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The African Landscape of Primary Immunodeficiencies and Allergies - in the Era of Personalised Medicine.

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Meeting Abstracts

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ASID MEETING ABSTRACTS 2025

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X-Linked Lymphoproliferative Syndrome in a Kenyan Child with Bronchiectasis

Elizabeth Mwailongo, MBChB[1], Diana Marangu-Boore, MBChB-PhD[1], B. Ombaba Osano, MBChB, MMed[1], Saada Harith, MBChB[5], Eunice Omamo, MBChB, MMed[5], Benjamin Gaston, MD[2], Evans Machogu, MD[2], Irene Nzamu, MBChB, MMed[4], and Anne Barasa, MBChB, MMed[3]

[1]Department of Paediatrics and Child Health, University of Nairobi, Kenya; [2]Department of Radiology, University of Nairobi, Kenya; [3]Department of Pediatrics, Indiana University, USA; [4]Division of Hematology and Oncology, Kenyatta National Hospital, Kenya; [5]Immunology Unit, Department of Human Pathology, University of Nairobi, Kenya

Background: X-linked lymphoproliferative syndrome (XLP) is a rare genetic condition characterized by immune dysregulation, clinically manifesting as either an abnormal immune reaction to Epstein-Barr virus infection causing hemophagocytic lymphohistiocytosis (HLH), lymphoproliferative disorders, and/or hypogammaglobulinemia with recurrent infections. There are two subtypes, XLP1, due to mutations in the *SH2D1A* gene, and XLP2, due to mutations in the *XIAP* gene. Mutations in *SH2D1A* lead to deficiency in signaling lymphocyte activation molecule-associated protein, which is involved in intracellular signaling and activation of T cells and T-dependent B cell activation.
Case Report: We present an 11-year-old Kenyan boy with a history of recurrent pneumonia, otitis media, chronic rhinosinusitis, and cor pulmonale who was being evaluated for primary ciliary dyskinesia (PCD) given the phenotypic features consistent with this diagnosis. Targeted panel genetic testing for PCD, primary immunodeficiencies, and cystic fibrosis (CF) identified a pathogenic mutation in the *SH2D1A* gene (c.245dup [p.Asn82Lysfs*22]), confirming his XLP diagnosis. Immunological testing identified hypogammaglobulinemia. Although he had elevated ferritin and CRP levels during his hospitalization, he did not meet HLH criteria, and these levels normalized following antibiotic therapy. Chest computed tomography revealed bilateral patchy opacities, left-sided thick-walled cavitation, worsening bronchiectasis, and dilated pulmonary arteries in comparison to similar imaging done two years prior. Echocardiography confirmed pulmonary hypertension. He was initiated on monthly intravenous immunoglobulin replacement and treatment for pulmonary hypertension. We managed his acute bronchiectasis exacerbation and implemented preventive measures including prophylactic microbial agents and continued daily airway clearance. He is scheduled for multidisciplinary follow-up and potential for hematopoietic stem cell transplantation.
Discussion: Inborn errors of immunity often present with recurrent sinopulmonary infections and bronchiectasis. The clinical features overlap with other diagnoses such as PCD and CF. A multidisciplinary team approach is crucial for an optimal outcome in patients with inborn errors of immunity and multiple comorbidities.

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HSCT in Wiskott-Aldrich Syndrome

Aicha Ben Taieb[1,2], Amal Bouraoui[1,2], Ilhem Ben Fraj[1,2], Samia Rekaya[1,2], Ameni Merdassi[1,2], Fethi Mellouli[1,2], Mohamed Bejaoui[1,2], Monia Ben Khaled[1,2], and Monia Ouederni[1,2]

[1]Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, Bone Marrow Transplant Center, Tunis, Tunisia; [2]University Tunis El Manar, Faculty of Medicine, Tunis, Tunisia

Introduction: Wiskott-Aldrich syndrome (WAS) is a rare genetic disorder primarily affecting males, characterized by a combination of immunodeficiency, thrombocytopenia, and eczema. This condition is caused by a mutation in the WASP gene, which is essential for the proper functioning of immune cells. HSCT remains the treatment of choice for severe forms of the disease, enabling the restoration of immune function. The aim of this study was to evaluate the outcomes after HSCT in children with Wiskott-Aldrich syndrome.
Methods: This is a retrospective descriptive study including children with WAS who underwent HSCT.

Results: Five boys with WAS were included. The age at diagnosis ranged from 1 month to 7 years, with a mean age of 31.2 months. Two patients received haploidentical grafts, and three received geno-identical grafts. Three patients received a protocol based on fludarabine and busulfan; one patient received busulfan, fludarabine, and antithymocyte globulin; and the last patient received fludarabine, thiotepa, and treosulfan. In vivo T depletion was based on post-transplant cyclophosphamide in the two patients receiving haploidentical HSCT. Post-transplant complications included bacterial infections in all patients, viral reactivation (CMV) in two patients, and acute graft-versus-host disease (GVHD) in two patients. Chronic GVHD was observed in one case. Furthermore, two patients developed thrombotic microangiopathy. All patients achieved engraftment with full donor chimerism. Finally, one patient out of five died at the age of 3 years and 5 months from extensive chronic GVHD. Four patients are alive and cured.
Conclusion: HSCT is a curative treatment in most patients with severe forms of WAS. However, post-transplant complications, including bacterial infections, viral reactivation, and GVHD, remain significant challenges in the management of these patients.

