increased plasmacytoid dendritic cells. The ISG score was elevated in all individuals carrying the variant, including the asymptomatic mother from family 2. Phosphorylation of STAT1 was elevated in response to IFN-α and IFN-γ. This was explained by increased basal STAT1 gene expression compared to controls. We observed both P2 and carrier had reduced γH2AX levels compared to healthy controls at 2 hours post-irradiation recovery, as reported in TREX1 knock-out cells.

Conclusions:

Heterozygous mutation in TREX1 (p.Ser27Phe) affects cellular function, however, there is incomplete penetrance of the clinical phenotype.

P-45

Abstract Title:

Mycobacterial infections in patients with Mendelian Susceptibility to Mycobacterial disease : An experience from North India

Abstract no: 68

All authors: Ahmed Zaid Jamal[1], Jhumki Das[1], Pandiarajan Vignesh[1], Abarna Thangaraj[1], Satish Kumar Loganathan[1], Aditya Dod[1], Rakesh Yadav[1], Rakesh Pilania[1], Ankur Jindal[1], Manpreet Dhaliwal[1], Saniya Sharma[1], Deepti Suri1[1], Sunil Sethi[1], Surjit Singh[1]

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Abstract:

Background:

Mendelian Susceptibility to Mycobacterial disease (MSMD) is a rare innate immunity disorder, predisposing to infections by weakly virulent mycobacteria such as the Bacillus Calmette-Guérin (BCG) vaccine, nontuberculous

mycobacteria (NTM), or environmental mycobacteria (EM). Infections due to more virulent M. tuberculosis have also been reported in patients with MSMD. We report the mycobacterial infection profile in MSMD patient cohort from North India.

Methods:

A retrospective review of clinical and laboratory records was carried out for patients with MSMD registered at Pediatric Immunodeficiency Clinic, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Results:

Of the 30 patients with MSMD, pathogenic homozygous defects in IL12RB1, IL12B, IFNGR1, IFNGR2, ISG15 were seen in 16, 3, 3, 2, and 2 patients respectively. A novel hemizygous defect in IKBKG was seen in 1 patient. Furthermore, 2 patients had partial dominant IFNGR1 defect. Of the 29 patients who received BCG vaccine at birth, 19 (63%) of them had evidence of BCG infection in the infancy age group. Of these 19 patients, 9 had disseminated form of the disease, of which 4 had IL12RB1 defect, 1 had partial dominant IFNGR1 defect but with dissemination limited to musculoskeletal system, 2 had IFNGR2 defect and 2 had IL12B defect. Recurrent and disseminated forms of M. tuberculosis were seen in 9 patients (30%). Multi drug resistant (MDR) forms of tuberculosis were seen in 2 patients. 1 patient with IL12RB1 defect had renal involvement due to M. tuberculosis infection. Multifocal bone infection due to M. avium complex was seen in a child with partial dominant IFNGR1 defect. Disseminated infections with M. fortuitum and M. saskatchewanense were seen in 2 patients with IFNGR1 and IL12B defects respectively. Mixed mycobacterial infections with M. bovis and NTM were seen in 2 patients with IL12RB1 and IL12B defect. The age at diagnosis varied from 1 month to 14 years. Mortality was seen in 7 patients.

Conclusion:

MSMD is a complex heterogenous disorder. M. bovis (BCG) is the most common infection with its disseminated form being the most common manifestation, due to universal BCG vaccination at birth practiced in our country. Additionally, infections with M. tuberculosis and NTM are also seen commonly and therefore a high suspicion for screening for the same must be kept.

P-46

Abstract Title:

Clinical and Laboratory Profile of Agammaglobulinemia: A Retrospective Analysis from a Tertiary Care Center

Abstract no: 69

All authors: Kavitha Shanigaram[1], Keerthivardhan Yerram[1], Devarasetti Phani Kumar[1], Tara Roshni Paul[1], Liza Rajasekhar[1]

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Abstract:

Introduction:

Agammaglobulinemia is a rare primary immunodeficiency disorder characterized by markedly low levels of

immunoglobulins and a profound reduction or absence of peripheral B cells due to impaired bone marrow development. The disease typically manifests within the first year of life, presenting with recurrent infections caused primarily by encapsulated bacteria. These infections commonly affect the respiratory and gastrointestinal tracts, skin, joints, and central nervous system.

Methods:

A retrospective analysis was conducted using data from the Primary Immunodeficiency Registry at Nizam's Institute of Medical Sciences (Nizam's Institute of Medical Sciences), Hyderabad, covering the period from 2021 to 2024. The dataset included demographic information, genetic findings from Whole Exome Sequencing (WES), clinical presentations, systemic manifestations, and treatment details. Patients with confirmed agammaglobulinemia were identified, and relevant data were extracted and analyzed.

Results:

The study cohort comprised 22 male patients diagnosed with agammaglobulinemia. Their mean age at diagnosis was 29 months. Clinical Manifestations included lower respiratory tract infections (LRTI): 21 cases (95%), upper respiratory tract infections (URTI)in 15 cases (68%), chronic suppurative otitis media (CSOM): 12 cases (54%), osteomyelitis: 4 cases (18%), blood cultures positive for *Pseudomonas aeruginosa*: 5 cases (22%). Autoimmune Features included arthritis in 14 cases (63%), cytopenias (anemia, thrombocytopenia) in 9 cases (40%). All patients had B cell counts below 1%. Serum
immunoglobulin levels (IgG, IgA, and IgM) were uniformly low. Additional findings included growth retardation in 6 cases (27%). One patient succumbed to severe infections at the age of 18 months
Whole Exome Sequencing (WES) was performed for 14 patients: BTK* mutation: 10 cases, BLNK mutation: 2 cases. No pathogenic variant detected: 2 cases (Table 1).
All patients were placed on a regular follow-up regimen. Monthly intravenous immunoglobulin (IVIG) replacement therapy at a dose of 0.4 mg/kg was administered. Cotrimoxazole prophylaxis was provided to prevent opportunistic infections.

