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EDITORIAL

Primary immunodeficiencies: a diagnostic challenge?

Dirceu Solé

Universidade Federal de São Paulo, Escola Paulista de Medicina, Departamento de Pediatria, Disciplina de Alergia, Imunologia Clínica e Reumatologia„ São Paulo, SP, Brazil

Primary immunodeficiencies constitute an important aspect of daily clinical practice and are currently called ''Inborn Errors of Immunity (IEI)''. They represent a group that comprise of more than 400 diseases, mostly monogenic and associated with pathogenic variations of more than 430 genes.[1]

The IEI represent a group of diseases that primarily affect the components of the immune response and have a variable presentation depending on the immune defect manifestation.[1,2] Clinically, IEI have as their main clinical manifestations: increased susceptibility to infections, autoimmunity, inflammation, severe allergies and malignancy.[1,2] Generally, the most severe, life-threatening conditions start in the first months of life, which has caused IEI to be mistakenly associated with exclusive childhood diseases.

According to the most recent report by the International Union of Immunological Societies (IUIS), the identified IEI were classified in 10 groups: (a) immunodeficiencies that affect cell and humoral immunities; (b) immunodeficiencies combined with associated characteristics or syndromes; (c) predominantly antibody deficiencies; (d) immune dysregulation diseases; (e) quantitative or functional phagocyte defects; (f) innate immunity defects; (g) autoinflammatory diseases; (h) complement system deficiencies; (i) bone marrow failure or insufficiency and (j) IEI phenocopies.[1,2]

In the last two decades, molecular biology advances have allowed better knowledge of the immune system, as well as of the adaptive mechanisms that occur during the neonatal period, the transplacental transport of antibodies and during breastfeeding.[3,4] These aspects are addressed in the article on the acquisition of immunological competence, including how young infants are protected from diseases which allows them to have an adequate postnatal development. Innate immunity is represented by physical, chemical and biological barriers, epithelial cells, intraepithelial T lymphocytes, hair, cilia, mucus, macrophages, neutrophils, dendritic cells, natural-killer cells, and complement system proteins, whereas adaptive immunity is represented by T and Blymphocytes. Both types of immunity guarantee the body integrity, protecting it from harm.[3]

The absence or malfunction of any of these components can determine the clinical presentation of an IEI. Although the infectious, frequent, severe conditions that are sometimes limited to some specific infectious agents are the most indicated as suggestive of probable IEI, severe allergies, inflammatory processes, lymphoproliferation, autoimmunity and malignancies can also comprise the clinical picture of patients with IEI.[5] Obtaining clinical, personal and family data is of great importance. The identification of the pathogenic agent involved in the infectious conditions can very often lead us to the diagnosis of a certain immune system compartment impairment. This can facilitate the request for complementary tests, from a simple blood count, serum immunoglobulin levels, to complete sequencing of the exome or genome.[6]

Extensive anamnesis and clinical evaluation are the weapons that pediatricians have for a suspected diagnosis of IEI. Therefore, in this supplement, the warning signs are characterized,[7] as well as the clinical manifestations of the main groups of IEI, aiming to guide the pediatrician in the search for an initial complementary immunological assessment with the goal of identifying the most common IEIs. It is worth mentioning that the non-infectious manifestations of IEI are also addressed.

E-mail: sole.dirceu@gmail.com

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The acquisition of new diagnostic tools associated with molecular biology made it possible to increase the knowledge of medical genetics, which allowed fora better characterization of certain IEI patterns, in addition to establishing correlations with genetic variants carried by these patients. Initially limited to university or research centers, the access to these techniques is still difficult in our country. Nonetheless, the number of new IEIs has grown significantly. If, on one hand, they have enabled the definitive diagnosis of the disease, on the other hand they have allowed family genetic counseling and the implementation of better targeted and precise treatment, consequently improving the quality of life of these patients.[8]

In addition to addressing the immune system defects involved in each of the IEI groups, which include the characteristic clinical manifestations and associated diagnostic evidence, the therapeutic approach is also shown depending on the immune defect involved. Considerations about the different therapeutic approaches (general measures, antibiotics, among others) are also presented. Special emphasis is given to the replacement therapy with human immunoglobulins and curative treatment with hematopoietic stem cell transplantation from healthy individuals, or gene therapy.

In conclusion, this supplement discusses the screening for severe combined immunodeficiencies and a gamaglobulinemias. In brief, the possibility of measuring products released into the bloodstream during the development of B and T lymphocytes corresponds to a revolution in clinical immunology, since they infer defects in the development of these two cell types, allowing the investigation and diagnosis of severe diseases before their clinical manifestations. The indication of TREC (T-cell Receptor Excision Circles) and KREC (Kappa-deleting Recombination Excision Circles) in the neonatal period is a paradigm break, as it allows an early diagnosis and the implementation of effective treatments. A new era for children and their families with the decrease in the number of deaths and quality of life improvement will be possible with the implementation of large-scale screening.[9]

Conflicts of interest

The author declares no conflicts of interest.

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