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Early-Onset Inflammatory Bowel Disease: Diagnostic and Therapeutic Challenges in a Child

Aicha Ben Taieb[1,2], Rania Naffeti[1,2], Samia Rekaya[1,2], Ilhem Ben Fraj[1,2], Meriem Tira[2,3], Ameni Merdassi[1,2], Nejla Mekki[2,3], Fethi Mellouli[1,2], Mohamed Bejaoui[1,2], Imen Ben Mustapha[2,3], Monia Ben Khaled[1,2], and Monia Ouederni[1,2]

[1]Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, Bone Marrow Transplant Center, Tunis, Tunisia; [2]University of Tunis El Manar, Faculty of Medicine, Tunis, Tunisia; [3]Laboratory of Immunology, Institut Pasteur, Tunis, Tunisia

Introduction: Growing evidence suggests a link between specific mutations involved in monogenic autoinflammatory diseases, primary immunodeficiencies (PIDs), and early-onset inflammatory bowel disease (EIBD), including Crohn's disease-like phenotypes. Understanding these genetic interactions is crucial for elucidating the underlying pathophysiological mechanisms and optimizing the therapeutic management of these early and complex forms of EIBD.
Methods: Through this case report, we aim to describe the clinical presentation and outcomes of EIBD in a 16-year-old child and to discuss etiological and therapeutic options.
Results: At the age of 12, the patient presented with severe hemophagocytic lymphohistiocytosis (HLH) syndrome associated with EBV infection, involving both cardiac and hepatic systems. He had a history of recurrent diarrhea since 40 days of life, hypoxemic pneumonia, and recurrent ear, nose, and throat infections. Later, he was diagnosed with Crohn-like inflammatory manifestations, including rectosigmoiditis, severe congestive colitis, and an inflammatory digestive syndrome (calprotectin >1,000 µg/g), which were resistant to immunosuppressive therapy. The immune workup revealed a decrease in NK cells and an inversion of the CD4/CD8 (T4/T8) ratio. Genetic testing identified a hemizygous mutation in the XIAP gene and a heterozygous mutation in the NLRP12 gene. The patient was considered for hematopoietic stem cell transplantation (HSCT) from his 20-year-old asymptomatic brother, a matched sibling donor (MSD). However, genetic analysis of the donor revealed the same NLRP12 mutation. While bone marrow transplantation is a potentially curative option for the XIAP mutation, its efficacy is uncertain in this case due to the coexisting NLRP12 mutation in the donor. The contribution of each mutation to the patient's complex inflammatory manifestations remains difficult to determine.
Conclusion: A better understanding of the underlying immunological interactions may help identify new therapeutic targets and improve the clinical management of patients with EIBD.

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Putting the Pieces Together: A Case of Good's Syndrome

Adil Salyani[1] and Anne Barasa[2]

[1]Infectious Diseases Section, Department of Medicine, Aga Khan University Hospital, Nairobi; [2]Immunology Unit, Department of Pathology, University of Nairobi

Case Description: A 68-year-old female presented for evaluation of a recurrent large painful genital ulcer. She had developed a similar lesion nine years earlier in conjunction with a mediastinal mass, which was excised, revealing a thymoma. The ulcer was grafted with

healing but recurred four years later; a swab was positive for herpes simplex virus-2, and biopsy revealed viral cytopathic effects suggestive of a herpetic ulcer. She received a course of valacyclovir without improvement in symptoms. Medical history was significant for a chronic cough and an admission for pneumonia in the past. Examination revealed a large perineal ulcer and lower lung coarse crepitations. Testing for human immunodeficiency viruses 1 and 2 was negative. Immunoglobulin testing revealed profound hypogammaglobulinemia with markedly low IgG (0.94 g/L), IgA (0.05 g/L), and total IgM levels (<0.25 g/L). Lymphocyte subset enumeration revealed profound B cell lymphopenia, CD4 T cell lymphopenia, and mild NK cell lymphopenia. Chest imaging revealed bronchiectasis. A diagnosis of Good's syndrome (thymoma with immunodeficiency) was made. She was reinitiated on valacyclovir therapy and is receiving four weekly intravenous immunoglobulins with an aim to achieve and maintain an IgG trough level of 6 g/L, following which she will undergo wound grafting.

Discussion: Recurrent or unusually severe presentations of infections should raise the possibility of an underlying immunodeficiency. Good's syndrome is a rare, acquired cause of immunodeficiency affecting both humoral and cell-mediated immunity. Patients typically present in the fourth to sixth decade of life with symptoms attributable to mass effect from thymoma and/or recurrent infections. Defects in humoral immunity predispose to sinopulmonary infections, while defects in cell-mediated immunity lead to fungal and viral infections, including those of the human herpes virus family. Immunologic testing reveals hypogammaglobulinemia and B and CD4 T cell lymphopenia. Management includes excision of thymoma and immunoglobulin replacement.

