EDITORIAL

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Staphylococcal enterotoxin B sensitization in eosinophilic asthma

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Staphylococcus aureus is a Gram-positive bacterium that commonly colonizes the human body, occasionally emerging as a significant pathogen. Its primary colonization sites include the anterior nares in humans [1], but it can also inhabit other regions, including the axilla, groin, pharynx, intestine, and perineum. The prevalence of nasal *S. aureus* colonization varies regionally [2], typically affecting 20–30% of the healthy population. However, individuals with chronic airway diseases, including asthma and nasal polyps, exhibit significantly higher *S. aureus* colonization rates, reaching up to 90% [3].

Colonized *S. aureus* may release various IgE-reactive enzymes and toxins, including staphylococcal enterotoxins (SEs), serine protease-like proteins, and fibronectin-binding protein [4]. Elevated colonization rates correlate with increased IgE formation against SEs in patients with chronic airway diseases, such as chronic rhinosinusitis and asthma, compared to healthy individuals.

SE-IgE sensitization, defined as a high serum level of SE-IgE, plays a significant role in the pathogenesis of asthma, chronic rhinosinusitis, and atopic dermatitis [5]. SE-IgE sensitization is associated with severe asthma, increased risk of severe exacerbations, and eosinophilic inflammation. *S. aureus* induces SE-IgE-sensitized eosinophilic inflammation through multiple mechanisms [6]. The bacterium releases δ-toxin, damaging epithelial barriers and facilitating allergen penetration. SE and other superantigens induce excessive release of Th2 cytokines, including interleukin-4 (IL-4), IL-5, and IL-13, from tissue T cells. Recent studies have reported eosinophilic migration through the human airway epithelium in response to *S. aureus* exposure, resulting in eosinophil extracellular trap formation and persistent inflammatory responses. IL-5-activated eosinophils can be recruited by *S. aureus* to further degrade the epithelium by inducing the release of major basic proteins, the epithelial-toxic components of the eosinophil extracellular trap.

SEs and other T cell superantigens are exceptionally stable and significantly influence the immune system. They can circumvent the T cells' requirement for antigen recognition by directly crosslinking T cell receptors with major histocompatibility complex class II molecules, leading to the polyclonal activation of T cells, including T helper-2 cells, regardless of their antigen specificity. *S. aureus* can secrete staphylococcal protein A, which acts as a B cell superantigen to induce mast cell degranulation [6].

Based on these findings, several studies have examined the associations between *S. aureus* colonization and asthma. A meta-analysis in Korea reported a significant association between nasal *S. aureus* colonization and adult asthma (odds ratio: 1.19; 95% confidence interval: 1.06–1.34; I^2 = 1%) [7]. Investigating asthma severity, Caruso et al. [8] reported that SE-B-specific IgE was associated with chronic rhinosinusitis with or without nasal polyps in severe asthma. However, there was no correlation between SE-B-specific antigens and eosinophilia, severity, or steroid dosage. Several recent studies have focused on *S. aureus* enterotoxins and asthma severity, particularly airflow limitations. Schleich et al. [9] demonstrated that asthma patients sensitized to SEs had later disease onset, higher incidence of exacerbations and nasal polyps, and more severe airway obstruction. They also had higher fractional exhaled nitric oxide and sputum concentrations of IgE and IL-5. Won et al. [10] recently reported a 2-year follow-up study that demonstrated correlations among SE-IgE sensitization, asthma exacerbations, and fixed airflow limitation in elderly asthmatics, which suggest-

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ed that SE-IgE sensitization may mediate airway remodeling.

A study by Sim et al. [11] in the current issue of the *Korean Journal of Internal Medicine* found that high SE-B-specific IgE levels correlated strongly with eosinophilic activation markers, including eosinophil cationic protein and eosinophil-derived neurotoxin. This supports the possibility that SE-B-specific IgE sensitization might be associated with the pathogenesis of eosinophilic asthma. This study contributes to a deeper understanding of the asthma phenotype through the association of *S. aureus* sensitization with eosinophilic inflammation.

In conclusion, *S. aureus* plays a prominent role in orchestrating severe airway inflammation in asthma.

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