CHILDHOOD ATOPIC DERMATITIS AND SYSTEMIC COMORBIDITIES

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ABSTRACT
Atopic dermatitis (AD) is now becoming very common and is being diagnosed in a vast majority of children. AD is known to be associated with several comorbidities. The connection seems to be due to more than one reason – genomes, skin barrier dysfunction, and inflammation.

Keywords: Atopy, Dermatitis, Comorbidities.

INTRODUCTION

The relationship between atopic dermatitis, food allergies and asthma is believed to be due to altered skin barrier function present in atopic dermatitis, which predisposes to cutaneous allergen sensitization. Mutations in the filaggrin gene lead to barrier dysfunction, allowing the allergens to be transferred across the skin to Langerhans cells leading to a TH2 immune response with IgE production by B cells. Asthmatic patients with filaggrin mutations have more difficult to manage asthma, though the filaggrin is not expressed on the respiratory epithelia. In children with AD there is an increased risk of allergies, mental health, and infectious diseases compared to their normal counterparts.

Cutaneous infection:
Patients with AD have increased colonization with staphylococcus aureus and have a higher risk of developing bacterial and viral infections. Recent attention has been paid to the pathogenetic role of defects of TLR2 (Toll like Receptors).

TLR2 recognizes peptidoglycan and lipoteichoic acid, components of the cell wall of S. aureus and other gram-positive bacteria. It is interesting that obesity is associated with numerous effects on the innate immune system, including TLR2 expression. It is also possible that obesity predisposes AD patients to even higher risk of cutaneous infections [1,2].

Atopic march
The development of AD often heralds the beginning of the “atopic march,” a term used to describe the increased risk these children have of developing one or more of the atopic diseases, which include asthma, food allergy, and allergic rhinitis. Studies found that childhood eczema was associated with increased incidence of asthma in childhood, adolescence and adult life. Childhood eczema predicts atopic but not nonatopic asthma in adulthood. Risk factors for the development of asthma in children with AD include persistent or more severe AD, IgE sensitization, and filaggrin deficiency. Filaggrin deficiency, even in the absence of AD, may increase the risk for asthma supporting the idea of epicutaneous sensitization. The hygiene hypothesis states that atopic diseases result from reduced microbial exposure during early childhood, leading to the defective development of the immune system. Recently, the finding that mutations in the epidermal gene, filaggrin, predispose to the development of AD and asthma provides a new possible explanation for the link between AD and allergic diseases [3,4].

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Metabolic disorders and AD
There are conflicting results about the association between AD and diabetes. Multiple large-scale epidemiological studies demonstrated that obesity is a risk factor for atopic disorders, including asthma and atopy. FLG and other genetic mutations involved in AD result in both an AD phenotype and increased risk for obesity and its sequel. Obesity is considered to be a trigger or exacerbating factor for AD, and not merely an epiphenomenon. There is growing use of the term “overweight hypothesis”, which states that being obese early in childhood may guide the immature immune system towards a pro-atopic state or inflammatory state.

Adipokines play an important role in allergic inflammation. Adiponectin tend to be lower in obesity. Leptin is an adipokine that is unregulated in obesity. It has been shown to induce eosinophils in vitro and stimulate chemokines. Leptons may play a role in allergic asthma.

The associations between AD, obesity, and other metabolic factors have important clinical ramifications. These associations highlight the importance of maintaining ideal BMI, especially during early childhood, and suggest that weight loss may actually improve AD in some children [5].

Cancer and Atopic Dermatitis:
Older literature suggests having atopic disease decreases one’s risk of a variety of cancers. More recent data suggest a more mixed picture, with the protective effects of various atopic diseases being specific to cancer type. In addition, some other studies have found increased rates of a variety of cancers in patients with a history of AD, including cutaneous T cell lymphoma and brain cancer. The risk of lymphoma is likely to be increased in AD, especially in those patients with severe disease [6,7].

Mental health and Atopic Dermatitis:
Children with AD demonstrate psychological disturbances more frequently than do their healthy peers, and that this association correlates with the severity of the skin disease. Having a child with AD negatively affects the mental state of parents as well. Mothers of children with AD report higher stress levels, less employment, more difficulty with child discipline, and a lack of social support networks compared to parents in a control group. There is a relationship between AD and attention deficit hyperactive disorder (ADHD). Despite the compelling evidence of a comorbidity of AD and ADHD the underlying pathophysiologic mechanisms linking the two disorders are unknown. The manifestation and chronification of AD in early childhood increases the risk for ADHD. Main diagnostic schemata for childhood ADHD are defined by three core symptoms hyperactivity, inattention and impulsivity that had to be present before school age. A dose-dependent relationship between the reported severity of AD and the prevalence of ADHD, suggests a causal relationship. Several studies have shown an association between atopic disease and anxiety, depression, and autism. Controlled studies have found increased rates of anxiety, depression, and suicidal ideation in adults with AD that correlate with disease severity [8,9].

Erectile dysfunction and Atopic Dermatitis:
A recent population-based study of 23,982 subjects from the Taiwan National Health Insurance program found that erectile dysfunction (ED) was associated with a higher prevalence of AD than non-ED controls.

ED in AD patients may have a neuropathic or vascular occlusive component secondary to comorbidities (e.g., obesity and/or diabetes) [10].

Fatty liver and Atopic Dermatitis:
Children with AD were found to have increased fatty liver. Children with AD had increased serum leptin levels and even higher leptin levels in AD with fatty liver. It is possible that the association between fatty liver and AD is secondary to circulating free fatty acids in chronic obesity [11].

CONCLUSION
AD’s negative impact often extends beyond the skin. Children with AD experience increased rates of infectious, mental health, and allergic diseases compared to their non-atopic counterparts. The mechanisms underlying these associations remain unidentified. New insights from genetic and epidermal research identify the skin barrier as a primary initiator of AD. Epicutaneous sensitization represents an exciting new model which links a disrupted skin barrier to the later development of IgE-mediated diseases in patients with AD. Recent epidemiological studies have identified new comorbidities linked to AD as well, including several mental health disorders and obesity.

REFERENCES
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