Chapter 27

Approach to primary immunodeficiency

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ABSTRACT

Primary immunodeficiency diseases (PID) are inherited defects of the innate or adaptive arms of the immune system that lead to an increase in the incidence, frequency, or severity of infections. There may be defects in the adaptive arm of the immune system that include, combined immunodeficiency and antibody deficiency syndromes or by abnormalities in innate immunity such as disorders of phagocytes, the complement pathway, or Toll-Like receptor (TLR) mediated signaling. Recurrent sinopulmonary infections with encapsulated bacteria such as Haemophilus influenza type B or Streptococcus pneumoniae may be characteristic of an IgG antibody deficiency or dysfunction. Frequent viral, fungal, or protozoal infections may suggest T lymphocyte dysfunction. Multiple staphylococcal skin infections and fungal infections may imply neutrophil dysfunction or the hyper-IgE syndrome, and recurrent neisserial infection is a characteristic manifestation of late complement component (C5-9, or the membrane attack complex) defects. Recurrent viral or pyogenic bacterial infections often without the presence of a significant inflammatory response suggest a defect in TLR signaling. Mycobacterial infections are characteristic of defects in interleukin (IL)-12, interferon (IFN) gamma, or their receptors. Screening of newborns for T-cell lymphopenia using a polymerase chain reaction to amplify T-cell receptor excision circles (TRECs), which are formed when a T cell rearranges the variable region of its receptor, serves as a surrogate for newly synthesized naive T cells. Because of very low numbers of TRECs, severe combined immunodeficiency, DiGeorge syndrome, and other causes of T-cell lymphopenia have been identified in newborns.


Primary immunodeficiency diseases (PID) are inherited defects of the innate or adaptive arms of the immune system that lead to an increase in the incidence, frequency, or severity of infections.1-3 In general, PIDs are uncommon, but the associated morbidity and mortality may be high. The overall prevalence of PID is not known but is estimated to be 1:10,000 live births. However, IgA deficiency occurs more frequently; as many as 1:333 individuals may be affected. An early diagnosis of PID is essential because prompt treatment may help prevent associated morbidity and mortality.

PRIMARY IMMUNE DEFICIENCY DISEASES

PIDs may be caused by defects in the adaptive arm of the immune system that include combined immunodeficiencies (CID) and antibody deficiency syndromes or by abnormalities in innate immunity such as disorders of phagocytes, the complement pathway or Toll-like receptor (TLR) mediated signaling.

Severe CID (SCID), results from the absence of T lymphocytes or T lymphocyte function with the presence or absence of B cells and/or natural killer (NK) cells. Even if B cells are present, antibody production is impaired because of lack of T cell help. SCID is characterized by early onset of infections caused by bacterial, viral, or fungal pathogens; chronic diarrhea; and failure to thrive. Pneumocystis jiroveci pneumonia is commonly observed in these patients as well as pulmonary infections by adenovirus, RSV, CMV, and parainfluenza viruses. Isolated CD4 T-cell deficiency caused by MHC class II deficiency or idiopathic CD4 lymphopenia and isolated CD8 T-cell deficiency from absence of MHC class I molecule expression or caused by ZAP 70 also cause a severe T-cell immunodeficiency.

DiGeorge syndrome results from a developmental defect in the third and fourth pharyngeal pouches resulting in impaired formation of the thymus, parathyroid glands, and the heart. Affected patients have a spectrum of T-cell deficiency from mild or moderate in partial DiGeorge syndrome to severe T-cell deficiency in complete DiGeorge syndrome, which is a condition