EXPLORATION OF PRIMARY IMMUNODEFICIENCY: DIAGNOSTIC APPROACH AND CURRENT STATUS IN MAURITANIA.

Abstract

Primary immunodeficiencies (PIDs) are a heterogeneous group of inherited disorders of the immune system, often severe and still underdiagnosed in low-resource settings. Their clinical expression is highly variable, ranging from recurrent or unusual infections to complex syndromic presentations. This article reviews a practical diagnostic approach to PIDs and highlights the current situation in Mauritania based on local clinical experience. Clinical suspicion remains the cornerstone of diagnosis and should be raised in front of severe, persistent, recurrent, or unusual infections. Initial work-up relies on simple first-line investigations, including complete blood count, HIV testing, serum protein electrophoresis, and quantitative immunoglobulins, followed when possible by lymphocyte phenotyping and genetic characterization. In Mauritania, underdiagnosis is favored by limited awareness, lack of a national registry, restricted technical resources, and poor availability of some essential therapies. Strengthening physician awareness, developing diagnostic capacity, and improving access to immunoglobulins and specialized care are necessary to improve outcomes.

Key words:-
PRIMARY IMMUNODEFICIENCY, PID, DIAGNOSIS, RECURRENT INFECTIONS, SEVERE COMBINED IMMUNODEFICIENCY, MAURITANIA

INTRODUCTION:-

Primary immunodeficiencies (PIDs) are inherited disorders affecting one or more components of the immune system. Once considered exceptionally rare, they are now recognized as an expanding group of diseases due to the progress of immunology and molecular genetics. They may lead to severe infectious complications, chronic organ damage, growth impairment, and major social and educational consequences when diagnosis is delayed.

The pathogenic mechanisms are complex but increasingly better understood. Although several hundred entities have been described worldwide, PIDs remain under-recognized in many developing countries. In Mauritania, the challenge is even greater because of limited diagnostic facilities, insufficient awareness among health professionals, the absence of a national registry, and the competing burden of other public health priorities.

In a setting where consanguinity is frequent, early recognition of PIDs is particularly important. Timely diagnosis may improve survival, guide treatment, and support genetic counseling. The aim of this article is to present a practical diagnostic approach to primary immunodeficiency and to describe the current situation in Mauritania from a local hospital perspective.

I. CURRENT SITUATION IN MAURITANIA:-

Primary immunodeficiencies are still largely underdiagnosed in Mauritania. According to local experience presented in the source material, awareness remains limited and many physicians do not

routinely consider PID in the differential diagnosis of recurrent or severe infections. In addition, no national registry is currently available, which makes it difficult to estimate the real burden of disease.

The major barriers include insufficient technical facilities, restricted access to specialized immunological investigations, dependence on external laboratories for some confirmatory tests, and poor availability of certain treatments for economically vulnerable patients. These constraints justify the need for a pragmatic, stepwise, and context-adapted strategy for diagnosis and management.

II. LOCAL HOSPITAL EXPERIENCE:-

Nine patients were followed for suspected or confirmed PID. Among them, four cases were diagnosed as ataxia telangiectasia, three as severe combined immunodeficiency, and two remained under investigation. The mean age was 7 years, with five boys and four girls. Consanguinity was found in all cases. Outcomes reflected the severity of these disorders and the challenges of care, with three deaths and two patients lost to follow-up.

Illustrative cases included children presenting with recurrent respiratory infections, otitis, bronchopneumonia, developmental delay, telangiectasia, or severe lymphopenia. These observations highlight the importance of considering PID when infections are repetitive, severe, or associated with syndromic manifestations.

III. ORGANIZATION OF CARE:-

A dedicated team for PID care was established locally in November 2015. The available infrastructure included a limited but functional care area with three beds, a refrigerator, a washbasin, sanitary facilities, and air conditioning. The team consisted of one pediatrician, one general practitioner, one nurse trained in immunoglobulin administration, and one biologist.

