

IMMUNOLOGY

APPLIED IMMUNOLOGY AND CLINICAL CLUES FOR INBORN ERRORS OF IMMUNITY

*Geeta M. Govindaraj
**Kalpana George

Abstract: Primary immune deficiency disorders or inborn errors of immunity are one of the commonest genetic disorders caused by variants in more than 400 genes. This is manifested by susceptibility to severe, persistent, unusual or recurrent infections encompassing a broad or narrow range of pathogens. Autoimmune, allergic and autoinflammatory manifestations and susceptibility to early onset malignancies may be the other manifestations. These disorders are often undiagnosed or misdiagnosed and enhancing awareness among pediatricians is key to improving outcomes, since a high index of suspicion is crucial.

Keywords: Primary immune deficiency, Inborn errors of immunity, Autoinflammation.

Points to Remember

- *A high index of suspicion is essential to diagnose primary immune deficiency disorders (PIDDs).*
- *Infections of unusual severity, frequency, etiology and suboptimal response to treatment are the hallmark of these disorders.*
- *Apart from susceptibility to infections, autoimmune, allergic and autoinflammatory features occur as well as early onset malignancies.*
- *Important clues from the history include age at onset, types of infections, adverse events following immunization and the family history.*
- *Examination often reveals valuable clues including syndromic features, paucity or proliferation of lymphoid tissue, other systemic manifestations and failure to thrive.*

References

1. Tangye SG, Al-Herz W, Bousfiha A, Chatila T, Cunningham-Rundles C, Etzioni A, et al. Human Inborn Errors of Immunity: 2019 Update on the Classification from the International Union of Immunological Societies Expert Committee. *J Clin Immunol* 2020; 40(1):24-64.
2. Bousfiha AA, Jeddane L, Ailal F, Benhsaien I, Mahlaoui N, Casanova JL, et al. Primary immunodeficiency diseases worldwide: more common than generally thought. *J Clin Immunol* 2013; 33(1):1-7.
3. Marshall JS, Warrington R, Watson W, Kim HL. An introduction to immunology and immunopathology. *Allergy Asthma Clin Immunol* 2018; 14(Suppl2):49.
4. Tasher D, Dalal I. The genetic basis of severe combined immunodeficiency and its variants. *Appl Clin Genet* 2012; 5:67-80.
5. Kumrah R, Vignesh P, Patra P, Singh A, Anjani G, Saini P, et al. Genetics of severe combined immunodeficiency. *Genes Dis* 2020; 7(1):52-61.
6. Amado MC. Primary Immunodeficiency Update and Newborn Screening. *Mo Med* 2011; 108(5):350-353.
7. Suri D, Rawat A, Singh S. X-linked Agammaglobulinemia. *Indian J Pediatr* 2016; 83(4):331-337.
8. Blundell MP, Worth A, Bouma G, Thrasher AJ. The Wiskott-Aldrich Syndrome: The Actin Cytoskeleton

* Professor,
Department of Pediatrics

** Associate Professor,
Department of Microbiology,
Government Medical College, Kozhikode, Kerala,
FPID Regional Diagnostic Centre, Kozhikode
email: geetakkumar@gmail.com

- and Immune Cell Function. *Dis Markers* 2010; 29 (3-4):157-175.
9. Das J, Sharma A, Jindal A, Aggarwal V, Rawat A. Leukocyte adhesion defect: Where do we stand circa 2019? *Genes Dis* 2020; 7(1):107-114.
 10. Arnold DE, Heimall JR. A Review of Chronic Granulomatous Disease. *Adv Ther* 2017; 34(12):2543-2557.
 11. Bustamante J, Boisson-Dupuis S, Abel L, Casanova JL. Mendelian susceptibility to mycobacterial disease: genetic, immunological, and clinical features of inborn errors of IFN- γ immunity. *Semin Immunol* 2014; 26(6):454-470.
 12. Gathmann B, Mahlaoui N, Gérard L, Oksenhendler E, Warnatz K, Schulze I, et al. Clinical picture and treatment of 2212 patients with common variable immunodeficiency. *J Allergy Clin Immunol* 2014; 134(1):116-126.
 13. Griffith LM, Cowan MJ, Notarangelo LD, Puck JM, Buckley RH, Candotti F, et al. Improving cellular therapy for primary immune deficiency diseases: recognition, diagnosis, and management. *J Allergy Clin Immunol* 2009; 124(6):1152-1160.e12.
 14. Barron MA, Makhija M, Hagen LE, Pencharz P, Grunebaum E, Roifman CM. Increased resting energy expenditure is associated with failure to thrive in infants with severe combined immunodeficiency. *J Pediatr* 2011; 159(4):628-632.e1.
 15. Hambleton S, Goodbourn S, Young DF, Dickinson P, Mohamad SMB, Valappil M, et al. STAT₂ deficiency and susceptibility to viral illness in humans. *Proc Natl Acad Sci U S A*. 2013; 110(8):3053-3058.
 16. Govindaraj GM, Riyaz A, Krishnan C, Scaria V. Rapid Transition of Facial Features from Early to Mid - Adolescence in Autosomal Dominant Hyper IgE Syndrome with a STAT₃ Variation. *Indian J Pediatr* 2018; 85(7): 595-596.
 17. Natkunam Y, Gratzinger D, Chadburn A, Goodlad JR, Chan JKC, Said J, et al. Immunodeficiency-associated lymphoproliferative disorders: time for reappraisal? *Blood* 2018; 132(18):1871-1878.
 18. Carneiro-Sampaio M, Coutinho A. Early-onset autoimmune disease as a manifestation of primary immunodeficiency. *Front Immunol* 2015; 6:185.
 19. DeSanctis S, Nozzi M, Del Torto MD, Scardapane A, Gaspari S, de Michele G, et al. Autoinflammatory syndromes: diagnosis and management. *Ital J Pediatr* 2010; 36:57.
 20. Mayor PC, Eng KH, Singel KL, Abrams SI, Odunsi K, Moysich KB, et al. Cancer in primary immunodeficiency diseases: Cancer incidence in the United States Immune Deficiency Network Registry. *J Allergy Clin Immunol* 2018; 141(3):1028-1035.