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When Neutropenia Hides a Genetic Disorder: A Case of ALPS Type 2 Due to CASP10 Mutation

Aicha Ben Taieb[1,2], Amal Bouraoui[1,2], Samia Rekaya[1,2], Ilhem Ben Fraj[1,2], Ameni Merdassi[1,2], Fethi Mellouli[1,2], Mohamed Bejaoui[1,2], Monia Ben Khaled[1,2], and Monia Ouederni[1,2]

[1]Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, Bone Marrow Transplant Center, Tunis, Tunisia; [2]University Tunis El Manar, Faculty of Medicine, Tunis, Tunisia

Introduction: Autoimmune lymphoproliferative syndrome (ALPS) is a rare genetic disorder caused by impaired lymphocyte apoptosis. It is typically characterized by chronic nonmalignant lymphoproliferation, autoimmune cytopenias, and an increased risk of lymphoma. ALPS type 2, associated with *CASP10* gene mutations, is an uncommon autosomal dominant variant that may present with mild or atypical features.

Case Report: We present the case of a male infant born September 2020, to non-consanguineous parents, with an unremarkable perinatal course. At one year of age, routine blood work unexpectedly revealed persistent neutropenia, accompanied by eczematous skin lesions. Clinical examination revealed normal somatic and neurodevelopmental parameters, with no evidence of hepatosplenomegaly or lymphadenopathy. Bone marrow aspiration demonstrated a reduced number of neutrophils and a predominance of eosinophils. Immunological evaluation revealed an IgA level at the lower limit of normal, with normal IgG and IgM levels. Lymphocyte immunophenotyping showed normal T cell subsets ($CD3^+$, $CD4^+$, and $CD8^+$), along with a mildly decreased B cell count. The patient subsequently experienced recurrent febrile episodes that responded favorably to antibiotic treatment. Neutropenia persisted, while hemoglobin and platelet levels remained within normal ranges. His growth and neurodevelopment continued to progress appropriately. Genetic analysis revealed a heterozygous pathogenic variant in the *CASP10* gene (c.1202_1208del, p.(C401Lfs*15)), confirming the diagnosis of autoimmune lymphoproliferative syndrome type 2 (ALPS-2). Autoimmune serologies were negative, and no clinical or radiological evidence of lymphoproliferation has been observed to date.

Conclusion: This case highlights an atypical and mild presentation of ALPS-2, revealed by isolated neutropenia. It underscores the importance of thorough evaluation in persistent unexplained neutropenia, even in the absence of classical ALPS features, to enable early diagnosis and appropriate genetic counselling.

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The Diagnostic Dilemma of NEMO Syndrome

Aicha Ben Taieb[1,2], Altaf Garbaa[1,2], Samia Rekaya[1,2], Jihene Ben Hfaiedh[3,2], Ilhem Ben Fraj[1,2], Ameni Merdassi[1,2], Nadia Siala[3,2], Fethi Mellouli[1,2], Mohamed Bejaoui[1,2], Monia Ben Khaled[1,2], and Monia Ouederni[1,2]

[1]Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, Bone Marrow Transplant Center, Tunis, Tunisia; [2]University of Tunis El Manar, Faculty of Medicine, Tunis, Tunisia; [3]Department of Paediatrics, Mongi Slim University Hospital, La Marsa, Tunisia

Introduction: NEMO syndrome is an X-linked primary immunodeficiency disorder characterized by phenotypic heterogeneity, which complicates its diagnosis and management.
Methods: This case report describes an 11-year-old patient diagnosed with NEMO syndrome, presenting with early-onset auto-inflammatory manifestations and recurrent infections.
Case Report: The index patient was born to consanguineous parents and developed atopic dermatitis at 2 months of age. At 5 months, he presented with a Kawasaki-like syndrome, followed by recurrent broncho-pneumopathies from ages 3 to 6. A quantitative immunoglobulin assay showed normal levels. At age 7, he was diagnosed with ectodermal anhidrosis, suspected due to the absence of sweating during febrile episodes and the presence of pointed teeth, which was confirmed by skin biopsy. Subsequently, he developed a severe Crohn-like digestive condition with abdominal pain, weight loss, erythema nodosum, and wrist arthritis, accompanied by a persistent inflammatory syndrome. Colonoscopy and MRI revealed inflammatory lesions. Partial remission was achieved with corticosteroids and azathioprine, but infliximab was eventually required. A later immunoglobulin assay revealed hypogammaglobulinemia. These findings, along with recurrent infections and digestive relapses, raised suspicion of an underlying immunodeficiency. An immunological workup and IV immunoglobulin therapy were initially unremarkable. High-throughput sequencing identified a hemizygous IKBKG c.524G>C (p. Arg175Pro) variant—a de novo mutation that does not exist in the mother—which impairs NEMO function and explains the combined phenotype of recurrent infections and immune dysregulation. The child remains stable on regular immunoglobulin therapy, corticosteroids, and immunosuppressive treatment, with no current indication for bone marrow transplantation.
Conclusion: This case highlights the importance of considering NEMO syndrome in patients with early-onset infections and auto-inflammatory manifestations, even in the absence of overt immunological abnormalities. It underscores the critical diagnostic role of genetic testing, particularly targeted sequencing, in atypical and complex presentations.