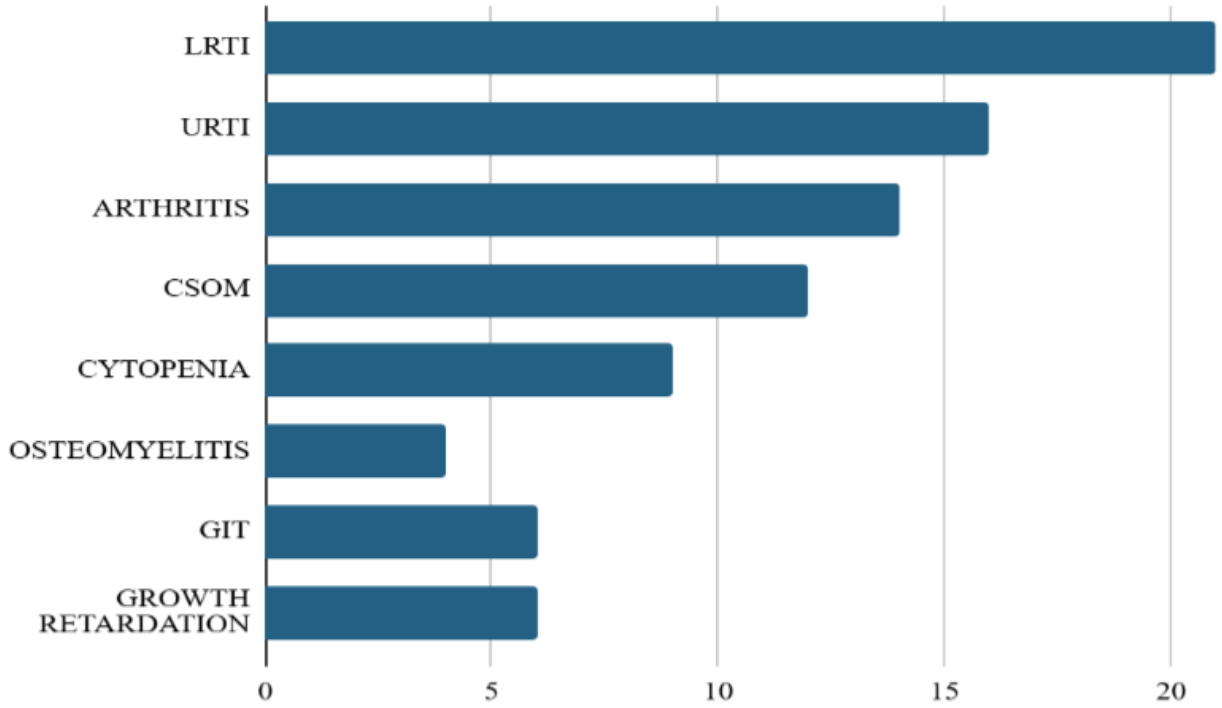
Conclusion:

This study highlights that respiratory infections were the predominant clinical manifestation in patients with agammaglobulinemia, with significant autoimmune complications, including arthritis and cytopenias, also being observed. Early diagnosis, timely administration of antibiotics, and regular immunoglobulin replacement therapy are crucial in improving patient outcomes. Consistent follow-up and prophylactic measures can ensure a longer lifespan with fewer complications in affected individuals.

Figures, Tables:

No.	Gender	Age at Presentation (months)	Age at onset of symptoms (months)	No. of LRTI	CSOM	Arthritis	WES
1	Male	24	12	>5	Yes	Yes	BTK (-)/Intron 11/Hemizygous X Linked Agammaglobulinemia/XR
2	Male	60	36	>5	Yes	Yes	BTK (-) Intron 9 variant/c.838_839+2del/Hemizygous/Agammaglobulinemia/XR
3	Male	24	12	>4	Yes	Yes	BTK(-) Exon 8 variant/c.7del Hemizygous/XLA/XR
4	Male	48	24	>6	No	Yes	BTK (-)/Intron 11/ Variant c.974+5G>A/Hemizygous X Linked Agammaglobulinemia/XR
5	Male	60	48	>7	No	No	BLNK (-), Intron 10/Variant c.774+1G>A/ Homozygous/Agammaglobulinemia/AR
6	Male	3	2	>2	No	Yes	BTK (-)/Exon 15/ Variant c.1559G>A/Hemizygous/Agammaglobulinemia/XL
7	Male	36	24	>5	No	yes	BTK (-) Exon 8 variant/c.7del Hemizygous/XLA/XR
8	Male	24	8	>5	Yes	Yes	BTK (-)
9	Male	36	12	>5	Yes	No	BTK (-)
10	Male	30	15	>5	No	No	BTK (-) Exon 8 variant/c.7del Hemizygous/XLA/XR

Table 1. Phenotype and Genotype correlation



Dig.1 Clinical features

P-47

Abstract Title:

Siblings With Recurrent Fever: A Journey From Diagnosis To Treatment- Is It Truly Enough?

Abstract no: 70

All authors: Anjani Gummadi[1], Prof Deepti Suri[2]

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Abstract:

Introduction:

Hyper-IgD syndrome (HIDS) is characterized by recurrent and lifelong episodes of fever, arthritis, headache, abdominal pain, vomiting, hepatosplenomegaly, lymphadenopathy, and skin rashes. In this report, we describe two siblings from India who presented with fever, abdominal pain, and lymphadenopathy. They were diagnosed with HIDS and initiated on anakinra, but unfortunately, their response has been partial.

Case Report:

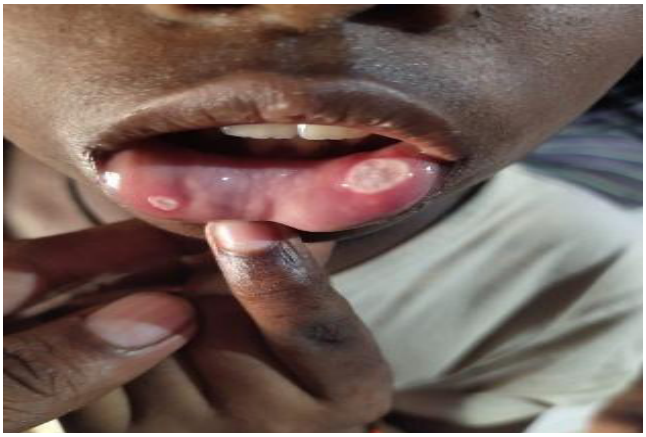
A 6-year-old girl, born to healthy, unrelated parents, presented to us with recurrent fever associated with abdominal pain, vomiting, and headache. She had a history of recurrent fever episodes since the age of 3. Each episode lasted 4–5 days and occurred every 2 weeks, accompanied by chills, fatigue, and abdominal pain. During the asymptomatic periods, the patient appeared completely well. She had been admitted multiple times and treated with antibiotics on several occasions. On clinical examination, cervical lymphadenopathy, a palpable liver enlargement of 2 cm, and a spleen enlargement of 4 cm were noted. Previous laboratory tests revealed elevated inflammatory markers. Given the recurrent fever pattern, an autoinflammatory disease was suspected, and whole exome sequencing was performed. Colchicine was started as a preliminary treatment. The diagnosis of HIDS was confirmed based on a double heterozygosity for the MVK mutations 1129G>A and 768G>A. The patient was subsequently treated with oral prednisolone and colchicine, and the parents were counseled regarding anakinra therapy.

Meanwhile, the younger male sibling, aged 3 years, began experiencing recurrent episodes of fever, oral ulcers, abdominal pain, and headache. Sanger sequencing confirmed the same mutations in this child. Despite significant challenges in accessing the medication, anakinra was initiated at a dose of 1-2 mg/kg/day via daily subcutaneous injections and titrated accordingly. Although both siblings experienced some symptomatic improvement, neither achieved complete remission. The older sibling also began developing aphthous ulcers while on anakinra treatment. As a result, colchicine was continued for both children.

