Atopic Dermatitis and Allergic Urticaria

Cutaneous Manifestations of Immunodeficiency

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KEYWORDS

• Atopic dermatitis • Urticaria • Immunodeficiency

KEY POINTS

- Atopic dermatitis and allergic urticaria are common conditions of the skin that can also be the presenting symptoms of uncommon diseases.
- Defects leading to immunodeficiency may be associated with atopic dermatitis or allergic urticaria.
- Unusually severe or otherwise atypical presentations of atopic dermatitis or allergic urticaria may lead to clinical suspicion of an underlying immunodeficiency.

...for people who feel disgraced blush, and those who fear death turn pale.[1]

INTRODUCTION

Alterations in the skin can give the astute clinician insight into the inner workings of the immune system that may otherwise remain invisible. The skin can be altered in numerous ways via numerous pathologic mechanisms. This review focuses on 2 of those alterations: atopic dermatitis (AD) and allergic urticaria (AU). Although AD and AU are common in themselves, they may also serve to be the presenting sign of an uncommon underlying disease. More specifically, this review focuses on how these 2 conditions may be accompanied by other sentinel symptoms serving to comprise a distinct syndromic phenotype. The presence of the syndromic phenotype may then serve as a clue to the presence of an underlying immune defect. The objective of this review is to provide a differential diagnosis for both conditions as they relate to those immune defects to provide a diagnostic pathway to aid in establishing a diagnosis. Infectious, oncologic, or other causes leading to AD and AU will not be considered here.

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ATOPIC DERMATITIS

AD is a chronic condition characterized by pruritic skin lesions related to epithelial barrier dysfunction with an immunologic involvement. It affects between 10% and 20% of children in developed countries, making it one of the most common diseases of childhood.[2] Adult presentation of AD should prompt consideration of an alternate diagnosis. AD is a complex disorder consisting of a constellation of historical and physical features but lacking a pathognomonic sign or biomarker. As such, diagnostic criteria have been established to support AD as a clinical diagnosis. The modified UK Working Party's Diagnostic Criteria for Atopic Dermatitis[3] (**Box 1**) is widely used and validated.[4] The lesions can affect the scalp, face, and extensor surfaces in infants, whereas the flexor surfaces become more commonly affected in older children and adults. Immunoglobulin E (IgE) and peripheral eosinophilia frequently accompany AD. The loss of skin epithelial barrier integrity is a key concept in understanding the structural defects leading to AD. Genetic studies of AD have been able to provide insights into some of the genes involved in epithelial integrity.[5] Treatment of AD is meant to reestablish epithelial barrier integrity and limit the effects of allergic inflammation.

ALLERGIC URTICARIA

Urticaria can be either acute or chronic and is characterized by mast cell degranulation leading to a raised central wheal with surrounding erythematous flaring. Mast cell degranulation may be prompted by a variety of triggers. As such, urticarial lesions may be due to physical, allergic, or autoimmune causes. Physical urticarias cause direct mast cell degranulation and comprise 20% to 30% of chronic urticaria.[6] Stimuli can include heat, cold, and vibration even in the absence of specific antigens. In addition, autoantibodies are associated with 30% to 50% of chronic urticaria.[7] Acute urticarial lesions may develop as a result of IgE-mediated responses of mast cells to a specific antigen. Treatment of urticaria is aimed at limiting the affects of products released during mast cell degranulation as well as stabilizing or otherwise preventing mast cells from degranulating in the first place. Although physical and autoimmune urticaria needs to be within the differential of chronic urticaria, this review focuses on conditions for which urticaria is feature of a broader syndromic phenotype.

Box 1
Revised criteria for the diagnosis of atopic dermatitis

- Pruritis

Plus 3 or more of the following:

- History of flexural dermatitis (front of elbows, back of knees, front of ankles, neck, around the eyes) or involvement of cheeks and/or extensor surfaces in children aged less than 18 months
- Visible flexural dermatitis involving the skin creases (or the cheeks and/or extensor surfaces in children aged <18 months)
- History of a dry skin in the past year
- History of asthma or hay fever (or atopic disease in a first degree relative in children <4 years of age)
- Onset less than 2 years of age (for children aged $\geq$4 years at time of diagnosis)