Genes & Diseases (2020) 7, 1–2

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://ees.elsevier.com/gendis/default.asp

PERSPECTIVES

Primary Immune Deficiencies – A rapidly emerging area of basic and clinical research

In this special issue of *Genes & Diseases*, Primary Immune Deficiencies (PIDs) are the main focus. This is an exciting and a rapidly emerging field of basic and clinical immunology wherein upwards of 400 clinical conditions, with approximately 350 defined mutations, are now recognized. Contrary to common perception, PIDs as a group are not uncommon. Epidemiologic studies show that population prevalence of PIDs is approximately 1:2000. Statistical extrapolations of this figure would suggest that in a large country like China or India, approximately 1 million individuals would be expected to have a PID. However, at present because of lack of awareness of these conditions amongst both the laity as well as medical professionals, majority of these patients remain undiagnosed and untreated in many developing countries. This is clearly unfortunate.

PIDs can affect children as well as adults. While serious forms of combined immunodeficiencies are medical emergencies and usually present in early infancy, no age seems to be exempt from these disorders. The term Common Variable Immunodeficiency (CVID) refers to a heterogenous group of disorders that usually affect older children and adults. As its name suggests, the clinical and laboratory phenotype of CVID is variable. Because of this heterogeneity in clinical presentation, patients with CVID may, at times, remain undiagnosed for prolonged periods especially in regions wherein awareness about PIDs is not high.

In this issue, Jindal et al[1] present an overview of current status of PIDs in Asia and show that while countries such as Japan and Korea have advanced laboratory and treatment facilities for PIDs that are comparable to the best in the world, there are several other regions in Asia that need to improve their infrastructure. This is followed by a succinct review on the newly recognized clinical entity, phenocopies of PIDs, by Jindal et al[2] and an update on genetics of CVID by Aggarwal et al.[3] The field of PIDs is advancing so rapidly that the gap between bench and bedside is narrowing down every year. Gene therapy and gene editing for PIDs, hitherto considered experimental therapy, is now a well-recognized clinical option for patients with disorders such as Severe Combined Immunodeficiency (SCID), Wiskott-Aldrich syndrome and Chronic Granulomatous Disease (CGD). Zhang et al[4] discuss these exciting therapeutic options that have recently become available.

SCID is a syndrome that can have heterogenous clinical phenotypes and several genotypes. Pandiarajan et al[5] provide an updated overview of genetics of SCID and detail how the clinician can go about diagnosing these children.

Kawasaki disease (KD) is a common pediatric vasculitis whose etiopathogenesis is still not clearly understood. Both innate and acquired immune mechanisms are believed to play a role in pathogenesis of this enigmatic condition. Jindal et al[6] discuss the emerging role of platelets in development of the cytokine cascade that is so very characteristic of KD.

Several new phenotypes of PIDs have been identified in the last few years. Activated PI3 Kinase Delta Syndrome (APKDS) is one such disorder – Rawat et al[7] explain the clinical and laboratory profile of this fascinating condition. Hereditary angioedema is an uncommon immunological disorder but the acute exacerbations can be fatal if there are delays in diagnosis and treatment. Jindal et al[8] discuss the genetics and pathogenesis of this disorder and show how a clear understanding of the underlying defect goes a long way in developing appropriate therapeutic interventions.

CGD is a phagocytic defect involving the innate immune system and can have both X-linked recessive and autosomal recessive forms of inheritance. Pandiarajan et al[9] discuss some of the recent advances in diagnosis and management of this condition.

It is not often realized that early onset inflammatory bowel disease (IBD) can sometimes be the manifestation of an underlying PID. Suri et al[10] provide an update on the genetic basis of IBD and show how it is of paramount importance

Peer review under responsibility of Chongqing Medical University.

https://doi.org/10.1016/j.gendis.2020.01.006

to consider this differential diagnosis while managing infants with severe forms of IBD. Leucocyte adhesion deficiency (LAD) is an uncommon defect of the innate immune system. It can have protean clinical manifestations and requires a high index of suspicion for early diagnosis. Sharma et al[11] discuss some of the diagnostic and therapeutic challenges of managing children with LAD. Hematopoietic stem cell transplantation is curative in LAD and gene therapy is rapidly emerging as an alternative therapeutic option in situations wherein HSCT is not suitable.

Selective IgA deficiency is a complex PID and several patients may go on to develop CVID later in life. Some patients with IgA deficiency may also have associated IgG subclass deficiency. Song et al[12] provide a clinical review based on their experience of 16 patients with selective IgA deficiency in China.

