Mucosal Cytokine Expression in Allergic Rhinitis

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Key Words

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Introduction

Allergic rhinitis is associated with mucosal inflammation characterised by an epithelial accumulation of activated mast cells and eosinophils, an increase in eosinophils within the lamina propria and local up-regulation of the endothelial expression of leucocyte endothelial cell adhesion molecules. These cellular changes, which are triggered by antigen recognition, are considered to be cytokine orchestrated [1]. Attention has focused on the interleukin (IL)-4 family of cytokines encoded on chromosome 5 [IL-3, IL-4, IL-5, IL-13 and granulocyte/macrophage-colony-stimulating factor (GM-CSF)] as potential key cytokines in this process, along with tumour necrosis factor (TNF)- α . These cytokines may be generated by the Th2 subpopulation of T lymphocytes, because the cytokine profile of this cell population includes IL-3, IL-4, IL-5, IL-13, TNF- α and GM-CSF.

To investigate the expression of cytokines relevant to allergic inflammation and to identify their cellular localisation within the nasal mucosa, we have undertaken specific immunohistochemistry staining of thin sections of inferior turbinate biopsies from patients with perennial allergic rhinitis and, for comparison, from non-atopic healthy volunteers [2,3].

Subjects and Methods

Fifteen atopic house-dust-mite-allergic patients with perennial rhinitis (7 men/8 women, mean age 40.5 years) and 12 healthy non-atopic non-rhinitic volunteers (4 men/8 women, mean age 35.6 years) participated in the study. None of the rhinitic subjects, who were all symptomatic, were receiving topical or systemic corticosteroids.

Nasal biopsies were taken under direct vision from the inferior or inferomedian border of the inferior turbinate after prior local anaesthesia with topical 1% tetracaine containing 1:10,000 adrenaline. The biopsies were immediately fixed in ice-cooled acetone and processed subsequently into glycolmethacrylate resin. Immunostaining was undertaken for IL-4 using monoclonal antibodies (mAbs) 4D9 and 3H4, IL-5 (mAbs 7 and 8), IL-6 (mAb 104-B11), IL-8

(mAbs 499/A5/A7) and TNF- α (mAb 52B83) and the positive cells, detected by the streptavidin-biotin peroxidase system, enumerated both within the epithelium (cells/mm epithelium) and submucosa (cells/mm²). Additional thin sections (2 μ) were immunostained for mast cells (AA1), eosinophils (EG2) and T lymphocytes (UCHT1) to localise the cytokine positive immunostaining to specific cell types.

Results

The nasal biopsies of rhinitic subjects contained more eosinophils in the submucosa and epithelium and more mast cells within the epithelium than the normal volunteers.

IL-4, -5, -6 and -8 along with TNF- α immunoreactivity was present in biopsies from both rhinitic and non-rhinitic subjects. There were significantly greater submucosal numbers of IL-4-immunoreactive cells in the rhinitics for both

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4D9 and 3H4 (medians 27.4 and 35.6, respectively) in comparison with the healthy controls [medians 22.5 ($p < 0.08$) and 14.5 ($p < 0.02$), respectively]. The two IL-4 antibodies gave a different pattern of immunostaining, 4D9 staining cytoplasmic IL-4 and 3H4 delineating cell-surface-associated IL-4. No differences were identified between the two groups in the number of IL-5-, IL-6-, IL-8- or TNF- α -immunoreactive cells. IL-8 was almost exclusively present within the nasal epithelium, IL-4, IL-5, IL-6 and TNF- α were predominantly identified in association with mast cells, with a small percentage of eosinophils also revealing positive immunoreactivity for IL-4 and IL-5.

Discussion

These studies identify the presence of performed cytokines within the nasal mucosa in both the normal nose and in perennial allergic rhinitis. The cytokines are predominantly within mast cells with, in addition, some IL-4 and IL-5 stored in eosinophil granules and IL-8 expressed on the airway epithelium. No immunolocalisation of preformed cytokines was evident in T lymphocytes, compatible with the inability of these cells to store products. The differing pattern of IL-4 immunoreactivity seen with the two antibodies suggests active IL-4 secretion in rhinitis and identifies a potential role for mast cell cytokine secretion in the genesis and maintenance of chronic airway inflammation in rhinitis.

References

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