Primary Immunodeficiency Masquerading as Allergic Disease

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KEYWORDS

• Primary immune deficiency • Corticosteroids • Eczema • Elevated IgE
• Allergic disease

KEY POINTS

- Primary immune deficiencies (PIDs) are uncommon diseases, including several with overlapping clinical presentations to common allergic and autoimmune diseases.
- Early recognition and diagnosis of PIDs is critical.
- Immune suppression should be initiated judiciously because it can increase the susceptibility to life-threatening diseases in PID patients.

INTRODUCTION

Primary immune deficiencies (PIDs) are an uncommon heterogeneous group of diseases that result from fundamental defects in the proteins and cells that enable specific immune responses. Most are inherited and often appear in family members. Remarkably, many of these diseases do not demonstrate predictable clear-cut clinical patterns. For many, the hallmark is an increased susceptibility to infection; and different pathogens associate with different defects of the immune system. The true incidence and prevalence of these primary immunodeficiencies are unknown, but are estimated to be 1:10,000 to 1:2000 from registries in more than 40 countries.[1] This is likely an underestimation because many cases remain undiagnosed; a random telephone survey in the United States estimated the prevalence of all PIDs at 1:2000 to 1:800.[2] Early diagnosis of a PID has a significant bearing on outcome. For example, newborn screening for severe combined immune deficiency (SCID) has resulted in important early diagnoses and when treated with hematopoietic stem cell transplantation (HSCT) before 3.5 months of age, a 94% success rate can be achieved compared with older individuals with infections at the time of transplant (50%).[3]

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What is increasingly being recognized is that common allergic symptoms can also be manifestations of an underlying and severe immune deficiency (Fig. 1). The immune system relies on a complex balance of activation, to protect against invading pathogens, and control, to discriminate between self, nonself, and foreign matter. Hypersensitivity (allergic) reactions (eczema, allergic rhinitis, asthma, and food allergies) are exaggerated immune responses against specific allergens. Classic testing used to investigate allergic diseases often reveals increased immunoglobulin (Ig)E, peripheral blood eosinophilia, and immediate skin responses after percutaneous or intradermal injection. It is now clear that some of these PIDs do not manifest with a predominant susceptibility to infection, but rather present with what seems to be more common allergic symptoms or autoimmunity.[4] Recognition of these immunodeficiencies is important because their treatments are profoundly different than the treatments for an allergic condition, the latter often involving use of immunosuppressive therapies. In PID patients, further suppression of the immune system increases susceptibility to a life-threatening event, namely, infection. If the classic allergic triad includes increased IgE, eosinophilia, and eczema, then under this umbrella are a number of genetically defined PIDs that masquerade as allergy and warrant different therapeutic approaches (Table 1).

ALL THAT ITCHES IS NOT ALWAYS ECZEMA

Eczema is a complex, chronic, relapsing inflammatory skin disorder with a lifetime prevalence in the United States of 17%.[5] Interestingly, 80% have an elevated serum IgE.[6] It is the earliest part of the allergic march toward allergic rhinitis and asthma, with 66% of patients progressing to develop asthma plus at least 1 allergy by 3 years of age.[7]

Pathophysiology

Eczema and atopic dermatitis present early in infancy, usually between 1 and 6 months of age. Resolution occurs in 50% by adolescence, but factors that suggest a poorer prognosis include family medical history of eczema, early infantile disease, gender (female), coexistent allergic rhinitis, or asthma.[8] Although the exact mechanism remains unclear, breaks in the skin barrier lead to sensitization to allergens, increased IgE levels, and increased numbers of eosinophils.

PRIMARY IMMUNE DEFICIENCY PRESENTING WITH NEWBORN AND INFANT ECZEMA

Although a common condition, eczema in a newborn warrants a number of diagnostic considerations and concerns. Severe whole body dermatitis appearing as an

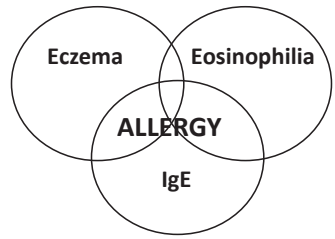

Fig. 1. The allergic triad. Allergic diseases share common factors with primary immunodeficiencies including skin rashes such as eczema, increased immunoglobulin (Ig)E, and eosinophilia.