Conclusion:

Anakinra has been shown to reduce the frequency of fever episodes and improve the quality of life in patients with HIDS. However, it may not lead to complete remission in all cases. Further studies are needed to explore the optimal treatment strategies for this condition, especially in resource limited settings

Figures, Tables:



P-48

Abstract Title:

From Griscellic Syndrome To Inflammatory Myositis: A Rare Pediatric Case Of Multisystem Challenges And Successful Interventions

Abstract no: 71

All authors: Rahul Vijayan[1], P S Arulrajamurugan[1], Arockiaraj B[1]

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Abstract:

CASE REPORT:

A male child, born to a third-degree consanguineous marriage, was normal until the age of 3. He developed high-grade continuous fever and abdominal swelling for one week. On examination, he had triangular facies, grey scalp hair, hypopigmented hair on his limbs, and a hypopigmented patch on the left side of his chest [Figure 1]. Laboratory investigations revealed pancytopenia, raised serum ferritin, and elevated serum triglycerides. Ultrasound imaging demonstrated hepatosplenomegaly. A bone marrow biopsy confirmed HLH and hair shaft examination revealed irregular pigmentation [Figure 2], leading to a diagnosis of Griscelli syndrome (probable type 2). A genetic study was not performed due to financial constraints. Skin biopsy also supported the diagnosis of Griscelli syndrome with lymphohistiocytosis.The patient was treated with steroids and etoposide, followed by maintenance therapy with etoposide and cyclosporine. His symptoms improved, pancytopenia resolved, and he was scheduled for a bone marrow transplant. On October 26, 2018, the patient underwent HSCT from his sister, who was a 10/10 HLA match. Post-transplant, he developed urticarial rashes and elevated liver enzymes, suspected to be graft-versus-host disease (GVHD), which resolved with increased steroid doses. A bone marrow study in February 2019 confirmed graft engraftment with 100% XX pattern on FISH In 2019, the patient presented with fatigue and vomiting, and tests revealed elevated liver enzymes and hepatitis C infection. He was treated with direct-acting antivirals (DAAT), leading to negative HCV RNA and recovery. After three asymptomatic years, the patient presented in 2024 with muscle weakness, difficulty rising from a seated position, and elevated creatine kinase levels (CK-8233 IU/L). Viral markers and myositis profile were negative. Infectious panels for myositis were negative. MRI showed diffuse hyperintensities in the lower limbs [Figure 3] and a

muscle biopsy suggested inflammatory myositis. Steroid therapy led to significant improvement, and his creatine kinase levels normalized.

Conclusion:

Griscelli syndrome type 2, a rare autosomal recessive disorder, is often associated with hemophagocytic lymphohistiocytosis (HLH). It presents with immunodeficiency, pigmentation abnormalities, and life-threatening systemic inflammation. HSCT is a curative treatment. In this case, the patient developed weakness suggestive of myositis (myositis and infectious panel – negative) which is inflammatory probable Chronic graft versus host disease Disease duration(>3mon),100% donor engraftment and good response to steroid also favours GVHD. Graft-versus-host disease (GVHD) is a recognized complication of allogeneic stem cell transplantation (allo-SCT) and may affect muscle.

Figures, Tables:

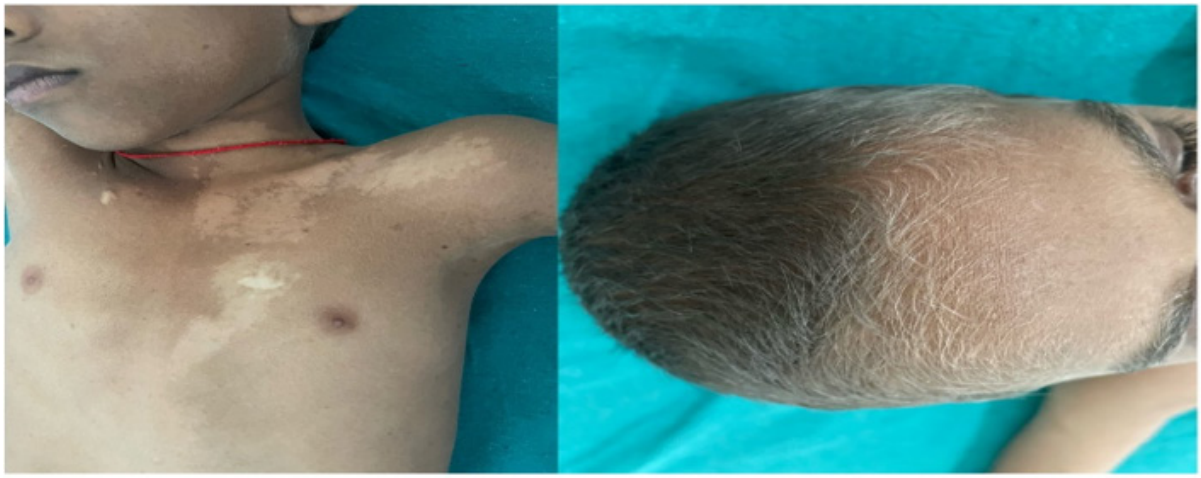
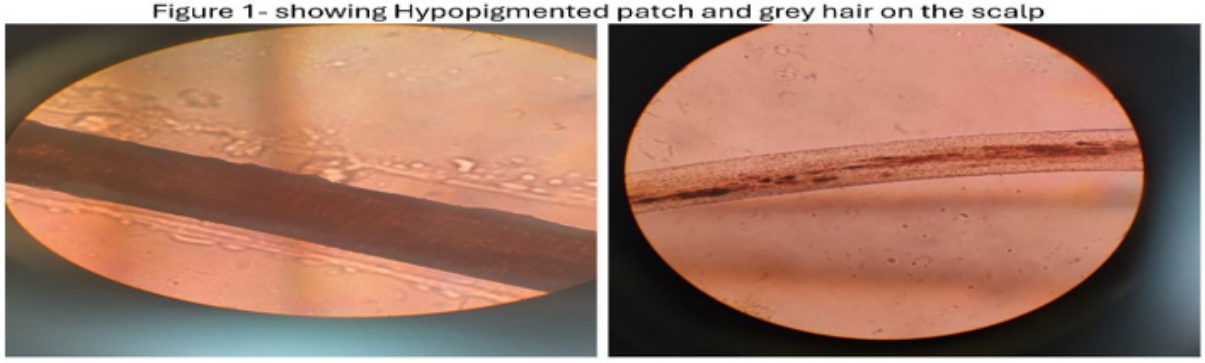


Figure 1- showing Hypopigmented patch and grey hair on the scalp



A B

Figure 2 – Hair shaft microscopy showing normal hair(A) and patient hair(B)