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Recurrent Infections in a Kenyan Child with X-Linked Agammaglobulinemia: A Case Report

Yusuf Rasheed, MBChB, MMed[1], Diana Marangu-Boore, MBChB-PhD, ATSF[2], and Anne Barasa, MBChB, MMed[3]

[1]Department of Paediatrics, Malindi Sub County Hospital, Kenya; [2]Department of Paediatrics and Child Health, University of Nairobi, Kenya; [3]Immunology Unit, Department of Human Pathology, University of Nairobi, Kenya

Background: X-linked agammaglobulinemia (XLA) is a rare inherited immune deficiency characterized by absence or paucity of circulating B lymphocytes and hypogammaglobulinemia. Patients with XLA present at varying ages and have different presentations. The most common presentation is related to recurrent respiratory tract infections. Patients can also present with severe infections such as meningitis or severe sepsis.
Case Report: We present a case of an 8-year-old school-going boy with a history of recurrent throat infections and bilateral suppurative otitis media. In 2021, he had an episode of severe dengue infection complicated by pancytopenia presenting with mucosal bleeding, petechiae, and purpura, requiring blood and platelet transfusion. The child developed meningitis presenting with convulsions and headaches and was hospitalized for 14 days. Immunological evaluation upon referral revealed markedly reduced serum immunoglobulins (Ig) G (<1.1 g/L), Ig M (0.20 g/L), Ig A (<0.05 g/L), and Ig E (<2.0 KU/L) levels and CD 19+ B lymphopenia (9 cells/μL). Absolute T (4022 cells/μL) and natural killer cell (397 cells/μL) counts were normal. Targeted genetic panel testing confirmed a hemizygous pathogenic variant in the *BTK* gene (c.62C>A), establishing a diagnosis of XLA. The patient is currently on monthly intravenous immunoglobulin (IVIG)

replacement therapy and prophylactic co-trimoxazole. No episode of severe infection has been reported since the onset of treatment over a year ago. He is currently doing well on regular multidisciplinary follow-up and lung-protective strategies.

Discussion: This case highlights the need to consider inborn errors of immunity in patients presenting with recurrent, severe, or unusual infections. Early immunological assessment is essential for timely diagnosis and intervention. IVIG remains the mainstay of treatment for XLA, significantly reducing morbidity from recurrent infections. IVIG is given either intravenously or subcutaneously every 3 to 4 weeks to the patient. There is also a role of prophylactic antibiotics in prevention of severe infections. Daily co-trimoxazole is a widely agreed choice of therapy. Thrice weekly azithromycin is also added to prevent respiratory exacerbations and to reduce the risk of developing bronchiectasis. Hematopoietic stem cell transplantation has been considered in some centers as a possible curative therapy.

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Early-Onset Atopy as an Initial Manifestation of Combined Immunodeficiency in a Sudanese Child

Tamadur B. Abbas[1], Omaima M.S. Abdel Allah[2], Aalaa M. Awoda[3], and Nahla H. Erwa[4]

[1]Department of Allergy and Immunology, Haj ALSafi Teaching Hospital, Khartoum, Sudan; [2]Department of Pediatrics, Faculty of Medicine, Omdurman Islamic University, Omdurman, Sudan; [3]National Center of Allergy, Asthma, and Immunology, Riyadh, Saudi Arabia; [4]Faculty of Medicine and Soba University Hospital, University of Khartoum

Introduction: Combined immunodeficiencies (CIDs) are inherited disorders affecting T and/or B cell function, presenting with recurrent infections, autoimmunity, and severe allergic disease [1].

Objective: To highlight atopy as a manifestation of CID and to outline feasible management in resource-limited settings.

Case Description: A female infant developed severe atopic dermatitis by week two of life. By 2 months, she was hospitalized repeatedly for bronchiolitis, diarrhea, and oral thrush. At 15 months, she was diagnosed with asthma and allergic rhinitis; her symptoms remained uncontrolled despite standard therapies. She exhibited multiple food allergies and required a restrictive diet. At 18 months, she had severe chest infections, necessitating intravenous antibiotics. Growth was normal; physical examination revealed pallor and turbinate hypertrophy.

Investigations: Initial evaluations revealed iron deficiency anemia with normal WBC counts. Hypogammaglobulinemia: IgG: 284 mg/dL (330–1,160 mg/dL); normal IgE: 18.67 kU/L; normal IgM: 101 mg/dL; IgA: 122 mg/dL; allergy workup: polysensitization. At 18 months: (1) leukopenia: WBC – 2.6 × 10^3 cells/mm^3 (ref range: 3.0–9.5 × 10^3); (2) moderate neutropenia: 0.83 × 10^3 cells/mm^3; (3) lymphopenia: 1.56 × 10^3 cells/mm^3 (ref range 3.0–9.5 × 10^3). Lymphocyte subset analysis showed a reduction in: (1) $CD3^+$ T cells: 875 cells/µL (2,100–6,200); (2) $CD4^+$ T cells: 450 cells/µL (1,300–3,400); (3) $CD8^+$ T cells: 415 cells/µL (620–2,000); (4) $CD19^+$ B cells: 524 cells/µL (720–2,600); (5) $CD16^+/56^+$ NK cells: 88 cells/µL (180–920). HLA typing showed the mother as a haploidentical match.

Management: She was initially labeled as transient hypogammaglobulinemia and started azithromycin prophylaxis. Progressive symptoms led to a CID diagnosis. She was given prophylactic antimicrobials. IVIG was added, but faced many difficulties. Hematopoietic stem cell transplantation (HSCT) was recommended but unavailable.

