Effectors and Pathogenesis of Allergic Diseases

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Neutrophil Influx and Interleukin-8 Release after Segmental Allergen or Saline Challenge in Asthmatics

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Key Words

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Abstract

Neutrophils have been associated with the late asthmatic reaction. However, their role in this disease is not well understood. In this study, we have measured neutrophil influx and release of interleukin-8 into asthmatic airways after endobronchial challenge with either allergen or saline solution.

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Introduction

During the last decade, segmental airway challenge has been used increasingly to study the inflammatory changes induced by the local application of allergen in sensitised asthmatic airways [1, 2]. Despite a number of groups showing neutrophil influx, the role of these cells in allergic asthma remains controversial. Thus, while some authors have reported increased numbers of neutrophils in broncho-alveolar lavage (BAL) fluid after allergen challenge [1], others have failed to show this [2]. The lack of consistency among these studies may be due to the fact that the inflammatory changes in asthmatic airways induced by the bronchoscopy itself have not been rigorously analysed. Therefore, we have investigated the profile of granulocyte recruitment after local bronchial allergen challenge and its relationship to the neutrophil chemoattractant, interleukin (IL)-8 in BAL fluid.

Methods

Subjects taking part in this study were divided in two groups (A, n=13; B, n=9). Both groups had allergen instilled into the right middle lobe (RML) and saline solution in the right upper lobe (RUL). Group A had a second bronchoscopy for BAL of the RML and RUL, 4 h after challenge;

group B were sampled at 24 h. In addition, in group A (n=6) and group B (n=3), a baseline lavage was performed before performing the bronchial challenge.

Results

When compared with baseline lavages, lavages from both saline and allergen sites of exposure contained greater numbers of neutrophils 4 and 24 h after challenge ($p < 0.05$). However, there was no significant difference between the numbers of neutrophils in lavages obtained from these two sites ($p > 0.05$). In contrast, eosinophil numbers were only elevated in BAL fluid obtained from the allergen site ($p < 0.05$). Measurements of albumin in BAL showed

that albumin concentrations were higher in the antigen lav-age when compared with the baseline lavage. However, no statistical difference was found between the allergen and saline lavages. Immunoreactive IL-8 (measured by ELISA, Sandoz) was below the limit of detection (< 20 pg/ml) in baseline lavages. Four hours after allergen or saline challenge, median BAL fluid IL-8 concentrations were 200 and 123 pg/ml, respectively; these declined to 23 and 43 pg/ml, respectively, 24 h after exposure.

Discussion

We have demonstrated that neutrophil influx into asthmatic airways in response to local allergen challenge, but there was a similar degree of BAL neutrophilia after saline challenge, suggesting that the neutrophil response is largely due to the non-specific bronchial insult rather than being a specific response induced by allergen. Others have recently reported that bronchoscopy and BAL in normal subjects also causes neutrophil influx which can be detected 2, 7, and 24 h after BAL, but this completely resolves by 72 h [3]. Taken together, these observations make a convincing case for local recruitment of neutrophils following airway instrumentation in asthma. However, BAL eosinophilia was localised to the allergen challenge site. This is consistent with a number of studies which have documented increased

numbers of eosinophils in BAL fluid obtained 18-24 h after segmental allergen challenge [1, 2]. The absence of BAL eosinophilia at the saline-challenged sites suggests that the neutrophilia at the saline site and the generalised changes in pulmonary function are not due to allergen spreading out from the middle lobe to other bronchial segments. Since eo-sinophil recruitment is confined to allergen-exposed sites, the mechanisms underlying eosinophil and neutrophil recruitment in segmental challenge would appear to be quite distinct.

The present study shows that while the levels of IL-8 in baseline lavages were undetectable, high levels of this cyto-kine were detected in BAL fluid 4 and 24 h after either segmental allergen or saline exposure, with higher levels being observed 4 h after challenge. Furthermore, the parallel elevation in the number of neutrophils and concentrations of IL-8 in the BAL fluid following saline or allergen exposure suggests that IL-8 may be responsible for recruiting neutrophils into asthmatic airways. Other cytokines with neutrophil chemotactic properties have been implicated in asthma, but their role in this disease remains to be determined [4].

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