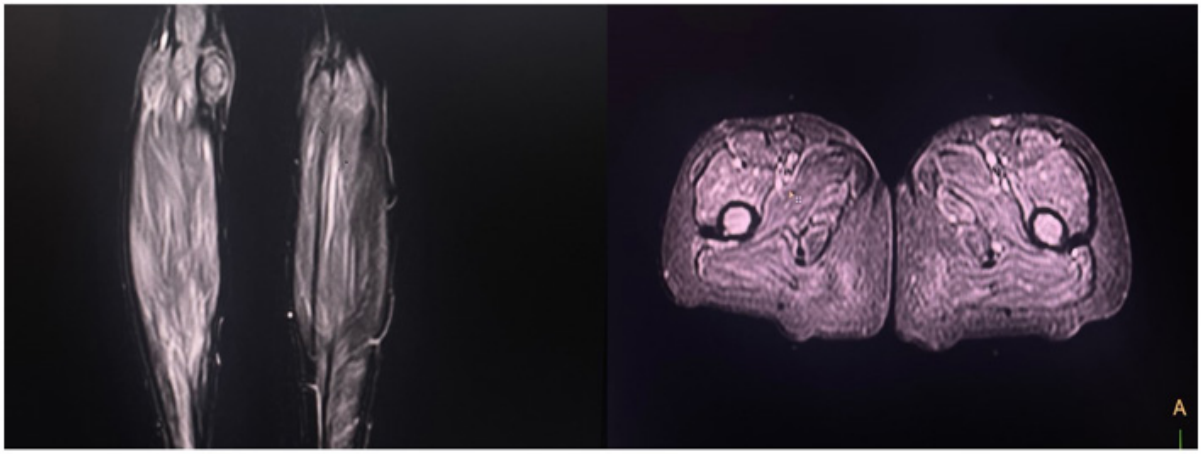
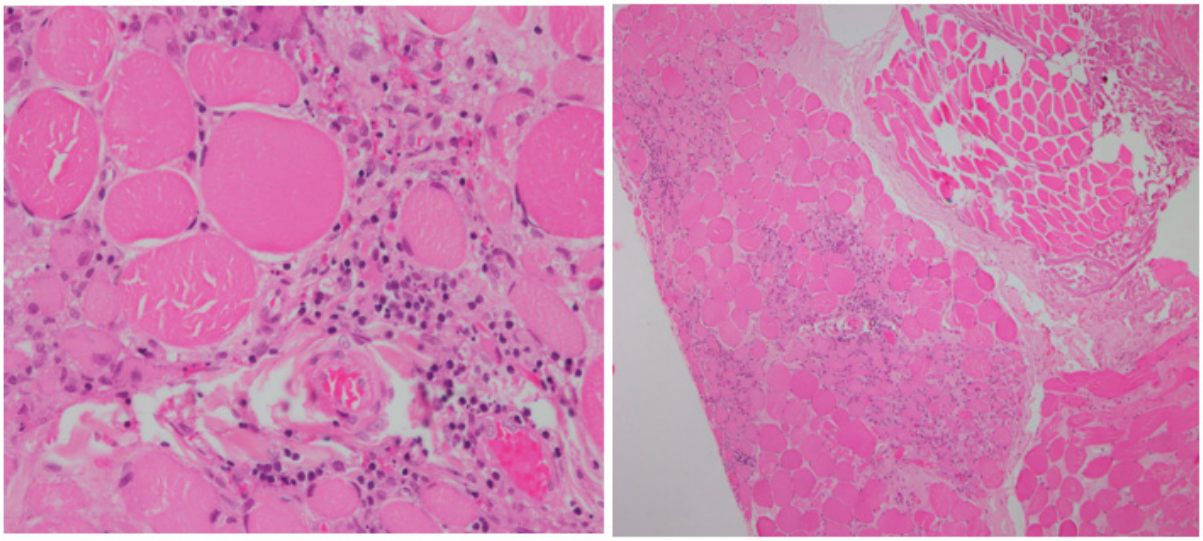


Figure 3- MRI of Lower limb showing diffuse hyperintensities



H&E –Consistent with inflammatory myositis. Specific type of inflammatory myopathy is difficult to identify- ? Immune mediated Vs Infective

P-49

Abstract Title:

PASH Syndrome

Abstract no: 72

All authors: Vishnu Koneru[1], Dr. Molly Mary Thabah[1], Dr. Aishwarya[1], Dr. Christina Mary Mariaselvam[1]

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Abstract:

Introduction

Autoinflammatory syndromes are characterized by repeated episodes of sterile inflammation without circulating autoantibodies or autoreactive T cells. PASH syndrome is a newly recognized hereditary autoinflammatory condition marked by neutrophilic dermatoses such as pyoderma gangrenosum (PG), acne, and hidradenitis suppurativa (HS)

Case

An 18-year-old man presented in 2022 with a 2-year history of painful pus-filled blisters in the axillae, groin, and ankle, followed by the development of papulonodular acneiform lesions in the same areas, including the face. These acneiform lesions evolved into painful, interconnected nodules and abscesses, often forming deep, inflamed cysts. He also had chronic right medial femoral condyle pain without joint line tenderness, likely enthesitis. He later developed left hypochondriac region pain, which, upon evaluation, revealed a splenic abscess. The review of systems was otherwise negative.

The patient was initially treated with prednisone, dapsone, and adalimumab, which resulted in good response. However, due to affordability issues, he switched to cyclosporine and later to tofacitinib, with no improvement. On current admission, he was in a disease flare and showed signs of steroid toxicity, including obesity, gynaecomastia, osteopenia, and dyslipidemia. Physical examination revealed cysts, papules, and pustules with hyperpigmentation and scarring on the back and chest. Multiple inflammatory abscesses with sinus tracts and scarring were present. Despite treatment with high-dose prednisone, cyclosporine A, and tofacitinib, the eruptions recurred.

The patient was evaluated thoroughly and clinically diagnosed with PASH syndrome, characterized by pyoderma gangrenosum, acne, and hidradenitis suppurativa. Given the previous positive response to adalimumab, treatment was resumed, resulting in excellent resolution of skin lesions in the following weeks.

Discussion:

The patient presented with the PASH phenotype, although the mutation identified was distinct from those reported in PSTPIP1 gene mutations. This highlights the genetic heterogeneity of PASH syndrome. Although mutations in PSTPIP1 and NCSTN have been identified in some patients, the genetic basis of PASH remains largely unknown. The treatment of PASH syndrome is challenging, and traditional immunosuppressive treatments may not always be effective. TNF-alpha inhibitors have shown significant improvement in skin symptoms, and anakinra, potentially combined with cyclosporine, has demonstrated considerable effectiveness. The increased expression of IL-17 in the affected skin of patients with PG further supports the clinical use of IL-17 inhibitors.

