異位性皮膚炎的致病機轉與臨床表徵

Atopic dermatitis: Pathogenesis and clinical manifestation

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Atopic dermatitis (AD) is a complex disease with multifactorial etiology, involving immune system dysregulation and epidermal barrier dysfunction, which are both influenced by genetic and environmental factors. Both the microbiota and the sensory nerves contribute to disease propagation by driving each loop through barrier dysfunction and keratinocyte activation in AD

Barrier dysfunction due to impaired terminal differentiation of keratinocytes is thought to allow increased penetration of cutaneous antigens that results in the initiation of AD. Barrier dysfunction of the skin is considered central to AD. Damaged keratinocytes produce alarmins such as TSLP, IL-25 and IL-33 following barrier disruption. Alarmins are a divers group of proteins and can induces inflammation. These mediators expand and activate skin-resident group 2 innate lymphoid cells (ILC2s) and Th2 cell-mediated immune responses. Type 2 inflammation is considered to be essential for the pathogenesis of AD in lesional and even nonlesional skin. Among type 2 immune mediators, IL-4 and IL-13 have been demonstrated to play a key role in acute lesions. IL-31, a cytokine associated with itch, shows large increases in acute lesions. Besides type 2 cytokines, Th22, Th17/IL-23, and Th1 cytokine pathways also have a role in disease, particularly in some AD subtypes. Th17-associated molecules are consistently upregulated in both patients with acute and those with chronic AD. Th2 and Th22 responses are intensified in chronic AD lesions, with parallel activation of the TH1 axis rather than a ‘‘switch’’ to a TH1-only signature. IL-22 has also been identified as a key mediator of epidermal hyperplasia.

Pruritus is the most suffering symptom in AD patients. The skin is innervated by a meshwork of peripheral nerves consisting of sparse autonomic fibers and abundant sensory fibers, along with inflammatory type 2 mediators, such as TSLP, IL-4, IL-13 and IL-31, that drive the itching that exacerbates the disease via scratching.

This complex pathophysiology translates into a heterogeneous clinical presentation (phenotype) with differences in age of onset, lesion localization, severity, sensitization profiles, disease persistence, presence of comorbid atopic and nonatopic conditions and longitudinal trajectories of disease progression.

In this lecture, we will detailing talk about the complex pathophysiology and clinical presentation of AD.