
◎原 著

Lymphocytes in the airways of patients with bronchial asthma. Is there any relationship to IgE-mediated allergic reaction.

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Abstract : Relationship of the proportion of lymphocytes in bronchoalveolar lavage (BAL) fluid to IgE-mediated reactions and to ventilatory function was studied in two age-matched asthma groups : group A of 11 subjects with BAL lymphocytes over 30% and group B of 11 subjects with BAL lymphocytes less than 10%. Of the eleven subjects in group A, 3 (27.3%) were atopic and 4 (36.4%) were non-atopic. The proportion of BAL lymphocytes in subjects with serum IgE level more than 300 IU/ml, who were all older than 50 years, was significantly higher than that in subjects with serum IgE less than 100 IU/ml in group A ($p < 0.05$). While of the eleven subjects of group B, 5 (45.5%) were atopic and 4 (36.4%) were non-atopic. The value of $\% \dot{V}_E$ was significantly higher in the atopics compared with the non-atopics in group A ($p < 0.05$), although no significant difference was found in the value of $\% \dot{V}_E$ between the two asthma types in group B. The results show that an increased number of lymphocytes in BAL fluid may be enhanced by IgE-mediated allergic reactions in the elderly, and that the decreased value of $\% \dot{V}_E$ may be associated with an increased number of lymphocytes in BAL fluid in non-atopics.

Key words : Lymphocytes, BAL fluid, IgE antibody, bronchial asthma

Introduction

It is well known that an asthma attack is at first initiated by chemical mediators such as histamine and SRS-A (leukotrienes C₄, D₄ and E₄) released from mast cells. In addition to these humoral factors, recently cell infiltration into allergic reaction site in airways has been noted by analysis of the cells in

bronchoalveolar lavage (BAL) fluid¹⁻⁹⁾. Lymphocytes, one of the inflammatory cells, have been reported to be increased in BAL fluid of patients with bronchial asthma^{6, 10)}. The increased number of lymphocytes in BAL fluid is confined to the T cell population¹¹⁾. Role of lymphocytes is, however, unclear in the airways of asthma patients, although it

is hypothesized to modulate local immunological reactions.

One of the major allergeo-immunological reactions, which participate in the onset mechanism of bronchial asthma, is IgE-mediated reaction. The presence of IgE-mediated allergic reaction in patients with asthma can be clinically shown by high serum IgE levels, positive skin reaction to allergens, specific IgE antibodies, positive bronchial challenge and high reactivity of blood basophils to allergens¹²⁻¹⁸. The presence of IgE-mediated allergic reaction is, however, unclear in some adult patients with asthma.

In the present study, a correlation between the proportion of lymphocytes in BAL fluid and IgE-mediated reaction was discussed in patients with bronchial asthma.

Subjects and Methods

The subjects comprised 11 patients (6 females and 5 males) with bronchial asthma, whose proportion of lymphocytes in BAL fluid was more than 30% (group A, study group). Their mean age was 58.9 years (range, 42-72 years). The mean serum IgE level was 443 IU/ml (range, 11-2136 IU/ml). Another age-matched asthma group including 11 subjects (8 females and 3 males) whose proportion of lymphocytes in BAL fluid was less than 10% was prepared as control group (group B). The mean age in group B was 57.7 years (range, 40-71 years), and the mean serum IgE level was 615 IU/ml (range, 11-2430 IU/ml). All subjects in groups A and B were non-smokers.

Bronchoalveolar lavage (BAL) was performed in all subjects when they were attack free^{9,19,20}. Informed consent for the examination of BAL was obtained from all subjects. BAL fluid aspirated by the bronchofiberscope

was filtered through sterile steel mesh. The filtrates were centrifuged at 1200 rpm for 10 min at 4°C, and the cell pellet was resuspended in Tris ACM. Smear preparations were made using the cell suspension. The slides were air dried and stained with May-Giemsa. BAL cells were differentiated on 500 cells excluding epithelial cells. The results were expressed as a percentage of the total cells.

Ventilatory function test was carried out in all subjects using a Box Spiro 81-S (Chest Co) when they were asymptomatic.

Immediate skin reaction was examined to house dust (HD), ragweed, silk, Japanese cedar, alternaria, Cladosporium and Aspergillus (As). Skin reaction to *Candida albicans* was also examined, but the results were excluded in this study, because the antigen often produces nonspecific reaction.

Serum IgE levels were estimated by radioimmunosorbent test (RIST). Specific IgE antibodies for allergens were evaluated by radioallergosorbent test (RAST).