Discussion: This case highlights the importance of considering CID in infants with severe atopy [2]. In resource-limited settings, CBC, immunoglobulin levels, and lymphocyte phenotyping aid early recognition. Antibiotic prophylaxis and IVIG reduce infections while awaiting HSCT [3]. Infection control measures and nutritional assistance help decrease complications. Genetic testing, when accessible, confirms diagnosis and guides therapy [4].

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Inborn Errors of Immunity Management in Senegal: Inventory

I. Deme/Ly[1], A. Kane[1], I. Diop[1], M.S. Gueye[2], A. Nakoulima[3], A. Mbaye[1], Y.J. Dieng[1], B. Niang[1], I.D. Ba[1], P.M. Faye[1], A.L. Fall[1], Y.F. Mbodj/Diop[1], G. Ndiaye[1], M. Diallo[1], I. Diagne[4], T. Dieye[2], and O. Ndiaye[1]

[1]Cheikh Anta Diop University Dakar, Albert Royer National Children's Hospital; [2]Cheikh Anta Diop University Dakar, National Blood Transfusion Center Laboratory; [3]Dakar Main Hospital, Army Training Hospital; [4]Gaston Berger Saint-Louis University, UFR Sciences and Health

Introduction: Inborn errors of immunity are rare and underdiagnosed. The unavailability of some complementary tests contributes to delaying confirmation and management. This worsens the evolution and prognosis, with significant morbidity and mortality and impaired quality of life. Our aim was to present the challenges and perspectives in their management in Senegal.
Methodology: We recorded children monitored for inborn errors of immunity at the Albert Royer National Children's Hospital in Dakar, in specialized pediatric consultation, from 2014 to 2024. We report the overall evolution, mainly in the field of care activities organization, the training, patients' association, partnership, and collaboration.
Results: A total of 42 children are followed with an average of four new inclusions per year. The activity is provided by two pediatricians specialized in pediatric immunohematology, once a week, in addition to the children followed in dermatology. A teaching unit titled Immune Pathology has been taught in the fourth year of pediatric specialization since 2016. Since 2015, parents have been organized in a Senegalese Association Against Primary Immune Deficiencies (ASDIP), affiliated with the International Association of Patients (IPOPI) in 2024. Since 2022, some children have been included in poliovirus surveillance, in collaboration with the World Health Organization (WHO-AFRO), in the global polio eradication initiative. This recruitment concerned 10 children in 2022 and 9 in 2023, with negative results in all children. In addition, the Moroccan Society of Primary Immunodeficiencies (MSPID) contributes to the training through scientific conferences. The collaboration with the IMAGINE Institute of Necker in Paris has enabled the identification of genes in some children. However, the challenges remain genetic analysis, hematopoietic stem cell transplants, and genetic counseling.
Conclusion: Inborn errors of immunity are little-known and insufficiently explored conditions. The difficulties of their management are explained by a lack of training.

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Understanding the Hereditary Angioedema (HAE) Landscape in Sub-Saharan Africa

Priya Bowry, MBBS MRCGP DFFP DIC MSc (ALLERGY)[1], Tula Bowry, MBChB FRCPath[1], and Patricia Karani[2]

[1]The Allergy Clinic, Nairobi; [2]HAE Kenya

Background: Hereditary angioedema (HAE) is a rare, potentially life-threatening condition, with an estimated prevalence of 1 in 50,000 individuals. Despite global advances in diagnostics and treatment, data on HAE in sub-Saharan Africa remain scarce, highlighting a critical gap in awareness, diagnosis, and access to modern therapeutics in the region.
Objectives: This study aims to assess the current HAE landscape across a sample of sub-Saharan African countries, focusing on the number of diagnosed patients, availability of diagnostic testing, and access to prophylactic and acute treatments.
Methods: Doctors from the HAE African Regional Medical Advisory Panel (RMAP) completed a short survey covering: (1) Number of diagnosed HAE patients; (2) Available prophylactic and acute treatments; (3) Availability of diagnostic tests (local or abroad).
Results: 16 countries participated in the survey. The number of diagnosed HAE patients ranged from 0 to 117 per country. Diagnostic capabilities were limited, with C1 inhibitor levels and function tests often sent to South Africa (SA), Europe, or the USA. C1 inhibitor function testing was largely unavailable locally and for research in SA. While basic emergency treatments such as fresh frozen plasma (FFP), tranexamic acid, and danazol were widely available, access to modern HAE-specific therapies (e.g., icatibant and Ruconest) was restricted to only three countries—Kenya, DRC, and SA. SA and Kenya host Angioedema Centers of Reference and Excellence (ACARE). Overall, diagnostic services were mostly provided through private laboratories, with minimal integration into public health systems.
Conclusions: This study highlights the significant underdiagnosis of HAE in sub-Saharan Africa and the substantial disparities in access to diagnostic testing and modern treatments. The findings underscore an urgent need for increased awareness, improved public sector

diagnostic infrastructure, and equitable access to guideline-recommended therapies. Regional adaptations of international HAE management guidelines may be necessary to address local resource constraints and improve outcomes for affected individuals.

