Editorial
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Role of TSLP in Nasal Polyp Inflammation

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Thymic stromal lymphopoietin (TSLP) is an epithelial cell-derived cytokine expressed in skin, gut, lungs, and thymus. TSLP signals via the TSLP receptor (TSLPR), a heterodimer of the IL-7 receptor α chain and TSLPR chain. The TSLPR chain is closely related to the common receptor γ chain, which is expressed on a wide range of cell types in allergic inflammation. TSLP exerts a profound influence on the polarization of dendritic cells to drive T helper (Th) 2 cytokine production.[1] TSLP also promotes T-cell proliferation directly in response to T-cell receptor activation and Th2 cytokine production, and supports B-cell expansion and differentiation. TSLP further amplifies Th2 cytokine production by mast cells and natural killer T cells.[2] These properties confer a critical role on TSLP in driving Th2-mediated inflammation. Several studies have suggested an active role of TSLP in allergic diseases, including atopic dermatitis, asthma, and allergic rhinitis, because increased TSLP expression was noted in target tissues.[3,4] Additionally, increased TSLP expression is seen in inflammatory conditions in response to a wide variety of allergens and viral infections[5-7] and in eosinophilic esophagitis.[8,9] Regarding the role of TSLP in nasal polyps, one study suggested increased TSLP expression in nasal polyp tissue, but it did not demonstrate any relationship between TSLP and any major inflammatory parameter, such as eosinophilic infiltration.[4]

The study by Kimura et al.[10] in this issue of the AAIR clearly demonstrated increased in vivo expression of TSLP mRNA and protein in the epithelial and infiltrating cells of patients with nasal polyps regardless of their atopic status. Furthermore, they showed that the TSLP expression correlated closely with the degree of eosinophilic inflammation and local IgE level in nasal polyp tissue. These findings suggest a potential role of TSLP in the pathogenesis of chronic inflammation found in nasal polyps via regulating Th2 and eosinophilic inflammation. Moreover, the authors localized the source of TSLP within the nasal polyp tissue, and noted TSLP expression in inflammatory cells, various structural cells, and epithelial cells. These levels correlated significantly with the number of eosinophils in nasal polyp tissue, indicating that TSLP derived primarily from epithelial cells has a role in regulating eosinophilic inflammation in nasal polyps, possibly by driving Th2 type inflammation, which upregulates eosinophilic chemoattractants.

Several points should be clarified in future studies. First, increased TSLP expression was noted in both atopic and non-atopic groups. In the atopic group, allergen exposure could increase TSLP expression, as described in previous studies, because it was demonstrated that allergen exposure increased TSLP production from bronchial epithelial cells, which would enhance Th2-derived inflammation in asthmatic airways.[11,12] However, the mechanism of elevated TSLP expression in the nasal polyp tissue of the non-atopic group is not understood. Second, because the mast cell is a major inflammatory cell in nasal polyp tissue and TSLP can active mast cells as well as eosinophils, further studies should investigate the roles of TSLP in the survival and recruitment of mast cells in nasal polyps.

Recent interesting findings suggest that respiratory viral infections and the recruitment of Th2 cytokine-producing cells amplify Th2 inflammation via the induction of TSLP.[5] The clinical features of aspirin-exacerbated respiratory disease (AERD) include a very high prevalence of chronic rhinosinusitis and nasal polyposis in which Th2 and eosinophilic inflammations are the major findings.[13] Compared with other types of nasal polyp, the increased activated status of eosinophils is a characteristic finding of chronic nasal polyp tissue in AERD patients.[14] In this

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study, the subjects were classified into two groups according to their atopic status. They did not enroll nasal polyps from AERD patients. Thus, the next strategy is to evaluate the role of TSLP in chronic eosinophilic inflammation of nasal polyp tissue in AERD patients compared with non-AERD patients.

Several studies suggest that AERD develops as a result of chronic viral infection,[15-17] and respiratory viral infections are the most frequent exacerbating factors in AERD patients.[18] Moreover, a recent study showed that two genetic polymorphisms of the Toll-like receptor, *TLR3*, at -299698G>T and 293391G>A, were associated with the AERD phenotype.[19] Further studies are needed to investigate the role of TSLP in the development and exacerbation of symptoms in AERD patients.

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