Basic and clinical immunology are closely related specialties. Our understanding of pathogenesis of newly emerging PID syndromes is dependent upon figuring out the underlying immunological mechanisms. This compendium of articles also has overviews of basic immunology covering RIPK1 deficiency[13], atypical SIFD and multiple immune defects[14], tissue engineering[15] and transcriptomic changes associated with PCK1 overexpression in hepatocellular carcinoma[16].

This issue of *Genes & Diseases* highlights some of the recent advances in field of clinical and basic immunology and also details the complexities of underlying genetic aberrations.

References

1. Pilania RK, Chaudhary H, Jindal AK, Rawat A, Singh S. Current status and prospects of primary immunodeficiency diseases in Asia. *Genes Dis*. 2020;7(1):3—11.
2. Singh A, Jindal AK, Joshi V, Gummadi Anjani, Rawat A. An updated review on phenocopies of primary immunodeficiency diseases. *Genes Dis*. 2020;7(1):12—25.
3. Aggarwal V, Banday AZ, Jindal AK, Das J, Rawat A. Recent advances in elucidating the genetics of common variable immunodeficiency. *Genes Dis*. 2020;7(1):26—37.
4. Zhang ZY, Thrasher A, Zhang F. Gene therapy and genome editing for primary immunodeficiency diseases. *Genes Dis*. 2020;7(1):38—51.
5. Kumrah R, Vignesh P, Patra P, et al. Genetics of severe combined immunodeficiency. *Genes Dis*. 2020;7(1):52—61.
6. Arora K, Guleria S, Jindal AK, Amit Rawat, Singh S. Platelets in Kawasaki disease: is this only a numbers game or something beyond? *Genes Dis*. 2020;7(1):62—66.
7. Singh A, Joshi V, Jindal AK, Mathew B, Rawat A. An updated review on activated PI3 kinase delta syndrome (APDS). *Genes Dis*. 2020;7(1):67—74.
8. Banday AZ, Kaur A, Jindal AK, Rawat A, Singh S. An update on the genetics and pathogenesis of hereditary angioedema. *Genes Dis*. 2020;7(1):75—83.
9. Anjani G, Vignesh P, Joshi V, et al. Recent advances in chronic granulomatous disease. *Genes Dis*. 2020;7(1):84—92.
10. Nameirakpam J, Rikhi R, Rawat SS, Sharma J, Suri D. Genetics on early onset inflammatory bowel disease: an update. *Genes Dis*. 2020;7(1):93—106.
11. Das J, Sharma A, Jindal A, Aggarwal V, Rawat A. Leukocyte adhesion defect: where do we stand in circa 2019? *Genes Dis*. 2020;7(1):107—114.
12. Wang W, Yao T, Zhang T, et al. Selective immunoglobulin A deficiency (SIgAD) primarily leads to recurrent infections and autoimmune diseases: a retrospective study of Chinese patients in the past 40 years. *Genes Dis*. 2020;7(1):115—121.
13. Lin L, Wang Y, Liu L, et al. Clinical phenotype of a Chinese patient with RIPK1 deficiency due to novel mutation. *Genes Dis*. 2020;7(1):122—127.
14. Yang Lu, Xue X, Zeng T, et al. Novel biallelic TRNT1 mutations lead to atypical SIFD and multiple immune defects. *Genes Dis*. 2020;7(1):128—137.
15. Zhang L, Tang J, Sun L, et al. Three-dimensional printed tissue engineered bone for canine mandibular defects. *Genes Dis*. 2020;7(1):138—149.
16. Xiang J, Zhang Y, Tuo L, et al. Transcriptomic changes associated with PCK1 overexpression in hepatocellular carcinoma cells detected by RNA-seq. *Genes Dis*. 2020;7(1):150—159.

Surjit Singh*
Allergy Immunology Unit, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, 160012, India

Xiaodong Zhao
Chongqing Key Laboratory of Child Infection and Immunity, Ministry of Education Key Laboratory of Child Development and Disorders, National Clinical Research Center for Child Health and Disorders (Chongqing), Children's Hospital of Chongqing Medical University, Chongqing, 400014, PR China
Department of Rheumatology and Immunology, Children's Hospital of Chongqing Medical University, Chongqing, 400014, PR China

Huijie Zhang
The Editorial Office of Genes & Diseases, Periodical Press of Chongqing Medical University, Chongqing, 401331, PR China

*Corresponding author.
E-mail addresses: surjitsinghpgi@rediffmail.com, surjitsinghapc@gmail.com (S. Singh)

7 January 2020