Figures, Tables:

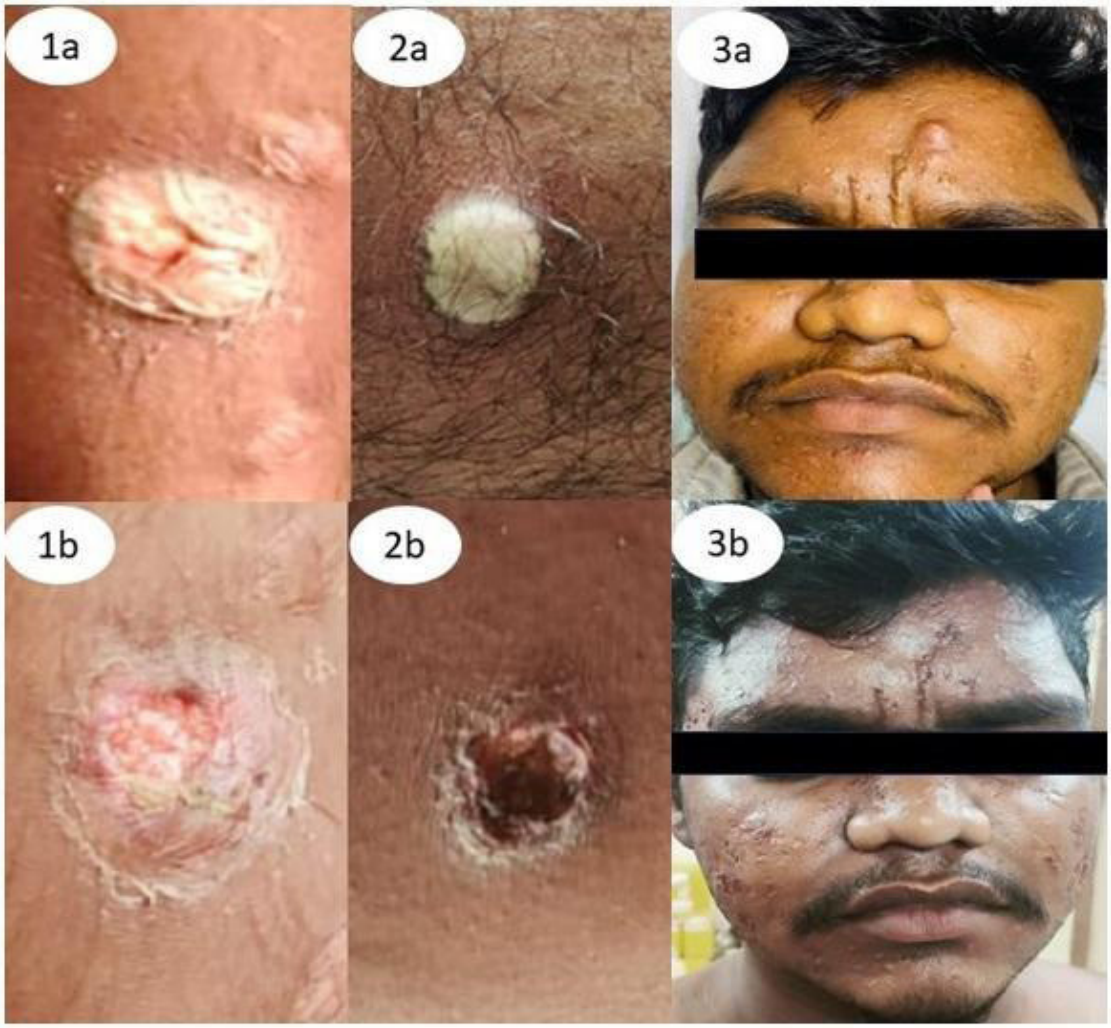

Fig 1: Blistering Pyoderma gangrenosum on dorsum of arm. a: Active and b: Healed

Fig 2: Pustular Pyoderma gangrenosum on thigh. a: Active and b: Healed

Fig 3: Acne conglobata on face. a: Active and b: Healed

Table 1: Summary of the manifestations and investigations

Clinical Manifestations	Pyoderma gangrenosum (Biopsy proven), Acne conglobata, Hidradenitis Suppurativa, Aseptic splenic abscess, Enthesitis, Neutrophilic leukocytosis
Basic lab investigations	Hb- 11.4 ; TLC – 10,700/mm^3; Platelet count – 380,000/mm^3 Urea/Creatinine – 45/1.0 mg/dL; Total protein / Albumin – 7.4/3.8 mg/dL; Total bilirubin / AST /ALT : 0.7 mg/dL/32/27 IU/mL Urine Routine – Normal Total cholesterol /Triglyceride / LDL / HDL – 190 / 210 / 164 / 48 mg/dL
Immunological profile	ANA- Negative hsCRP – 29.2 mg/L Lymphocyte profiling (TBNK) by flow cytometry: Normal DHR assay to rule chronic granulomatous disease (CGD) was normal Ig Profile-Raised IgE levels-1170 IU/ml (<100 IU/ml)
Genetic profile Whole Exome Sequencing	See nested table below
Disease activity markers	Hidradenitis Suppurativa: Hurley stage-I Pyoderma gangrenosum: Paracelsus score-20 Leeds Enthesitis Index-1/6

Gene (Transcript)	Location	Variant	Zygosity	Inheritance	Disease (OMIM)
EGFR (+) (ENST00000275493.8)	Exon 2	c.187G>A (p.Glu63Lys)	Heterozygous	Autosomal recessive	Neonatal inflammatory skin and bowel disease-2 (NISBD2) (OMIM#616069)
OSMR (+) (ENST00000275493.8)	Exon 5	c.515A>G (p.Asn172Ser)	Heterozygous	Autosomal dominant	Familial primary localized cutaneous amyloidosis-1 (OMIM#105250)

P-50

Abstract Title:

PRKDC Defect With PFAPA-Like Presentation: A Case Report

Abstract no: 74

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Abstract:

Introduction:

PRKDC gene encodes the DNA-dependent protein kinase catalytic subunit (DNA-PKcs) and is critical for DNA double-strand break repair and V(D)J recombination during lymphocyte development. Patients with PRKDC defect present with a varied spectrum of diseases from severe combined immunodeficiency to combined immunodeficiency with autoimmunity.

Objectives:

To describe a case of PRKDC defect with autoinflammatory phenotype

Methods:

A retrospective review of records was performed and the index case was analysed in detail.

Results:

Master L, a 5-year-old boy, born to a non-consanguineously married Indian couple, presented with recurrentfever from 1.5 years of age. The episodes recurred every month and lasted for 15-20 days. Each episode was associatedwith oral aphthosis and there were three records of documented tonsillitis. In the background, he also had a history offebrile seizures. On examination, he had cervical lymphadenopathy and membranous tonsillitis. The child otherwise waswell thriving, and family history was non-contributory.His laboratory investigations showed normal hemogram[Hb 123 g/L, TC 6.3 x 109/L (N 32% L 56%), PC 359 x 109/L] and high inflammatory markers(CRP 270 mg/L) during the fever episode, and the throat swab culture was sterile. He wasdiagnosed with Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis (PFAPA) syndrome and treated with asingle dose of steroid, which reduced the gap between episodes. Hence, he was started on colchicine, to which he hasresponded well. The whole exome sequencing picked a compound heterozygous mutation in the PRKDC gene[PRKDC c.10439G>A(p.Ser3480Asn) Exon 74 Heterozygous, c.4368G>T(p.Gln1456His) Exon 35 Heterozygous] and parental segregation analysis confirmed parents to be carriers. The immunological workup, showed normal naïve CD3 count[CD384.7%(3020), CD19 8.1%(287) CD56 3.8%(136), CD4 55.1%(1542), CD8 42.3%(1185), CD4 Naïve77.7%(1199), CD8Naïve91.5%(1084)] and immunoglobulin levels[IgG(3.4 – 12.4)11.4 g/L, IgA(0.1 – 1.6)1.2 g/L, IgM(0.4 – 2)0.8 g/L, IgE17.7 U/L].

