Airway-Like Inflammation of Minor Salivary Glands in Bronchial Asthma

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Key Words

Minor salivary gland
Asthma inflammation
Endothelial cell
Lymphocyte
Mast cell

Abstract

Bronchial asthma is characterized by a chronic inflammation with accumulation of eosinophils, mast cells and activated T lymphocytes that release a large panel of cytokines. As the mucosal immune system comprises a series of specialized lymphoid tissues with a **well-identified** lymphocyte traffic between different compartments, we initiated a study to evaluate the histological abnormalities of minor salivary glands (MSGs) in patients with bronchial asthma. 58 patients were studied (29 with allergic asthma, 29 with nonallergic asthma) and compared to 15 healthy controls and 15 patients with chronic obstructive pulmonary disease (COPD). MSGs were normal in all controls except one and in 14/15 COPD patients. 43/58 asthmatics (74%) exhibited MSG abnormalities with T lymphocyte infiltration (57%), mast cell infiltration (64%), basement membrane thickening (64%) and endothelial cell changes (26%). Histological abnormalities were predominantly observed in nonallergic asthmatics. We propose that activated T lymphocytes, present in the bronchial mucosal lymphoid tissue in chronic asthma might migrate, colonize other glandular and mucosal sites, and so trigger at a distance, an **airway-like** inflammation.

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Introduction

Material and Methods

The mucosal immune system comprises a series of specialized lymphoid tissues that interact with the external environment. There are many structural similarities and also a well-identified traffic of lymphocytes between the immune system in the lung and other glandular and mucosal sites [1,2]. As recent studies have emphasized the role of T lymphocytes in the pathogenesis of the local inflammatory reaction in bronchial asthma [3, 4, 5], we initiated a prospective study of pathological abnormalities of minor salivary glands (MSGs) in patients with allergic and nonallergic asthma. /

Fifty-eight patients with asthma were included in the study [37 female and 21 male, mean age 54 ± 6 years (range 18-71). Asthma was defined according to the criteria of the American Thoracic Society. The clinical severity was assessed according to the AAS scale. Asthmatic patients were

divided into two groups: allergic asthma and nonallergic asthma. Asthmatics were compared to 15 healthy controls and 15 patients with chronic obstructive pulmonary disease (COPD). In all patients, biopsy of the MSG was performed to obtain at least 4 glands. The four MSGs for each patient were cut into two: one half was fixed in 4% paraformaldehyde and further processed for paraffin embedding; the other was fixed in glutaraldehyde and further processed for electron microscope evaluation. A blind evaluation of MSG abnormalities was done without knowledge of the diagnosis.

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Results

43 of 58 asthmatics (74%) showed MSG abnormalities, more frequently in patients with nonallergic asthma (28/29; 97%) than in allergic asthma (15/29, 52%), while only 1 out of 15 patients with COPD and 1 healthy control subject presented abnormal features on MSG biopsy. Among asthmatic patients, the main feature was an inflammatory infiltrate, present in 33 of 58 patients (57%); the infiltrate was mainly composed of lymphocytes, located in perivascular areas. The lymphocytic infiltrate was more frequently observed in patients with nonallergic asthma than in patients with allergic asthma ($p < 0.01$). Mast cells were present in 37 of 58 (64%) asthmatics, and appeared as degranulated only in asthmatics but, paradoxically, more often in nonallergic asthmatics. A thickening of the basement membrane of the excretory duct epithelium was found in 37 of 58 asthmatics (64%) and often associated with the presence of degranulated mast cells. Endothelial abnormalities were detected, less frequently, in 15 of 58 patients (26%), especially in those with nonallergic asthma (14/15); they consisted in a narrowing of the lumen of the capillaries and venules; lymphocytes surrounded by edema were found within the vascular wall in

5 patients. In contrast, except for 2 asthmatics, no eosino-phil infiltration was detected in MSG sections.

Discussion

In this prospective study, we identified MSG abnormalities in patients with bronchial asthma, more frequently in the group of nonallergic asthmatics. Interestingly, except for eosinophil infiltration, these histological changes mimicked pathological findings in the bronchial mucosa and showed an inflammatory infiltrate of lymphocytes and mast cells, fully or partly degranulated, a thickened basal membrane and endothelial changes with vascular wall edema. In addition, overexpression of ICAM-1 on endothelial cells supported the hypothesis that endothelial cells were activated and might participate in T lymphocyte entry into the MSG tissues. However, the fact that eosinophils were absent in the MSGs of most asthmatic patients suggests that differences really exist in the triggering of the inflammatory process, perhaps linked to a different distribution of cell adhesion molecules in the bronchial mucosa and in MSGs or to different conditions of cell activation.

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