◎原 著

Role of eosinophils in the airways of patients with atopic asthma. Relationship to mucus hypersecretion

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Abstract : A correlation between the proportion of eosinophils in bronochoalveolar lavage (BAL) fluid and amount of expectoration was examined in patients with atopic asthma. The subjects were divided into two groups : cases with high proportion (20% of more) (group A) and low proportion (less than 5%) (group B) of eosinophils in the BAL fluid. Any significant difference was not paesent in the value of each ventilatory parameter between the two groups. The amount of expectoration/day was significantly higher in group A compared with group B ($p<0.001$). These results suggest that eosinophilia in BAL fluid correlates to mucus hypersecretion in the airways of patients with atopic asthma.

Key words : Eosinophilia, Hypersecretion, BAL fluid, bronchial asthma

Introduction

Eosinophilia in the peripheral blood is often observed in atopic asthma of children. Blood eosinophilia is also found in adult patients with bronchial asthma, whether they are atopic or non-atopic[1, 2)]. The increase in mumber of eosinophils in asthma patients shows a tendency to decrease during asthma attacks[3)]. The decrease in eosinophil count in the peripheral blood is due to the migration of the cells into local allergic reaction site[4, 5)]. These findings suggest that eosinophils play an important role in the pathophysiology of asthma. Although several roles of eosinophils in allergic reactions have been shown, the role of eosinophils closely related to clinical findings is still unclear.

In the present study, proportion of eosinophils in bronchoalveolar lavage (BAL) fluid was analyzed in relation to mucus hypersecretion in bronchial asthma.

Subjects and Methods

The subjects were 7 patients with bronchial asthma, whose proportion of eosinophils in the BAL fluid was 20% or more (group A). Of these, 4 were females and 3 were males. The mean age among them was 49.7 years with a range of 31 to 63 years. The mean serum IgE level was 884IU/mℓ (range, 87−

2439IU/mℓ). All of the subjects were sensitive to inhalant allergens, expressed by RAST score of 2+ or more(3 were sensitive to house dust mites, 2 to grass pollen and 2 to Candida albicans). Seven age-matched asthma patients (5 females and 2 males), whose proportion of eosinophils in the BAL fluid was less than 5%, were selected as control subjects (group B). Their mean age was 50.4 years (range, 36−65 years). The mean serum IgE level was 298 IU/mℓ (range, 65−1003 IU/mℓ). All subjects in group B showed a positive RAST score of 2+ or more to house dust mites. All subjects in groups A and B were admitted at our hospital because of their large asthma attacks.

Clinical symptoms, findings and signs including degree of wheezing and dyspanea, auscultation findings of the lung and amount of sputum were recorded every day during their admission. The results for amount of expectoration/day were expressed as a mean for three days when they had asthma attacks and larger amount of sputum.

The BAL examination was performed in all subjects of groups A and B during sttack-free stages, according to the method previously described[6,7]. Informed consent for the examination of BAL was obtained from all subjects. Smear preparations were made using the cells suspended in Tris ACM after filtration through sterile steel mesh. The slides were air dried and stained with May-Giemsa. A differential cell count was carried out on 500 cells excluding epithelial cells. The results were expressed as a percentage of the total cells.

Ventilayory function test was performed in all subjects using a Box Spiror 81−S (Chest Co) when they were attack free.

The total serum IgE concentration was measured by radiommunosoebent test (RIST). Specific IgE for allergens was estimated by radiollergosorbent test (RAST).

Results

Table 1 presents the characteristics of patients with bronchial asthma in group A (proportion of eosinophils of 20% or more in BAL fluid) and in group B (BAL eosinophils less than 5%). The mean proportion of eosinophils was markedly higher in group A compared with group B (Table 1).

Table 1. Characteristics of patients with bronchial asthma, classified by the proportion of eosinophils in BAL fluid.

Asthma group	No of cases	Age, years	Serum IgE (IU/ml)	%Eosinophils in BAL fluid
A	7	49.7	884±816*	39.6±17.5
B	7	50.4	298±293	2.1± 1.7

*Mean±sd. A: cases with BAL eosinophils of 20% or more, B: cases with BAL eosinophils less than 5%.

There was no difference in the values of %FVC and $FEV_{1.0\%}$ between groups A and B. The value of %PEFR was higher in group A than group B, although no significant difference was found between the two groups. The values of %MMF, $\%\dot{V}_{50}$ and $\%\dot{V}_{25}$ were slightly higher in group B compared with the values of group A, but the difference was not significant between the two groups (Table 2).

The mean amount of expectoration in the subjects of group A was 101.9±92.1mℓ/day. On the contrary, the mean amount of sputum in the subjects of group B was 15.7±10.5mℓ/day. A significantly larger amount of expectoration was observed in group A

compared with group B ($p<0.001$)(Fig. 1).

