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Time Course Development of Airway Remodeling in Mouse Chronic Asthma Model

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Introduction

Histological examination of biopsy or *postmortem* lung tissue from patients with asthma usually reveals thickened airway walls. This change is called airway remodeling, which is characterized by airway eosinophilia, hyperplasia of goblet cells and smooth muscle, and subepithelial fibrosis [1,2]. In this study, we investigated the time-course functional, morphological, biochemical changes of remodeling in a ovalbumin (OVA)-induced murine chronic asthma model.

Materials and Methods

BALB/c mice, after i.p. sensitization with OVA mixed with alum on Day 0, received intratracheal OVA challenge periodically Days 8-75 [3]. Airway hyperreactivity (AHR) measurement and bronchoalveolar lavage (BAL) was performed on 3w, 7w, 9w, and 11w after immunization. The number of total BAL fluid leukocyte and eosinophil was counted. Levels of total IgE, VEGF, TGF-β, IL-13 was determined by ELISA method. Lung section was stained with H&E and Trichrome stain. Immunohistochemical localization of TGF-β was performed with the lung sections.

Results

OVA-treated mice developed AHR and extensive eosinophilic airway inflammatory response. Mucus occlusion and goblet cell hyperplasia was also observed. Collagen deposition in the subepithelial layer and lung interstitium was apparent from 7w after immunization. TGF-β lelel in the BAL fluid gradually increased from 3w to 9w and it was maintained until 11w. In contrast, VEGF level in the BAL fluid was not different from that of control mice at all time point. Major source of TGF-β was inflammatory cells in this model.

Discussion

Features of airway remodeling was developed by repeating airway challenges with OVA after systemic immunization. Subepithelial and peribronchial fibrosis was apparent as early as 7w after immunization and its severity increased as repeating challenges. TGF-β seemed have a significant role in the process of remodeling changes, but not VEGF. This mouse chronic asthma model will be a useful model for understanding remodeling process in asthmatic disease and be a valuable model to evaluate therapeutics for chronic asthma.

References

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