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Glue Thistle Intoxication Revealing Familial Lymphohistiocytosis Type 3 in an Infant: About a Case

Ilhem Ben Fraj, Rania Naffeti, Monia Ben Khaled, Aicha Ben Taieb, Samia Rekaya, Altaf Garbaa, Eya Bouzidi, Fethi Mellouli, and Monia Ouederni

Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, National Center of Bone Marrow Transplantation, University of Tunis El Manar, Tunisia

Introduction: Familial lymphohistiocytosis (FHL) is a rare, potentially fatal primary immune deficiency characterized by uncontrolled activation of the immune system. Clinical manifestations are heterogeneous, ranging from trivial infectious pictures to severe multivisceral involvement. In some cases, the picture is dominated by liver failure, making diagnosis more difficult.
Result: An 8-month-old infant from a first-degree consanguineous marriage, born at 33 AW with an initial stay in neonatal intensive care. At 4 months of age, he presented with a prolonged fever and diarrhea, for which the mother administered an infusion of slime thistle. Clinical deterioration followed, with the appearance of pancytopenia, hepatic cytolysis, and cholestasis. The diagnosis of macrophagic activation syndrome (MAS) was made in the presence of fever, hepatosplenomegaly, pancytopenia, hypertriglyceridemia, hypofibrinogenemia, and hemophagocytosis on myelogram. The immune, infectious, and metabolic workup was completed by whole-exome sequencing. The evolution was marked by neurological damage (MRI: toxic-metabolic lesions of the basal ganglia) and major hepatic cytolysis with liver failure. Treatment according to the HLH-2004 protocol was instituted, with neurological improvement but persistent hepatic damage. The whole-exome sequencing revealed a pathogenic mutation in the UNC13D gene, confirming type 3 FHL. The child is currently undergoing haplo-identical stem cell transplantation.
Conclusion: This case illustrates the importance of suspecting a primary immune deficiency in early-onset MAS, even in the presence of a triggering factor, such as intoxication. Hepatic involvement may dominate the picture, masking the diagnosis. In atypical forms, genetic testing is essential for appropriate curative management.

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Successful Stem Cell Transplantation in a Girl with DOCK 2 Deficiency

Ilhem Ben Fraj, Samia Rekaya, Manel Gouja, Aicha Ben Taieb, Amani Merdassi, Fethi Mellouli, Mohamed Bejaoui, Monia Ben Khaled, and Monia Ouederni

Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, National Center of Bone Marrow Transplantation, University of Tunis El Manar, Tunisia

Introduction: The dedicator of cytokinesis 2 (DOCK2) protein deficiency is a very rare, combined immunodeficiency characterized by early-onset lymphopenia, recurrent infections, and lymphocyte dysfunction. The only cure is hematopoietic stem cell transplantation.
Result: Here, we report a case of an 8-month-old girl who was admitted for severe chronic diarrhea related to chronic inflammatory colitis. The immune assessment showed hypogammaglobulinemia and a decrease in T cells. Genetic study confirmed the diagnosis of DOCK2 deficiency. She underwent haploidentical stem cell transplantation at 10 months. Conditioning regimen was based on Busilvex and fludarabine. Cyclosporine and MMF were used for graft-versus-host prophylaxis. The child is currently asymptomatic after two years of transplantation.
Conclusion: DOCK2 deficiency is a rare cause of very early-onset inflammatory bowel disease. Early diagnosis and appropriate treatment are fundamental to improve post-HCST prognosis.

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Noninfectious Manifestations in Chronic Granulomatous Disease

Ilhem Ben Fraj, Manel Gouja, Monia Ben Khaled, Aicha Ben Taieb, Samia Rekaya, Ridha Kouki, Mohamed Bejaoui, Fethi Mellouli, and Monia Ouederni

Department of Pediatrics: Immune-Hematology and Stem Cell Transplantation, National Center of Bone Marrow Transplantation, University of Tunis El Manar, Tunisia

Introduction: Chronic granulomatous disease (CGD) is a primary immunodeficiency disorder caused by defects in the NADPH oxidase complex, which impairs the ability of phagocytes to generate reactive oxygen species, leaving patients vulnerable to recurrent infections. However, CGD patients often exhibit a variety of noninfectious manifestations.
Objectives: The aim of this study was to identify and characterize the noninfectious manifestations observed in patients with CGD.
Material and Methods: This retrospective study was conducted over a period of 33 years (1991–2024) and included all patients diagnosed with CGD and followed at our institution. Noninfectious complications were identified based on clinical, endoscopic, and histopathological evaluations.
Results: A wide range of noninfectious manifestations was observed in the 101 patients included in the study. One patient presented with Evans syndrome, which was successfully treated with corticosteroids, leading to complete remission. Inflammatory bowel disease affected four patients, all treated with corticosteroids and immunosuppressants, resulting in clinical improvement. Other manifestations included subcutaneous nodules (n = 3), cutaneous granulomas (n = 3), and hepatic granulomas (n = 2), one of which was complicated by hepatic cytolysis and splenic granuloma (n = 1). A significant proportion of patients (n = 46) exhibited growth retardation. Allergic manifestations included eczema (n = 9), cow's milk protein allergy (n = 2), and allergic conjunctivitis (n = 1).
Conclusion: Noninfectious manifestations in CGD patients are varied and can significantly affect clinical management. These complications, often due to dysregulated immune responses, require specific treatments. Early recognition and tailored management of these manifestations are crucial for improving the long-term prognosis of CGD patients.

