Overview of Immunodeficiency Disorders

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KEYWORDS

• Immunodeficiency • Antibody deficiency • Autoimmunity • Immune defect
• Innate immune defect • Lymphoproliferation • Immune dysregulation

KEY POINTS

- Primary immunodeficiencies lead to various combinations of recurrent infections, autoimmunity, lymphoproliferation, granulomatous disease, atopy, and malignancy.
- Immunodeficiency caused by defects in more than 1 gene can lead to similar manifestations and a defect in the same gene can cause varied manifestations.
- High index of suspicion along with meticulous history and physical examination are a key to early diagnosis of primary immunodeficiency.
- Early primary immunodeficiency diagnosis can be achieved with improved access to validated immunologic laboratory tests.

INTRODUCTION

In the past, primary immunodeficiency disorders (PIDs) have been described as diseases caused by 1 or more defects of the immune system, leading to increased susceptibility to infections. It is now known that PIDs are a group of heterogeneous disorders with immune system abnormalities characterized by various combinations of recurrent infections, autoimmunity, lymphoproliferation, granulomatous process, atopy, and malignancy (**Fig. 1**). The overall clinical picture is dictated by the specific type of underlying immune defect. Based on the type of PID, the types of infections can vary. Although bacterial infections may be a key feature of B-cell defects, infections with diverse pathogens (eg, viruses, fungi, and bacteria) are a feature of combined T-cell and B-cell immunodeficiencies. Similarly, autoimmune manifestations can range from autoimmune

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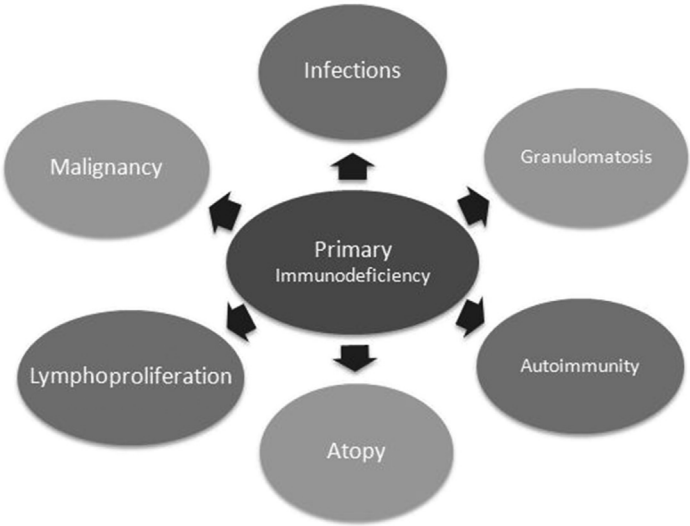

Fig. 1. Features of primary immunodeficiencies. (*Data from* Refs.[1,2,5–17,19–26])

cytopenias secondary to B-cell defects to systemic lupus erythematosus in complement disorders. Some PIDs (eg, X-linked lymphoproliferative disease) are characterized by lymphoproliferation, whereas others (such as those associated with chronic granulomatous disease) manifest with cutaneous, respiratory, or gastrointestinal tract granulomas caused by immune dysregulation. Although lymphomas and leukemias are the most common malignancies noted, other types of malignancies may also be seen. Atopic features such as asthma, atopic dermatitis, and food allergies can be observed in some patients with T-cell defects. Hence, the types of manifestations and involvement of other systems can provide a clue to the type of PID.

HISTORY

A few immune disorders, like ataxia telangiectasia (1926) and Wiskott-Aldrich syndrome (WAS) (1937), were discovered in the early part of the twentieth century. However, the landmark in the history of PIDs was the discovery of agammaglobulinemia by Colonel Ogden Bruton in 1952. In 1950, Eduard Glanzmann and Paul Riniker found that *Candida albicans* infections are associated with an absence of lymphocytes.[1] Two Swiss groups from Bern and Zurich (Hassig Cottier; R. Tobler and Walter Hitzig) discovered similar patients in 1958 and recognized the condition to be an immunodeficiency. The condition that was initially coined as Swiss-type agammaglobulinemia was renamed as severe combined immunodeficiency (SCID) by the World Health Organization (WHO) in 1970.[1] In 1954, Robert Good discovered a fatal granulomatous disease that is now known as chronic granulomatous disease (CGD).[1] Over the last 65 years, the field of PIDs has advanced greatly. With the advent of cutting-edge genetic technology, more than 240 PIDs have been discovered and the number continues to increase.[2]

EPIDEMIOLOGY

The prevalence of PID varies depending on the type of immunodeficiency. Although selective immunoglobulin (Ig) A deficiency is common (1 in 223 to 1 in 1000),[3] other immunodeficiencies, such as SCID, are rare (1 in 58,000).[4] Because immunodeficiencies are