Table 2. Ventilatory function in patients with bronchial asthma, classified by proportion of eosinophils in BAL fluid.

Asthma group	Ventilatory parameters					
	%FVC	$FEV_{1.0\%}$	%PEFR	%MMF	$\%V_{50}$	$\%V_{25}$
A	96.6* ±10.7	72.4 ±10.3	91.4 ±23.2	53.7 ±20.4	38.5 ±21.6	31.6 ±20.1
B	102.1 ±12.6	72.0 ± 9.7	82.3 ±28.7	54.1 ±20.0	49.8 ±15.5	36.5 ±16.9

*Mean±sd. A: cases with BAL eosinophils of 20% or more, B: cases with BAL eosinophils less than 5%.

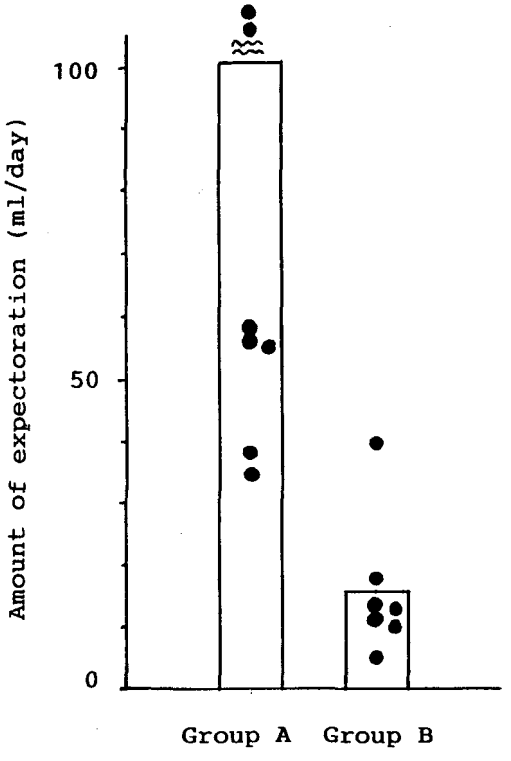

Fig. 1. Amount of expectoration in patients with bronchial asthma in relation to the proportion of eosinophils in BAL fluid. Group A ; cases with BAL eosinophils of 20% or more, group B : cases with BAL eosinophils less than 5%.

Discussion

Blood eosinophilia is a common feature in patients with bronchial asthma. Eosinophil infiltration into local allergic reaction site can be observed in sputum[5] and in skin vesicle[4] and in lung and bronchial biopsy specimens[8] of patients with bronchial asthma. Recently, airway inflammation has been noted to be associated with the pathophysiology of asyhma[9, 10], particularly of late asthmatic reaction (LAR)[11~13]. Analysis of cellular composition in the BAL fiuid of patients with bronchial asthma has demonstrated that lymphocytes, neutrophils and eosinophils migrating from bloodstream participate in the pathophysiology of bronchial asthma[14~16]. Of these cells, it has been often observed by many investigators that number of eosinophils increases in BAL fluid after challenge with allergen[17~19].

Several roles of eosinophils in allergic reactions have been pointed out, and their function are : 1) to secrete leukotrienes C_4, which can cause bronchial smooth muscle contraction, 2) to secrete platelet-activating factor (PAF), which produces bronchial hypersensiti vity and vascular permeability, 3) to secrete toxic granule basic proteins, including MBP and EPO, which can induce mucosal cell desquamation, and injury to ciliated epithelial cells, 4) to release reactive oxygen products, which can cause direct membrane damage to respiratory cells and 5) to stimulate mucus production from Goblet cells[20].

In the present study, pathophysiological changes of the airways of atopic asthmatics were compared between cases with marked

eosinophilia (group A) and cases without eosinophilia (group B) in BAL fluid in relation to ventilatory function and mucus hypersecretion. Regarding ventilatory function, any significant difference was not found between the two groups. On the contrary, amount of expectoration was significantly larger in group A compared with group B. The results reveal that an increased number of eosinophils in BAL fluid is closely related to mucus hypersecretion in adult patients with atopic asthma.

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気管支喘息における気道内への好酸球の出現とその意義．過分泌と関連して．

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アトピー型気管支喘息のなかから，気管支肺胞洗浄液（BALF）中の好酸球の出現頻度が20%以上の症例（グループA）と5%以下の症例（グループB）の2群を選び出し，それぞれの換気機能および喀痰量を比較検討した。その結果，換気機能には両群間に有意の差は見られなかったが，1日喀痰量は，BALF中好酸球の著明増多を示すグループAにおいて有意に多い傾向が見られた。これらの結果は，BALF中好酸球増多と過分泌との間にはある程度の関連があることを示しているものと考えられた。

キーワード：好酸球，過分泌，BAL，気管支喘息