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Mortalities Due to Inborn Errors of Immunity Where There Is a High Burden of Malaria and Other Infectious Diseases

Edwin Walong

Pathologist and Senior Lecturer, Maseno University School of Medicine, Site Pathologist – Child Health and Mortality Prevention, Surveillance (CHAMPS), Kenya

Introduction: Inborn errors of immunity, previously described as primary immune deficiencies, represent a group of diseases with inadequate development of immune responses to infectious diseases. This is due to a genetic disease that affects immune cell development and function. Characteristics of these diseases include failure to thrive, in addition to recurrent, persistent, and multipathogen infectious diseases. The CHAMPS series is a multicountry 20-year project implemented in sites with under-5 mortality rates of more than 100 per 1,000 live births. In this series, we seek to estimate the burden of inborn errors of immunity, in the Child Health and Mortality Prevention, Surveillance (CHAMPS) series.
Materials and Methods: This has been running for 7 years. In this project, all natural under-5 mortalities are recruited, and postmortem testing, consisting of minimally invasive tissue sampling (MITS) and detailed, advanced pathological testing, is performed within a defined health and demographic surveillance site (HDSS). In Kenya, these activities are performed within Siaya (Karemo) and Kisumu (Manyatta) HDSS, representing rural and urban deaths. In addition, risk factors are sought from clinical and demographic data. MITS specimens obtained are brain, lung, liver, blood, and cerebrospinal fluid. From these deaths, we identified potential inborn errors of immunity based on postneonatal age (child and infant) and clinical characteristics (history of previous child deaths, recurrent infections, and persistent disease) and presence of malnutrition. The final diagnosis, assigned as the immediate cause of death, and underlying causes of death are considered.

Results: In Kenya, a total of 1,602 subjects, out of an eligible population of 1,727, were recruited, and MITS performed. Of these, infant deaths were 352, consisting of 217 males and 172 females, while child deaths were 362, consisting of 192 males and 170 females. In this population, malnutrition, malaria, HIV disease, congenital birth defects, diarrheal diseases, and lower respiratory tract infections are major underlying causes of death. Malnutrition, malaria, HIV disease, and birth defects are major immediate causes of disease. In these cases, suboptimal clinical case management is a major contributor to mortality. Multipathogen infectious disease is common where a diagnosis of malnutrition and HIV disease are presented. In this series, two cases appear to fulfill diagnostic criteria for inborn errors of immunity. The first case is a 4-month-old male infant who is severely malnourished, with disseminated CMV disease and disseminated candida infection. The child presented with history of fever, with a temperature of 39 degrees. This child had undergone early weaning; the mother was a teenage pregnancy and had used herbal medicines. The second case is a 5-month-old female child whose cause of death is multipathogen sepsis and fungemia, with disseminated intravascular coagulation identified as a direct complication of these infections. There was also bowel gangrene and abdominal wall birth defects (gastroschisis). In this series, there are no incidences of infantile mycobacterial infections associated with universal BCG vaccination.

Conclusion: Due to high malaria, malnutrition, and HIV disease, and the limited nature of the MITS technique, potential cases of errors of immunity are difficult to identify. Two cases identified had multiple infections, consisting of disseminated fungal and bacterial infections, while one has additional disseminated CMV disease. As quality of care improves as a consequence of data- to action-driven interventions, more cases may be identified in this population.

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A Case of Gastrointestinal Tuberculosis in a 3-Month-Old Infant with Profound Immunodeficiency

Christine Karanja-Chege[1,2], David Mwakisha[2], Winnie Okoth[2], Joseph Mbuthia[2], Peter Ngwatu[1,2], Jeremiah Kamwetu[2,3], and Jacquie Oliwa[4,5]

[1]Kenyatta University, Nairobi, Kenya; [2]Gertrude's Children's Hospital, Nairobi, Kenya; [3]Kenyatta National Hospital, Kenya; [4]Health Services Unit, KEMRI-Wellcome Trust Research Programme, Nairobi, Kenya; [5]Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium

Gastrointestinal tract tuberculosis (GIT-TB) is a rare form of TB, but one that poses a serious challenge in diagnosis and management, particularly in the setting of severe immunosuppression. We present a case of intestinal TB in a 3-month-old immunosuppressed infant whose chief complaints were progressive abdominal distention and failure to thrive with features of intestinal obstruction with the diagnosis of GIT-TB confirmed on histology and culture. The resulting serious complications despite surgery included short bowel syndrome, enterocutaneous fistulae, and cholestasis, necessitating the use of total parenteral nutrition and a modified parenteral TB treatment regimen. During the two-month stay in hospital, irreversible liver failure and azotemia developed, with the patient eventually succumbing to these complications. This case highlights the importance of early recognition and treatment of GIT-TB to prevent adverse outcomes. Further, there is need to investigate for immunodeficiency in such presentations, particularly in young infants. The challenges encountered by the clinicians underscore the importance of the development of World Health Organization (WHO) guidelines on the specific management of GIT-TB.