Conclusion:

Patients with PRKDC defect present with immunodeficiency, autoimmunity, or unexplained granulomatous disease. This is, in all probability, the first reported case of a PRKDC defect presenting as a PFAPA variant in India.

P-51

Abstract Title:

Hyper Immunoglobulin E Syndrome- A Case Series From A Tertiary Referral Hospital In South India

Abstract no: 75

All authors: Suchitra Sivadas[1], C Jayakumar[1], Praveena Bhaskaran[1], Suma Balan[1], Sajith Kesavan[1], Arvind Perathur[1], Dhanya Yesodharan[1], Sheela Nampoothiri[1], Neeraj Siddharthan[1], Rema Ganapathy[1]

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Abstract:

Background/Objectives:

Hyper Immunoglobulin E syndrome is a rare primary immunodeficiency syndrome characterized by the presence

of atopic dermatitis and recurrent pulmonary and skin infections. The diagnosis is delayed in most cases due to the varying clinical presentations. We aimed to study the clinical profile, infection spectrum, genetic profile and outcomes in patients with this syndrome in a tertiary hospital

Materials And Methods:

The medical records of 8 patients diagnosed with Hyper Immunoglobulin E syndrome were reviewed and analyzed with respect to demographic data, age at presentation and diagnosis, clinical features, genetic profile, spectrum of infections and clinical course

Results:

A total of 8 patients were enrolled in the study. Six were autosomal dominant Hyper IgE and two were autosomal recessive DOCK 8 mutations. All the patients had onset of symptoms in infancy but were diagnosed late in the course of disease. Multiple specialities were involved in the treatment due to the varying clinical presentations. Novel gene mutations were seen in one of the patients. The index presentation was eczematous dermatitis seen in the majority of the patients. Recurrent subcutaneous abscesses and pulmonary infections requiring hospitalization were also seen in most of the cases. The characteristic coarse facies was seen in most patients with STAT 3 deficiency. Food allergies were most severe in patients with dock 8 mutations and anaphylaxis was seen in only one patient. Methicillin sensitive and resistant Staph Aureus were the most common organisms isolated. Most of the patients had bronchiectasis and failure to thrive . Sclerosing cholangitis requiring ERCP and stenting was seen in one patient. All the patients were on antibiotic prophylaxis ,immunoglobulin replacement ,bleach baths and multidisciplinary management.

Conclusion:

Hyper Immunoglobulin E syndrome can present with a wide variety of clinical presentations and diagnosis is often delayed in most of these patients. Genetic analysis is essential in all cases and early detection and management can lead to better long term outcomes.

P-52

Abstract Title:

Diagnosis and management of inborn errors of immunity at a tertiary healthcare center- a case series.

Abstract no: 76

All authors: Ritu Chadha[1], Neha Rastogi[1], Dhwanee Thakkar[1], Rajiv Uttam[1], Nitin Mathur[1], Praveen Khilnani[1], Satya Prakash Yadav[1], Renu Saxena[1]

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Abstract:

Background:

High index of clinical suspicion is required to diagnose inborn errors of immunity (IEI) in patients presenting with recurrent or unusual infections, autoimmunity, allergy, inflammation, malignancies and a positive family history.

Objective:

To describe clinical phenotype, immunology & genetic profile and treatment of patients with inborn errors of

immunity.

Methods:

We analyzed clinical phenotype, immunology and genetic profile of ~ 11 patients diagnosed with inborn errors of immunity and treated in our tertiary healthcare hospital between February 2023 to December 2024. Careful review of history including family history and physical examination was done for clue to underlying IEI. Laboratory investigations included complete blood counts, serum immunoglobulin levels, serum complement levels, flow cytometry for T, B, NK cells, DNT, DHR and Perforin assay. Whole exome sequencing was done on Illumina NextSeq 550. The sequencing data obtained is processed through in-house secondary and tertiary bioinformatics analysis pipeline, using Genome Reference Consortium Human Build 38 (GRCh38) as reference. The variants are prioritized based on the patient's phenotype, filtered based on their predicted pathogenicity and classified according to ACMG guidelines.

Results:

Median age at diagnosis of IEI in our cohort was 8 years with male to female ratio of 2.6:1. Fever was most common clinical symptom (6/11 patients) followed by upper & lower respiratory tract infection (5/11 patients) and skin involvement in 3/11 patients. Fungal and viral infections were equally noted in 4/11 cases each. Bacterial infections were noted in 3/11 cases. Anemia was observed in 9/11 patients; while, 3/11 patients showed neutropenia and 1/11 patient had pancytopenia. Immunology profile showed low immunoglobulin levels in 2 patients of SCID (both with IL2RG variants, T-B+NK-) and 1 patient of HLH with PRF mutation who also showed loss of perforin expression on NK and cytotoxic T cells. Elevated IgE was observed in 3 patients with DOCK8, STAT1 and ARPC1B genetic variants. Elevated levels of IgM were seen in 1 patient with CD40LG variant. 1 patient with elevated TCR alpha/beta positive double negative T cells (DNT) showed FAS (+) genetic mutation. One patient of SCID with IL2RG underwent matched sibling donor transplant and 3 patients (GATA2, PRF1 and DOCK8) received haploidentical transplant. Other patients received treatment in the form of IVIG, antibiotics, steroids and immunosuppressive therapy based on patient specific diagnosis and requirements.

Conclusion:

This is a single center study highlighting diagnostic details and patient specific management in inborn errors of immunity

Figures, tables:

Age	Gender	Genetic variant	Associated Disease	Treatment
6 months	Male	IL2RG	T-B+ severe combined immunodeficiency	Transplant planned
7 months	Male	IL2RG	X-linked severe combined immunodeficiency T-, B+, NK-	IV IG. MSD HSCT. Donor - Sister 10/10 matched, Conditioning - ATG+ TreoFlu.
6 years	Male	SH2D1A	X-linked lymphoproliferative disease	Received IV antibiotics, was started on Dexamethasone for HLH. Child received Rituximab at 100mg/m2. Inj Etoposide. Tab Ruxolitinib (Jakavi). Refractory HLH. Died.
12 years	Female	GATA2	Emberger syndrome, Immunodeficiency 21	Donor - Brother haploidentical donor, Conditioning - R+TF+ATG, GVHD prophylaxis - PTCy Tac MMF. Day+46 post BMT. Very well .
10 years	Male	CD40LG	X-linked immunodeficiency with hyper-IgM type-1	On regular IVIG since age of 1 yr. Has been on regular IVIG 15 gram IV once a month through government supply.

P-53
Abstract Title:
A Rare Cause of a Common Symptom
Abstract no: 79
All authors: Aashish Agrawal[1], Dr. C Balakrishnan[1]
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Abstract:

Background:

Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) is a rare autoinflammatory disorder caused by mutations in the TNFRSF1A gene. It is characterized by recurrent fever and systemic inflammation, often mimicking infectious or autoimmune conditions, leading to delayed diagnosis.

