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Bronchial hyperresponsiveness in type Ia (simple bronchoconstriction) asthma Relationship to patient age and the proportions of bronchoalveolar cells

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**Abstract :** Bronchial hyperresponsiveness was examined in relation to age, ventilatory function, and the proportion of bronchoalveolar lavage (BAL) cells in 39 patients with type Ia asthma (simple bronchoconstriction) (25 with type Ia-1 and 14 with type Ia-2), classified by clinical symptoms. 1. The proportion of BAL eosinophils was significantly higher in type Ia-2 than that in type Ia-1 asthma patients. 2. Bronchial reactivity to methacholine was not different between type Ia-1 and type Ia-2 asthma patients. 3. Bronchial hyperreactivity tended to decrease as patient age was higher in both types of asthma. Neither ventilatory function (FEV<sub>1.0</sub>%) nor the proportions of BAL lymphocytes and neutrophils was not correlated with bronchial hyperresponsiveness in both types of asthma. 4. Bronchial reactivity to methacholine more decreased with the increase in the proportion of BAL eosinophils in both type Ia-1 and Ia-2 asthma patients.

The results show that bronchial hyperresponsiveness in patients with type Ia asthma is correlated to patients age and the proportion of BAL eosinophils.

**Key words :** Bronchial hyperresponsiveness, Type Ia asthma, Patient age, BAL eosinophils

### Introduction

According to the classification system by clinical symptoms, bronchial asthma is divided into three types; Ia simple broncho-

constriction type, Ib bronchoconstriction + hypersecretion type, and II bronchiolar obstruction type<sup>1-3)</sup>. Type Ia is furthermore, classified into two subtypes according to expectoration per day; Ia-1 (0-49 ml/day)

and Ia-2 (50-99 ml/day). Among these types, clinical symptoms of type Ia is characterized by wheezing and transient dyspnea<sup>4)</sup>, which is mainly induced by bronchoconstriction. In contrast, the symptoms of type Ia-2 seems to be similar to those of type Ib hypersecretion (expectoration, more than 100 ml/day)<sup>5)</sup>.

It is well known that airway inflammation is a common feature of bronchial asthma<sup>6-10)</sup>, and among inflammatory cells, activated T cells and eosinophils play an important role during triggering event of asthma attacks<sup>11,12)</sup>. Regarding airway inflammation, the proportions of bronchoalveolar lavage (BAL) cells are not characteristic in type Ia asthma. However, increase in the proportion of BAL eosinophils is often observed in type Ia-2 asthma, which is associated with hypersecretion<sup>13)</sup>.

In this study, bronchial reactivity to methacholine is examined in relation to patient age, ventilatory function, and the proportions of BAL cells.

### Subjects and Methods

The subjects of this study were 39 patients (21 females and 18 males, mean age 55.1 years, range 21-72 years) with type Ia asthma (simple bronchoconstriction). The mean level of serum IgE was 422 IU/ml (18-2430 IU/ml). All patients were selected according to the classification system of asthma by clinical symptoms<sup>1-3)</sup>. Of these, 13 were patients with steroid-dependent intractable asthma.

Bronchial reactivity to methacholine was measured by an Astograph (TCK 6100, Chest Co.) Different concentrations of methacholine (49, 98, 195, 390, 781, 1563, 3125, 6250, 12500 and 25000  $\mu\text{g}/\text{ml}$ ) were prepared for bron-

chial challenge. The increase of total respiratory resistance (Rrs) after methacholine inhalation was measured by the oscillation method. A methacholine concentration causing a significant increase in Rre was assessed as Cmin (minimum concentration). All medications were stopped 12 hours prior to examination.

Bronchoalveolar lavage (BAL) was performed in all subjects when they were asymptomatic<sup>1-3)</sup>. Informed consent for BAL examination was obtained from all the subjects. A differential cell count was performed by observing 500 cells excluding epithelial cells, on smear preparations made from BAL cell suspension. The results were expressed as a percentage of the total cells.

Ventilatory function tests, using a Box Spiror 81-S (Chest Co.), were performed in all subjects when they were free of attack.