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When Recurrent Infections Don't Always Reveal a Primary Immunodeficiency

Doha Benchaji[1], Islam Mansouri[1], Zahra Aadam[1], Siham Satlane[2], Ikbal Belkhou[1,2], Ibtihal Benhsaien[1,2], Fatima Ailal[1,2], Fatima Adnane[1,2], Ahmed Aziz Bousfiha[1,2], and Naima Amenzoui[1,2]

[1]Clinical Immunology, Infection and Auto-Immunity Laboratory (LICIA), Faculty of Medicine and Pharmacy, Hassan II University, Casablanca, Morocco; [2]Department of Pediatric Infectious Diseases and Clinical Immunology, Children's Hospital, Ibn Rochd University Hospital, Casablanca, Morocco

Background: Recurrent infections often suggest an underlying immunodeficiency, particularly when local (e.g., an overlooked intra-bronchial foreign body) or systemic (e.g., retroviral infection) causes are excluded. Primary immunodeficiencies (PIDs) are a heterogeneous group of inherited disorders characterized by immune system defects, leading to increased susceptibility to infections, autoimmunity, and malignancies. Recurrent respiratory infections are a key clinical feature of PIDs and often prompt extensive

immunological evaluations. However, even when immune workups and cystic fibrosis testing are inconclusive, conditions that mimic PID must be considered to prevent misdiagnosis and treatment delays.

Objectives: This study aims to discuss cases of patients with recurrent infections initially suspected of having a PID and to evaluate the role of genetic testing in establishing a definitive diagnosis.

Methods: Patients with unexplained recurrent respiratory infections underwent a systematic evaluation, including immunoglobulin level measurements (IgG, IgA, IgM, and IgE), lymphocyte subset analysis, a sweat test for cystic fibrosis, HIV screening, and whole-exome sequencing (WES) to detect inborn errors of immunity and ciliopathy-related mutations.

Results: Seven patients (five males and two females) with a median age of 12.7 years were evaluated. Immunological testing was normal in five patients, while two had abnormal immune profiles: one female was diagnosed with combined immunodeficiency and one male with Wiskott-Aldrich syndrome. Notably, WES identified, in all seven patients, a homozygous pathogenic mutation in primary ciliary dyskinesia (PCD)-related genes, a disorder caused by defective ciliary function.

Conclusion: This study underscores the importance of considering PCD in the differential diagnosis of patients with recurrent respiratory infections suspected of PID, particularly when immunological tests yield inconclusive results. Additionally, PCD may coexist with other immunodeficiencies, complicating the diagnostic process. In populations with high consanguinity, incorporating genetic testing into routine diagnostic workflows is critical for accurate diagnosis, ultimately improving patient outcomes and preventing complications related to delayed treatment.

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A Novel Homozygous CRACR2A Variant Underlying CRACR2A-Associated Immunodeficiency in a Tunisian Patient

Mariem Tira[1], Najla Mekki[1], Aicha Ghariani[1], Meriem Ben Ali[1], Ilhem Ben Fraj[2], Koon Wing Chan[3], Xinxin Chen[3], Xingtian Yang[3], Jing Yang[3], Wanling Yang[3], Yu Lung Lau[3], Monia Ouederni[2], and Imen Ben Mustapha[1]

[1]Laboratory of Transmission, Control, and Immunobiology of Infections (LR11IPT02), Pasteur Institute of Tunis; [2]Pediatric Immuno-Hematology Unit, Bone Marrow Transplantation Center Tunis, Tunis, University Tunis El-Manar, Tunis, Tunisia; [3]Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong, China

The calcium release-activated calcium modulator-2A (CRACR2A) protein plays a critical role in regulating store-operated calcium entry (SOCE) through CRAC channels, a process essential for numerous cellular functions, particularly T cell activation. Herein, we report the first Tunisian patient harboring a homozygous CRACR2A mutation. The patient is a 45-year-old female, born to consanguineous parents, who presented with lymph node and urinary tuberculosis, as well as recurrent fungal infections, including oral, genital, and urinary candidiasis, raising suspicion of an inborn error of immunity (IEI). HIV serology was negative. Immunophenotypic analysis revealed profound CD4+ and CD8+ T cell lymphopenia associated with a markedly decreased percentage of naïve CD4 T lymphocytes (CD4+ naïve T cells: 17.3%, normal: 33–66%). Lymphocyte proliferation to phytohemagglutinin (PHA) was impaired, and functional studies of IL-12/IFN-γ and TH17 pathways studies were normal, excluding other primary immunodeficiencies (PIDs). Whole-exome sequencing identified a homozygous missense variant in CRACR2A (c.1058G>A, p.Gly353Glu), predicted as disease-causing by MutationTaster. This variation was confirmed by Sanger sequencing. To the best of our knowledge, only one case of CRACR2A deficiency has been reported in the literature. The previously reported Asian patient presented with chronic diarrhea and recurrent pulmonary infections since adolescence, associated with severe hypogammaglobulinemia, progressive CD4 T cell lymphopenia, and a reduced proliferative response to mitogens, consistent with a late-onset combined immunodeficiency (LOCID). CRACR2A deficiency is presumed to result in functional impairment of T lymphocytes. Further immunological investigations are needed to better characterize the impact of the novel variant described herein. In conclusion, we describe the first Tunisian patient with a homozygous *CRACR2A* mutation, making her the second reported case worldwide. This finding broadens the clinical and immunological spectrum of CRACR2A-associated immunodeficiency and contributes to expanding the catalogue of genetic variants underlying this rare inborn error of immunity.