Case Presentation:

A 33-year-old female presented with fever in January 2024 with mild hepatomegaly and elevated inflammatory markers. She was treated with antibiotics and steroids, but fever relapsed within days, now accompanied by polyarthritis.

Between February and May 2024, she had recurrent episodes of fever with vomiting, myalgia, hepatosplenomegaly, and elevated inflammatory markers. Investigations, including autoimmune and infectious panels, imaging, and bone marrow studies, were inconclusive. PET-CT revealed weakly metabolically active lymph nodes, heterogeneous bone marrow uptake, and minimal pleural and pericardial effusions. On detailed history, she gave history of four episodes of febrile illness between 2017-2018, each lasting five days, with no associated rash or joint symptoms. Following which she was asymptomatic till now. Whole exome sequencing identified a pathogenic variant in the TNFRSF1A gene, confirming TRAPS.

The patient was started on etanercept (50 mg weekly) and corticosteroids, leading to rapid symptom resolution. Steroids were tapered and discontinued by November 2024.

At follow-up in January 2025, the patient was symptom-free on etanercept monotherapy, with no recurrence of fever or systemic inflammation.

Conclusion:

This case highlights the challenges in diagnosing TRAPS, particularly in settings where it may mimic more common conditions. Genetic testing was crucial for diagnosis, and early initiation of biologic therapy with etanercept led to sustained remission. Awareness of TRAPS as a potential cause of recurrent fever and systemic inflammation is essential for timely diagnosis and effective treatment, significantly improving patient outcomes.

P-54
Abstract Title:
Presence of MEFV gene in Behcet's Disease: A Behcet-FMF overlap?
Abstract no: 82
All authors: Shaurav Khanna[1], Dr. C Balakrishnan[1]
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Abstract:
Background:
Behçet disease (BD) and familial Mediterranean fever (FMF) are two inflammatory conditions that overlap in various aspects, such as their historical background, ethnic prevalence, and inflammatory traits. MEFV gene mutations have been associated with both the diseases. We present a case of an overlap of FMF and BD in a young male who presented at our centre.
Case: A 20-year-old male presented with high-grade fever, oral and scrotal ulcers, abdominal pain, breathlessness, arthralgia, and myalgia. A year earlier, he had similar complaints, which led to hospitalization. During that episode, he developed dry gangrene of the left little finger, decreased cardiac output (ejection fraction 45%), and left radial artery thrombosis along with partial thrombosis of the left basilic and median cubital vein. He was diagnosed with sepsis-related cardiomyopathy and thrombosis, treated with antibiotics, and remained asymptomatic thereafter without medication. On current admission, he had painful oral and painless scrotal ulcers, proximal lower limb weakness (MRC grade 4/5), and serositis confirmed by imaging. Investigations revealed anemia, elevated liver enzymes, high ferritin (4376 ng/mL), elevated creatinine phosphokinase (2619 U/L), and 2 D Echocardiography showed global hypokinesia with an ejection fraction of 40%. MRI confirmed myositis. Given his episodic fever, arthralgia, serositis, oral and scrotal ulcers, arterial thrombosis and thrombophlebitis, Behçet's syndrome was suspected, supported by HLA-B51 positivity. However, absent ocular findings and presence of myositis, myocarditis, serositis and periodicity of fever raised concerns about FMF. Myocarditis, serositis, and myositis are rare in Behçet's. Genetic testing confirmed MEFV mutations associated with Familial Mediterranean Fever (FMF), without pathogenic variants for Behçet's disease. The patient was treated with colchicine, methotrexate, and prednisolone, showing significant improvement. He remains on close follow-up. This case highlights the diagnostic challenges in differentiating Behçet's syndrome from FMF in overlapping presentations.
Discussion: This case underscores the complexity of distinguishing Behçet's syndrome from FMF, particularly in regions with overlapping prevalence. Comprehensive genetic testing, alongside clinical evaluation, is crucial for accurate diagnosis and appropriate treatment

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P-55
Abstract Title:
Immunodeficiency or Autoimmunity? – Unravelling the mystery
Abstract no: 83
All authors: Mounika Reddy[1]
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Abstract:
Immune dysregulation can present with features of both autoimmunity and immunodeficiency. An 11-year-

boy presented with erythematous scaly itchy skin rash, recurrent ear discharge, and intermittent fever from 2years of age. At 5years, he started developing pustular lesions over scalp. He developed bilateral knee pain at 6 years age with progressive right knee deformity. There is history of recurrent painful subcutaneous nodules and abscesses over limbs, oral ulcers and photosensitivity. He had no history of recurrent pneumonia, sinusitis, loose stools, or frequent hospitalizations. He was born to consanguineous parents with 2.5kg birth weight, with normal development. Family history was non-contributory. Examination revealed stunted growth, generalized xerosis, icthyosis, dyspigmentation, seborrhoiec dermatitis, oozy crusted lesions over scalp with diffuse scarring alopecia, thin brittle hair, oral mucosal erosions, and crowded teeth. Tonsils and lymph nodes were present. He had reducible flexion deformity of right knee with terminal restriction. Other systemic examination was unremarkable. Possibilities of primary immunodeficiency including hyperIgE syndrome, chronic granulomatous disease, complement defect, Langerhans cell histiocytosis or early onset lupus were considered. Investigations revealed microcytic hypochromic anemia, mild thrombocytopenia, transaminitis and reversed albumin-to-globulin ratio. Renal functions, urine microscopy, urine protein: creatinine ratio, skull X-ray, chest X-ray and abdominal ultrasonogram were normal. He had elevated serum IgE (>3000/IU/mL), weakly positive mixed ANA pattern, negative anti-dsDNA, normal C3, C4 levels; and absent CH50 activity consistent with early classical complement component defect. Whole exome sequencing identified a novel homozygous missense variant c.227G>T (p.Gly76Val) in exon3 of C1qB gene (transcriptID NM_001378156.1). Diagnosis of monogenic lupus secondary to C1Q deficiency was made. Treatment included antihistamines, antibiotics, immunosuppressive therapy. Complement subcomponent C1Q deficiency though rare, can present with overlapping features of immunodeficiency and autoimmunity, necessitating high index of suspicion and genetic evaluation for accurate diagnosis and management. Variation from usual pattern of symptoms and antibody titers indicates the complexity in evaluation of monogenic childhood onset lupus. The novel mutation contributes to the growing understanding of genetic variations in complement deficiencies and their clinical consequences.