Available laboratory investigations included complete blood count, HIV serology, serum protein electrophoresis, and measurement of immunoglobulins A, M, E, and G. Agreements with laboratories in Tunisia and Morocco allowed access to lymphocyte subpopulation analysis and genetic testing when necessary.

IV. WHEN SHOULD PRIMARY IMMUNODEFICIENCY BE SUSPECTED?:-

Clinical suspicion is the most important step in the diagnosis of PID. A primary immunodeficiency should be considered in front of severe infections, persistent infections, recurrent infections, or unusual infections. The type of microorganism involved and the pattern of clinical manifestations are essential for orienting the diagnosis.

Some syndromic presentations are highly suggestive on clinical grounds alone, especially ataxia telangiectasia, Wiskott-Aldrich syndrome, Griscelli syndrome, DiGeorge syndrome, and Omenn syndrome. Before concluding that a patient has a PID, acquired causes of immune deficiency must be excluded, particularly HIV infection, protein loss, hematologic malignancies, exudative enteropathy, nephrotic syndrome, immunosuppressive therapy, and autoimmune disease.

V. PRACTICAL DIAGNOSTIC APPROACH:-

The diagnostic approach should be organized in successive steps. The first step is clinical orientation. The second step relies on first-line biological investigations, which should remain simple and accessible. The

third step is phenotypic characterization of the immune defect. The fourth step is genetic confirmation whenever feasible.

Complete blood count is a key investigation. Lymphopenia strongly suggests severe combined immunodeficiency, especially when it is marked and early in life. Neutropenia may indicate a phagocytic defect, while thrombocytopenia associated with small platelets may orient toward Wiskott-Aldrich syndrome.

Serum protein electrophoresis can suggest hypogammaglobulinemia and help exclude protein-losing conditions. Quantitative immunoglobulin measurement is essential to identify global hypogammaglobulinemia, selective deficiencies, hyper-IgM profiles, or hyper-IgE syndromes. Investigation of complement should be considered in patients with recurrent meningitis or severe invasive bacterial infections, beginning with total complement activity testing.

When first-line results support the diagnosis of PID, lymphocyte phenotyping using CD3, CD4, CD8, CD19, and NK markers allows a more precise classification of combined immunodeficiencies. Genetic characterization, in collaboration with specialized centers, remains the reference for definitive diagnosis and family counseling.

VI. Clinical orientation according to the type of immunodeficiency:-

Humoral immunodeficiencies usually become apparent after the age of 6 months and are characterized by recurrent infections due to extracellular bacteria, repeated otitis, recurrent pneumonia, chronic diarrhea, and bronchiectasis. Combined immunodeficiencies generally present earlier, often between 3 and 6 months of age, with opportunistic infections, persistent oral candidiasis, chronic diarrhea, interstitial pneumonitis, or septicemia.

Complex syndromic immunodeficiencies may combine infections with neurological, cutaneous, hematological, or developmental abnormalities, as seen in ataxia telangiectasia or Wiskott-Aldrich syndrome. Defects of innate immunity, including phagocytic disorders and complement deficiencies, may be suspected in the presence of deep abscesses, delayed cord separation, stomatitis, unusual pyogenic infections, or recurrent meningitis.

VII. Challenges in Mauritania:-

The Mauritanian context is characterized by under-recognition of PID, delayed referral, limited access to specialized tests, insufficient availability of immunoglobulin therapy, and difficult long-term follow-up. Social difficulties and geographic distance may also contribute to treatment interruption or loss to follow-up.

These realities explain why diagnosis is often made late, at a stage when severe complications have already occurred. As a result, mortality remains significant, particularly for severe combined immunodeficiency and other early-onset forms.

VIII. Perspectives and recommendations:-

Improvement of PID care in Mauritania requires a coordinated strategy. Physician education must be strengthened, especially among pediatricians, general practitioners, and physicians working in peripheral regions. Simple diagnostic algorithms should be disseminated widely to facilitate early suspicion and referral.

