

◎原 著

## Bronchial asthma in the elderly. Relationship to allergic reaction and airway inflammation

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**Abstract :** Clinical features of bronchial asthma in the elderly were analyzed by observing IgE-mediated allergic reactions evaluated by immediate skin reaction and specific IgE antibodies to allergens, ventilatory function and cellular composition in bronchoalveolar lavage (BAL) fluid. 1. The frequency of positive immediate skin reaction and positive RAST score to allergens was in general low in the elderly patients over age 70. 2. Ventilatory function was widely variegated, and fifteen cases (60%) of the 25 subjects showed considerably high values of FEV<sub>1.0%</sub>, %PEFR, %MMF, % $\dot{V}_{50}$  and % $\dot{V}_{25}$ , and the mean value of FEV<sub>1.0%</sub> in these cases was 71.3%. 3. The decreased value of % $\dot{V}_{25}$  was related to BAL neutrophilia in 2 cases, but any correlation was not found between BAL neutrophilia and decreased value of % $\dot{V}_{25}$  in 9 cases of the eleven subjects who had the BAL examination. The results show that in asthma of elderly patients, IgE-mediated allergic reactions are weak, and that a decreased value of % $\dot{V}_{25}$  can be observed without BAL neutrophilia.

**Key words :** elderly subjects, IgE-mediated allergic reaction, ventilatory function, BAL neutrophilia, bronchial asthma

### Introduction

It is widely accepted that the majority of atopic asthma in young subjects begins to occur before the age of 10. In atopic asthma, IgE-mediated allergic reactions can be usually observed<sup>1, 2)</sup>. The reaction is evaluated

by high levels of serum IgE, positive skin reaction and positive RAST score of 2+ or more to allergens, bronchial provocation test and basophil histamine release induced by allergen and anti-IgE<sup>3-5)</sup>.

Two major changes have been suggested in the elderly patients with bronchial asthma<sup>6, 7)</sup>.

The first one is the changes of allergic reactions with aging, which play the major role in the onset mechanism of bronchial asthma<sup>9</sup>. The second one is the organic change of the airways with aging, in which the organic change is mainly found in the peripheral lung regions including small airways. Thus, bronchial asthma in the elderly is characterized by the changes of allergic reaction and of airway structure with aging.

In the present study, characteristics of bronchial asthma in the elderly were observed in relation to age at onset of the disease, IgE-mediated allergic reaction, ventilatory function and airway inflammation represented by cells in bronchoalveolar lavage (BAL) fluid.

### Subjects and Methods

For this study, 25 elderly patients with bronchial asthma over the age of 70 were selected. Their mean age was 72.2 years with a range of 70 to 80 years. Of these, 12 were females and 13 were males. The mean level of serum IgE was 417 IU/ml (range, 14–2007 IU/ml). Their asthma is not so severe, and 4 patients (16%) had been on corticosteroid therapy for over two years.

Immediate skin reaction was examined with 0.02ml of commercial allergen extract (Torii Pharmaceutical Co). The diameters of flare and wheal at 20 min were measured in millimeters after the test. The diameter of flare larger than 20mm or wheal larger than 9mm was regarded as positive. Allergens used for skin reaction were house dust (HD), ragweed, silk, Japanese cedar (JC), *Candida* (Ca), *Alternaria* and *Aspergillus*.

BAL cytology was examined in eleven subjects by differentiating 500 cells excluding epithelial cells on smear preparations<sup>9, 10</sup>. The

results were expressed as a percentage of the total cells. Informed consent for the BAL examination was obtained from study subjects.

Ventilatory function was measured by using a Box Spiro 81 (Chest Co) when they were attack free.

Serum IgE was determined by radioimmunosorbent tests (RIST). Specific IgE antibodies were estimated by radioallergosorbent test (RAST).

### Results

#### 1. Allergic reaction

The level of serum IgE was widely varied, and a low level of serum IgE under 100 IU/ml was found in 9 cases (36%), while a high level over 500 IU/ml in 7 cases (28%) of the 25 subjects. Immediate skin reaction to allergens was positive in one case (4%) to house dust, 6 cases (24%) to *Candida* and 3 cases (12%) to Japanese cedar. A positive RAST score to allergens was found in 2 cases (8%) to HD and in 2 cases (8%) to Ca.