P-56

Abstract Title:

Focal lymphoedema with warts in a child with DOCK8 immunodeficiency syndrome – A novel association

Abstract no: 84

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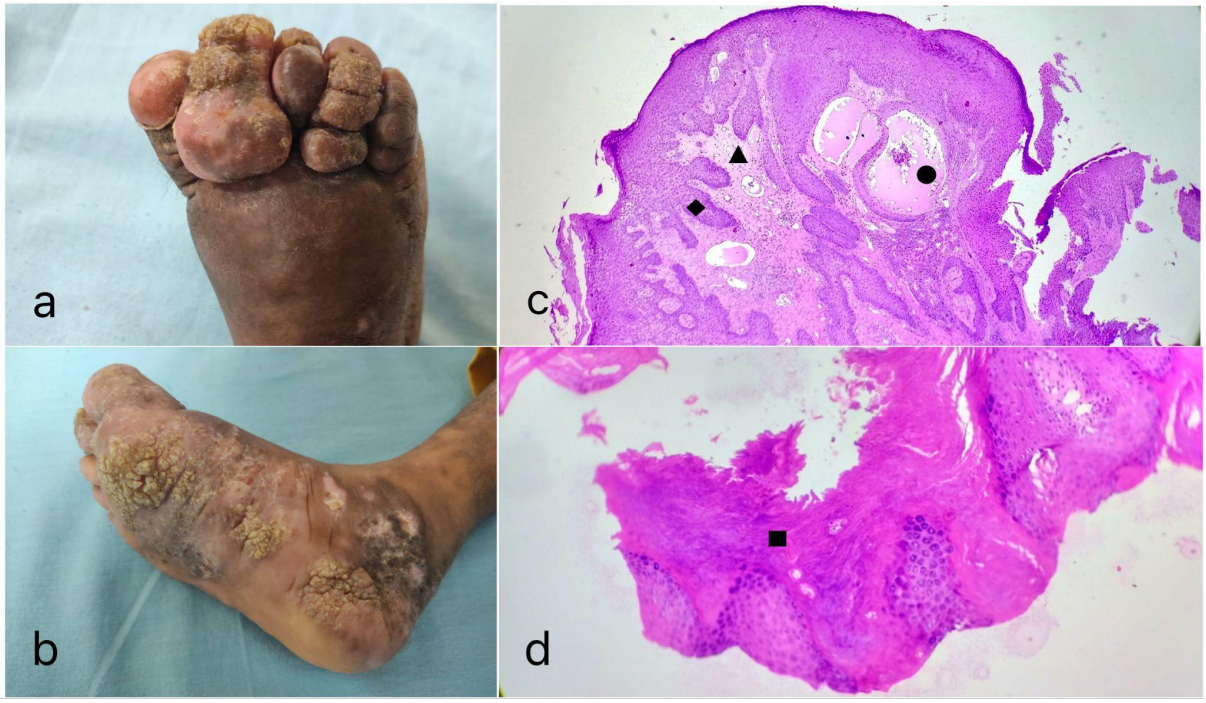
Abstract:

Dedicator of cytokinesis 8 (DOCK8) gene mutation results in combined immunodeficiency and predisposes to severe cutaneous viral infections. Our patient is a 4-year-old girl who developed widespread, red, itchy, scaly skin rash at 1 month age, and painless non-erythematous, soft-pitting swelling of right foot from 3 months age. She had right leg cellulitis at 9 months and left lobar pneumonia at 17 months, requiring intravenous antibiotics. She also had two episodes of ear discharge and multiple episodes of loose stools. Born in consanguineous

marriage, no adverse perinatal events, she weighed 2.75 kg at birth and had normal development. On examination, her weight and height were below -2 z scores, there was no dysmorphism, organomegaly, dental, or skeletal abnormalities. Tonsils and lymph nodes were present. Her elder female sibling had a similar skin rash and recurrent infections, along with developmental delay, microcephaly, spasticity, and dystonia. She had elevated serum Immunoglobulin E (IgE) levels (>3000 IU/ml), lymphopenia, and diffuse cerebral and cerebellar atrophy on neuroimaging. She died at 4 years of age after a life-threatening infection. There were no abortions or stillbirths. Index child had normal to mildly elevated serum IgE levels (187 and 12 IU/ml at 4 and 10 months respectively), high eosinophil count (1600/mm3), low CD3, CD4, and CD8 cell counts with low to normal CD19 and natural-killer cell counts. Clinical exome revealed DOCK8 gene homozygous deletion (exons 1-19), confirmed by multiplex ligation-dependent probe amplification (MLPA), indicative of autosomal recessive hyperIgE-recurrent infection syndrome 2. Both parents are heterozygous carriers. She was initiated on monthly intravenous immunoglobulin supplementation, anti-bacterial and anti-fungal prophylaxis. At 3 years, she developed extensive warty growths over the right foot, accompanied by further foot swelling and deformity. The swelling was non-pitting with indurated surface. Right leg doppler ultrasound examination ruled out arteriovenous malformation or deep venous thrombosis, and radiographs showed no bony deformity. Histopathological examination of the warty growth confirmed verruca vulgaris, while that of the soft tissue swelling showed features of lymphoedema with chronic inflammation. Filariasis was ruled out on peripheral blood smear examination and antigen testing. Our patient likely had onset of lymphoedema in the right foot at 3 months, and experienced complications involving cellulitis and warts, with progressive aggravation. Though DOCK8 mutation is known to predispose to generalized, extensive, and treatment-resistant cutaneous viral infections, in our patient, the warts are confined to the right foot with lymphoedema, presumably due to local immunodeficiency.

Figures, tables:



P-57

Abstract Title: Unveiling IEI: Chest Wall Abscess with Genetic Clues- A case report

Abstract no:16

All authors: Dr.BinitaGoswami[1],Dr.Pradeep[1],Ritika Srivastava[1],Dr.Rajeshwari[1],Dr.Anuradha[1],Dr.Sonal Saxena[1],Dr. Bidhan Chandra Koner[1], Dr.Ram Gopal Saini[2]

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Abstract:

Background:

Inborn errors of immunity (IEIs) are a heterogeneous group of disorders caused by immune system defects, leading to recurrent infections, autoimmunity, and malignancies. Genetic mutations significantly contribute to PID pathogenesis, with next-generation sequencing (NGS) emerging as a pivotal diagnostic tool.

Objective:

To report a case of suspected IEI presenting with a chest wall abscess and to detail the associated clinical findings, laboratory results, and genetic analysis.

Methods:

A 15-year-old male with a five-day history of redness and swelling of the left chest was evaluated. Clinical examination and imaging confirmed a chest wall abscess. Laboratory investigations included blood counts, immunoglobulin profiling, complement levels, flow cytometry, and NGS. In silico tools were utilized to assess the pathogenicity of identified mutations, and ACMG guidelines were applied for variant classification.

Results:

The patient exhibited leukocytosis (TLC 13,600/µL), elevated CRP (35 mg/L), neutrophilia (56%), and lymphopenia (37%). Immunoglobulin profiling showed elevated IgG (862 mg/dL) and IgA (>40 mg/dL), with normal IgM (44 mg/dL) and IgE (3.46 IU/mL). Flow cytometry revealed CD3+ T cells at 78.9%,CD8+ T cells at 33.01%, and reduced FOXP3 expression (2.16%). NGS identified a missense mutation in CR2 (chr1:207640084). In silico analysis suggested pathogenicity (PhyloP -4.09, SIFT 0.0, Grantham 205, PolyPhen 0.999). ACMG classification deemed the variant a Variant of Uncertain Significance (VUS).

Conclusions:

This case suggests a primary immunodeficiency with CD4+ T-cell dysfunction. Although the identified mutation is a VUS, it highlights the need for functional validation and extended genetic studies. Early diagnosis and a comprehensive workup are essential for effective management and improved outcomes.

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