It is also necessary to develop national diagnostic capacity, encourage collaboration with regional reference laboratories, create a registry of primary immunodeficiencies, and improve access to essential treatments such as intravenous immunoglobulins, anti-infective prophylaxis, and bone marrow transplantation when indicated. Public authorities, families, scientific societies, and patient associations all have a role to play in this process.

IX. CONCLUSION:-

Primary immunodeficiencies are severe but still underestimated diseases in Mauritania. Their diagnosis depends first on strong clinical suspicion and then on a rational stepwise work-up adapted to the available resources. Despite current limitations, progress is possible through better training, improved laboratory support, stronger collaboration between clinicians, and wider access to treatment. Earlier diagnosis would significantly improve prognosis and quality of life for affected children and their families.

X. REFERENCES:-

1. Ailal F, Benhsaien I, Kili A, Bousfiha AA, Najib J. Déficit immunitaire primitif au Maroc: diagnostic et prise en charge. Revue marocaine des maladies de l'enfant. 2008;18:107-108.

2. Barbouche MR, Galal N, Ben-Mustapha I, Jeddane L, Mellouli F, Ailal F, Bejaoui M, Boutros J, Marsafy A, Bousfiha AA. Primary immunodeficiencies in highly consanguineous North African populations. Ann N Y Acad Sci. 2011 Nov;1238:42-52.

3. Boisson-Dupuis S, El Baghdadi J, Parvaneh N, Bousfiha A, Bustamante J, Feinberg J, Abel L, Casanova JL. IL-12Rβ1 deficiency in two of fifty children with severe tuberculosis from Iran, Morocco, and Turkey. PLoS One. 2011 Apr 13;6(4):e18524.

4. Sancho-Shimizu V, Pérez de Diego R, Lorenzo L, Puel A, Zhang SY, Abel L, Al-Muhsen S, Casanova JL. Herpes simplex encephalitis in children with autosomal recessive and dominant TRIF deficiency. J Clin Invest. 2011 Dec;121(12):4889-4902.

5. Esser M. SPUR infections in PID. ASID. Available from: www.asid.ma.

6. Chapel H, Geha R, Rosen F; for the IUIS PID Classification Committees. Primary immunodeficiency diseases: an update. Clin Exp Immunol. 2003;132:9-15.

7. Bousfiha AA, Ailal F, Fellah H, Maataoui O, Farouki B, Sekkat S, Abid A. Évoquer, explorer et diagnostiquer un déficitimmunitaireprimitif. Rev Mar Mal Enf. 2005;5:64-70.

8. Admou B, Haouach K, Ailal F, Benhsaine I, Barbouch MR, Bejaoui M, Bousfiha AA. Déficits immunitaires primitifs: approche diagnostique pour les pays émergents. Immunol Biol Spec. 2010.

9. Mahlaoui N. Explorations immunitaires chez l'enfant suivi pour infections respiratoires récurrentes. Arch Pediatr. 2007;14:S203-S207.

10. Picard C. Comment explorer un déficit immunitaire héréditaire? Rev Prat. 2007;57:1671-1676.

11. Naamane H, El Maataoui O, Ailal F, Bennani S, Najib J, Hassar M, Saile R, Bousfiha AA. The 752delG26 mutation in the RFXANK gene associated with major histocompatibility complex class II deficiency: evidence for a founder effect in the Moroccan population. Eur J Pediatr. 2010 Sep;169(9):1069-1074.

12. Bousfiha AA, Picard C, Bustamante J, Puel A, Ailal F, El-Baghdadi J, Abel L, Casanova JL. Primary immunodeficiencies of protective immunity to primary infections. Clin Immunol. 2010 May;135(2):204-209.

13. Picard C, Casanova JL, Puel A. Infectious diseases in patients with IRAK-4, MyD88, NEMO, or IκBα deficiency. Clin Microbiol Rev. 2011 Jul;24(3):490-497.