#### 2. Age at onset of bronchial asthma

Age at onset of the disease in these subjects was considerably high. Their asthma attacks began most frequently to occur between the ages of 51 and 60. The age at onset was between 41 and 50 in 4 cases, between 51 and 60 in 7 cases, between 61 and 70 in 6 cases and over age 71 in 4 cases.

The results reveal that asthma attacks in the patients over age 70 start between the ages of 41 and 50, and the initiation of the attacks is most frequently found between 51 and 60 (Fig. 1).

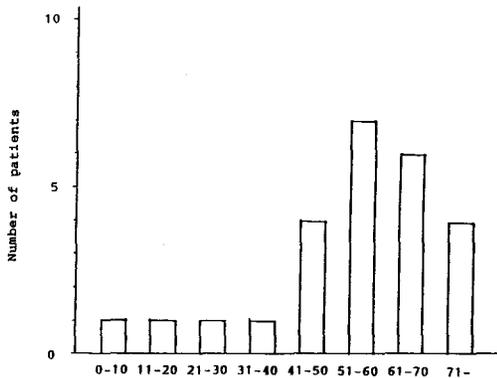


Fig. 1. Age at onset of bronchial asthma in patients over the age of 70 years

### 3. Ventilatory function

It has been suggested that bronchial asthma in the elderly shows ventilatory dysfunction in the small airways. In the present study, the value of  $\% \dot{V}_z$  less than 10% was observed in 10 cases (40%) of the 25 subjects, while 15 cases (60%) showed the value over 10%. Ventilatory parameters other than  $\% \dot{V}_z$  were compared between the subjects with the value of  $\% \dot{V}_z$  more than 10% (group A) and less than 10% (group B).

The ventilatory parameters such as FEV<sub>1.0%</sub>, %PEFR, %MMF and  $\% \dot{V}_{50}$  were significantly lower in group B than in group A, although no significant difference was present in the value of %FVC between the two groups. The values of ventilatory parameters representing obstructive ventilatory dysfunction were considerably high, and the mean value of FEV<sub>1.0%</sub> in the patients of group A was 71.3% (Fig. 2, Table 1.).

### 4. Cellular composition in BAL fluid

The proportion of macrophages and lymphocytes in the BAL fluid was not different between the subjects with the value of  $\% \dot{V}_z$  more than 10% (group A) and less than 10% (group B). The proportion of BAL

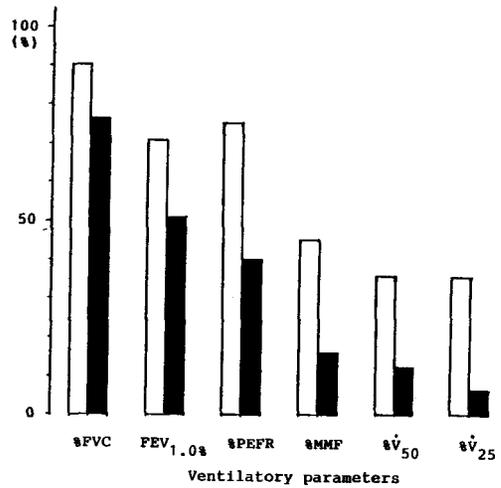


Fig. 2. Comparison of ventilatory function between the subjects with the value of  $\% \dot{V}_z$  more than 10% (□) and less than 10% (■)

Table 1. Comparison of ventilatory function between the patients with the value of  $\% \dot{V}_z$  more than 10% and less than 10%

Asthma group	Value of $\dot{V}_{25}$	No of cases	Ventilatory parameters					
			%FVC	%FEV <sub>1.0%</sub>	%PEFR	%MMF	$\dot{V}_{50}$	$\dot{V}_{25}$
A	10% <	15	91.1* ±14.2	71.3 <sup>a</sup> ±12.0	75.9 <sup>b</sup> ±27.7	45.4 <sup>c</sup> ±21.7	36.4 <sup>d</sup> ±20.7	35.9 ±18.5
B	<10%	10	75.9 ±17.7	50.7 <sup>a</sup> ±10.9	39.9 <sup>b</sup> ±14.2	15.9 <sup>c</sup> ± 4.5	12.1 <sup>d</sup> ± 7.6	6.0 ±2.0

\*Mean ± sd. a and d, p < 0.01; b, p < 0.02; c, p < 0.001. A: cases with the value of  $\dot{V}_{25}$  more than 10% and B: cases less than 10%

neutrophils was significantly higher in group B than in group A (p < 0.02). BAL neutrophilia was not observed in all of the six subjects of group A, and found in 2 cases of the five subjects of group B. On the contrary, the frequency of eosinophils in the BAL fluid was higher in group A compared with group B, although no significant difference was present between the groups A and B (Fig. 3).

