

Short Commentary

Atopic March; The Skin is the Clue

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Atopic Dermatitis (AD) is a chronic relapsing inflammatory skin disease characterized by recurrent eczematous skin lesions and intense itching. Globally, it affects 10-30% of children and 2-10% of adults, with a two- to three-fold increase in prevalence noted over the last decades [1]. AD pathogenesis is multifactorial, and involves a complex interaction between environmental factors, genetics, the immune system, and other factors such as microbiome, which contribute to skin barrier dysfunction and inflammation [2-4].

The concept of the atopic march provides a novel insight for the prediction, prevention, and treatment of atopic diseases. Skin barrier dysfunction has been proposed to be the first step in the development of atopic march as well as AD. These factors have been used to develop targeted therapeutic and preventative strategies of AD [5].

Cross-sectional and longitudinal studies have speculated that allergic diseases occur following a time-based order: from AD and food allergy in infancy to progressive development into Allergic Asthma (AA) and Allergic Rhinitis (AR) in childhood [6].

Dharmage SC et al. reported that, in infants who have AD within 2 years of age, the incidence of AA and AR increased dramatically during age 6–7 years. Specifically, early-onset, persistent, IgE-related AD was associated with a higher risk of developing AA and AR [7]. A longitudinal study on a Canadian birth cohort (2,311 children) has revealed that AD with sensitization at 1 year of age increased the prevalence of AA and AR at 3 years of age more than 11- and 7-fold, respectively [8]. In a study from Thailand, 102 children with AD (diagnosed at 1.5 years of age) were reviewed, and subsequently, AR and AA were diagnosed in 61.8 and 29.4%, respectively. Concomitantly, 67% of the AA patients also suffered AR [9]. A prospective cohort study (3,124 children aged 1–2 years) revealed that, compared with children with no history of AD, those once having AD, particularly moderate-to-severe, early persistent AD, were more prone to develop AA and AR [10].

Treatments to relieve itching in AD patients prevent skin damage aggravated by scratching. Ketotifen, an H1 antihistamine, significantly lowered AA risk in infants with AD or other pre-asthmatic conditions [11,12]. Dupilumab is a human IgG4 monoclonal antibody against IL-4 receptor subunit alpha (IL-4R α), and it can inhibit IL-4 and IL-13 signaling pathways by

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interacting with IL-4R α [13]. Dupilumab has been approved to treat infants, children and adults with moderate-to-severe AD [14]. Several trials revealed that dupilumab is effective and safe in patients with AD, severe AA and chronic AR [15]. These data suggest that dupilumab treatment in patients suffering from AD associated comorbidities may be a suitable single therapy to control AD, AA and AR. Such an outcome, although confirmation by trials is warranted, suggests the possibility to treat different atopic disorders with dupilumab, with favorable effects especially under the cost-effectiveness aspect [16].

In conclusion, the worldwide increase of atopic diseases' burden with the lowered quality of life, and the associated comorbidities with the theory of atopic march enhances our understandings of the pathophysiology of atopic diseases and further highlights the concept of early detection, prevention, and treatment of children at risk of allergic diseases. The discoveries mentioned above strongly support the natural process of the atopic march and the possibility of using a single treatment option to control all atopic diseases morphologies in the near future.

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