In the diagnosis of asthma type, cases with positive RAST score of 2+ or more to allergens or serum IgE over 500 IU/ml were evaluated as atopic type, and cases with negative RAST to allergens and serum IgE less than 100 IU/ml were assessed as non-atopic type of asthma.

Results

The proportion of lymphocytes in BAL fluid was $40.7 \pm 7.4\%$ in group A (lymphocytes in BAL fluid more than 30%) and $5.7 \pm 2.2\%$ in group B (BAL lymphocytes less than 10%). Of 11 subjects in group A, 3 cases (27.3%) were atopic and 4 cases (36.4%) were non-atopic. The proportion of lymphocytes in the BAL fluid was $44.1 \pm 8.3\%$ in the atopic su

jects and $36.7 \pm 3.9\%$ in the non-atopics. The proportion of BAL lymphocytes was 46.3% in subjects with serum level over 300 IU/ml. This proportion was significantly higher than that in subjects with serum IgE level less than 100 IU/ml ($p < 0.05$) (Table 1).

Table 1. Characteristics of patients with bronchial asthma with BAL lymphocytes over 30% (group A, study group)

Case	Age, years	Sex	Serum IgE (IU/ml)	Skin test	RAST	%Lymphocytes in BAL fluid
1	65	F	309	HD	HD	48.6
2	63	F	2136	Silk	-	51.3
3	63	M	1132	Silk	-	32.4
4	54	F	378	-	-	51.0
5	55	M	333	-	-	48.4
6	42	M	252	-	-	34.7
7	60	F	120	-	-	34.6
8	64	M	98	-	-	32.7
9	49	F	66	-	-	33.3
10	61	F	33	-	-	38.8
11	72	M	11	-	-	42.1

HD: house dust

On the contrary, of subjects in group B, 5 cases (45.5%) was atopic and 4 cases (36.4%) were non-atopic. The proportion of lymphocytes in the BAL fluid was 5.1% in the five atopics and 6.1% in the four non-atopics (Table 2).

Table 2. Characteristics of patients with bronchial asthma with BAL lymphocytes less than 10% (group B, control group)

Case	Age, years	Sex	Serum IgE (IU/ml)	Skin test	RAST	%Lymphocytes in BAL fluid
1	64	F	11	-	-	9.8
2	61	F	202	HD	HD	4.2
3	62	M	27	-	-	1.5
4	56	F	964	-	-	3.3
5	40	F	2430	As	-	7.3
6	60	F	236	-	-	5.6
7	61	F	43	-	-	6.0
8	47	M	1754	HD	HD	4.4
9	59	F	310	-	-	7.2
10	71	M	726	-	-	6.1
11	54	F	62	-	-	7.0

HD: house dust, As: Aspergillus

The values of $FEV_{1.0\%}$ and $\% \dot{V}_{25}$ were 67.4% and 24.7% in group A, respectively. While the value was 71.5% in $FEV_{1.0\%}$ and 26.2% in $\% \dot{V}_{25}$ in group B. Any significant difference was not found in the values of $FEV_{1.0\%}$ and $\% \dot{V}_{25}$ between groups A and B.

The value of $FEV_{1.0\%}$ was 73.5% in the three atopics and 64.1% in the four non-atopics of group A. The value of $FEV_{1.0\%}$ was higher in the atopics than in the non-atopics, but there was no significant difference between the two asthma types in group A. The value of $\% \dot{V}_{25}$ was 41.2% in the atopics and 17.6% in the non-atopics of group A. The value of $\% \dot{V}_{25}$ was significantly higher in the atopics compared with the non-atopics in group A ($p < 0.05$) (Fig. 1).

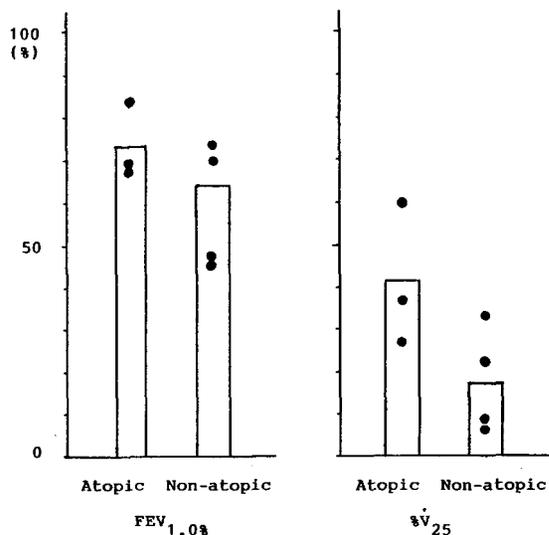


Fig. 1. Ventilatory function in patients with bronchial asthma in group A (BAL lymphocytes more than 30%)

On the other hand, the value of $FEV_{1.0\%}$ was 70.6% in the atopics and 74.1% in the non-atopics in group B. There was no significant difference between the two types in

group B (Fig. 2).