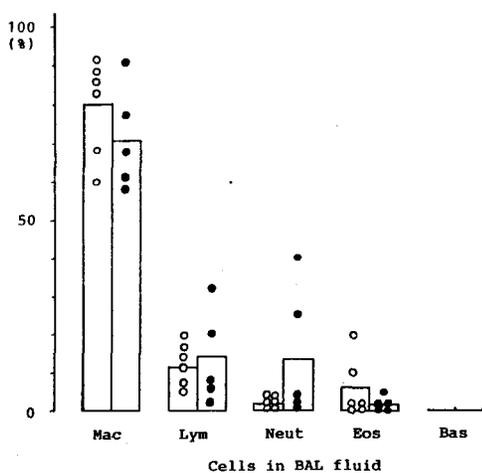


Fig. 3. Comparison of BAL cells between the patients with the value of %  $\dot{V}_A$  more than 10% (○) and less than 10% (●). Mac, macrophages; Lym, lymphocytes; Neut, neutrophils; Eos, eosinophils; Bas, basophils.

### Discussion

It has been considered that bronchial sthma in the elderly is different in several points from that in young adults. IgE-mediated allergic reactions, which participate in the onset mechanism of asthma<sup>1,2)</sup> and ventilatory function, which is affected by the pathophysiology of the airways, change with aging. In the present study, the two major changes by aging were examined.

IgE-mediated allergic reactions evaluated by immediate skin reaction and RAST score to allergens were in general weak in the elderly subjects over age 70, although high levels of serum IgE over 500 IU/ml were observed in 7 cases (28%) of the 25 subjects. Furthermore, specific IgE antibodies to allergens was present in only two cases (28.6%) of the seven subjects with serum IgE over 500 IU/ml.

Age at onset of the disease in the elderly subjects was higher, and in 21 cases (84%) of the 25 subjects, the age at onset was over age 41. The results reveal that asthma in the elderly subjects newly occurs after the age over 41, but does not continue from their childhood.

Ventilatory function in the elderly subjects is characterized by dysfunction in the peripheral lung region including bronchioles, which is related to BAL neutrophilia<sup>9,10)</sup>, and to aging<sup>8)</sup>. The data from this study demonstrate that the dysfunction in the peripheral lung region (expressed by the value less than 10%) of the elderly subjects is related to BAL neutrophilia in 2 cases and to aging in 9 cases of the eleven subjects receiving the BAL examination.

The results obtained here might show that bronchial asthma in the elderly is characterized by decrease of IgE-mediated allergic reaction and dysfunction in the small airways, which is partially caused by BAL neutrophilia and mainly by aging.

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#### 老年者の気管支喘息. アレルギー反応と気道細胞反応

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70才以上の老年者気管支喘息の特徴について, アレルゲンに対する即時型皮膚反応および特異的IgE抗体, 換気機能, 気管支肺胞洗浄液 (BAL) 中の細胞成分などにより検討した。1. アレルゲンに対する即時型皮膚反応および特異的IgE抗体

の陽性率は, 全般的にかなり低い傾向を示した。2. 換気機能にはかなりのばらつきが見られたが, 25例中15例 (60%) では, いずれの換気パラメーターもかなり高い値を示し, これらの症例の平均FEV<sub>1.0%</sub> は71.3%であった。3. BALを施行した11例中, % $\dot{V}_E$  値の低下とBAL中好中球増多との間に関連の見られた症例は2例のみで, 他の9例では% $\dot{V}_E$  値の高度な低下にもかかわらず, BAL中の好中球増多は見られなかった。これらの結果より, 老年者気管支喘息では, IgEにmediateされるアレルギー反応は全般的に弱いこと, またBAL液中好中球増多なしに% $\dot{V}_E$  値の高度な低下が出現してくることが示された。

キーワード: 老年者, IgE系反応, 換気機能, BAL好中球, 気管支喘息