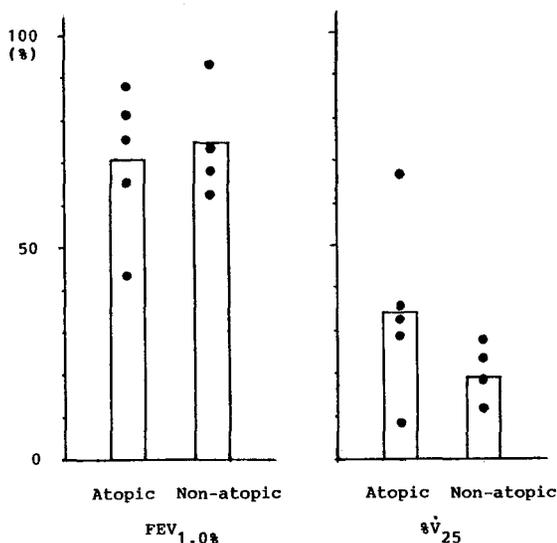


Fig. 2. Ventilatory function in patients with bronchial asthma in group B (BAL lymphocytes less than 10%)

Discussion

Analysis of BAL cells has suggested that the number of lymphocytes in BAL fluid is increased in patients with asthma compared with healthy subjects, and that the increased number of the cells is confined to the T cell population^{6,10,11}. It is, however, unclear whether there are some differences in clinical situation of asthma between cases with high and low proportions of lymphocytes in BAL fluid, and whether there is a correlation between the proportion of BAL lymphocytes and IgE-mediated allergic reaction. We do not know what is characteristic of asthma patients with high proportion of lymphocytes in BAL fluid.

In the present study, the degree of IgE-mediated allergic reactions in patients with increased proportion of lymphocytes (30% or more) (group A) was compared with that in subjects with the proportion of BAL lympho-

cytes less than 10%. The IgE-mediated allergic reaction was found in 3 out of the eleven subjects of group A. While IgE-mediated reaction was not observed in 4 cases of the eleven subjects in group A. The results suggest the an increased number of lymphocytes in BAL fluid is observed in atopic type and in non-atopic type of asthma. Whether functions of lymphocytes in the airways are different between atopic and non-atopic types of asthma is not known. One possibility for this question is shown by the results that the different values of $\% \dot{V}_{25}$ between the two asthma types of group A showing the increased number of lymphocytes in BAL fluid may suggest a different function of the cells.

A markedly increased proportion of lymphocytes in BAL fluid was found in subjects showing serum IgE level over 300 IU/ml. The proportion of BAL lymphocytes in these subjects was 46.3%, which was significantly higher than that in subjects with serum IgE less than 100 IU/ml. They were all older than 50 years. The results suggest that an increased number of lymphocytes in BAL fluid may be accelerated by IgE-mediated allergic reaction in the elderly.

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気管支喘息における気道内リンパ球の出現とその意義、IgE系反応との関連について。

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気管支喘息を対象に、気管支肺胞洗浄液(BALF)中のリンパ球の出現頻度と、IgE系反応および換気機能との関連について検討を加えた。対象は、同年齢の2つのグループ、すなわち、BALF中リンパ球出現頻度30%以上の症例(グループA)と10%以下の症例(グループB)に分けて、それぞれ11例ずつで比較検討を行った。グループ

Aでは、11例中3例がアトピー型、4例が非アトピー型であった。血清IgEが300IU/ml以上の症例(いずれも50才以上)では、100IU/ml以下の症例に比べ、BALF中リンパ球の出現頻度は、有意に高い傾向を示した。一方、グループBの11例では、アトピー型5例、非アトピー型4例であった。% \dot{V}_E 値は、グループAではアトピー型で、非アトピー型に比べ有意に高い値を示した。

これらの結果は、50才以上の症例では、IgE系の反応がリンパ球の出現頻度を増強させること、そして、非アトピー型では、リンパ球の出現頻度と% \dot{V}_E 値との間にある程度の関連が見られることを示唆しているものと考えられた。

キーワード：リンパ球, BAL液, IgE抗体, 気管支喘息