### Results

Table 1 shows characteristics of patients with type Ia-1 and type Ia-2 asthma. The mean age and mean level of serum IgE were not significantly different between the two types of asthma. The value of FEV1.0% was significantly higher in type Ia-1 than type Ia-2 asthma ( $p < 0.01$ ). The proportion of BAL eosinophils was significantly higher in type Ia-2 compared to type Ia-1 ( $p < 0.05$ ). Despite the difference in FEV1.0% value and the proportion of BAL eosinophils, bronchial hyperresponsiveness was not significantly different between the two asthma types, as shown in Fig. 1.

Association of bronchial hyperresponsiveness with patient age was found in both type Ia-1 and type Ia-2 asthma. The bronchial reactivity to methacholine tended to decrease as patient age was older (Fig.

Table 1. Characteristics of type Ia-1 and type Ia-2 asthma studied

Asthma type	No of patients	Age (years)	IgE (IU/ml)	FEV1.0%	BAL eosinophils(%)
Ia-1	25	54.0 (14-1932)	329 ±11.7	75.2 <sup>a</sup>	2.5±2.1% <sup>b</sup>
Ia-2	14	56.1 (62-2132)	543 ± 9.0	64.0 <sup>a</sup>	6.5±8.2% <sup>b</sup>

a:p<0.01, b:p<0.05.

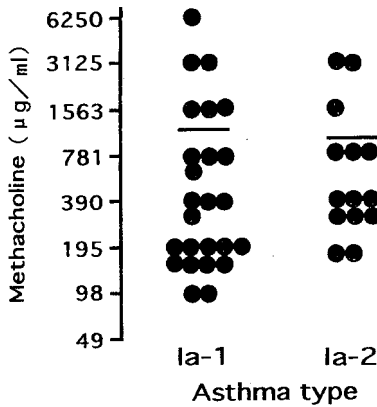


Fig. 1. Bronchial hyperresponsiveness in type Ia-1 (●) and type Ia-2 (⊗) asthma

2). Figure 3 represents a correlation between FEV1.0% value and bronchial hyperresponsiveness in type Ia asthma. There was not significant difference in bronchial hyperresponsiveness among three different values of FEV1.0%

A correlation between bronchial hyperresponsiveness and the proportions of BAL cells was examined in all subjects with type Ia-1 and Ia-2 asthma. The proportion of BAL lymphocytes did not correlated with bronchial hyperresponsiveness, as shown in Fig. 4. The mean Cmin of methacholine was highest in patients with the proportion

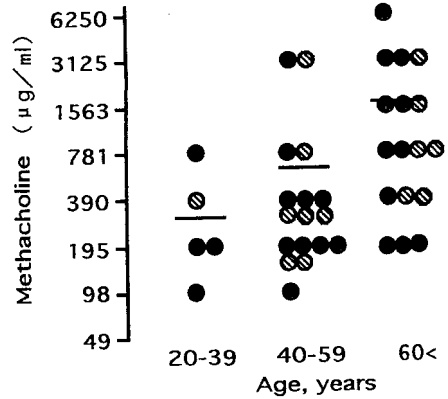


Fig. 2. Correlation between patient age and bronchial hyperresponsiveness in type Ia-1(●) and type Ia-2(⊗) asthma

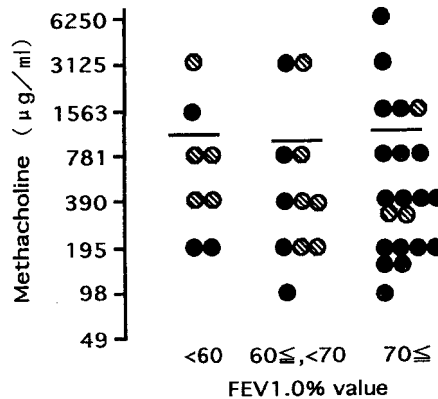


Fig. 3. FEV1.0% value and bronchial hyperresponsiveness in type Ia-1 (●) and type Ia-2 (⊗) asthma

of BAL neutrophils between 2.0-2.9%, however, there was no significant correlation between bronchial hyperresponsiveness and the proportion of BAL neutrophils (Fig. 5). Figure 6 shows a correlation between bronchial hyperresponsiveness and the proportion of BAL eosinophils in type Ia-1 and Ia-

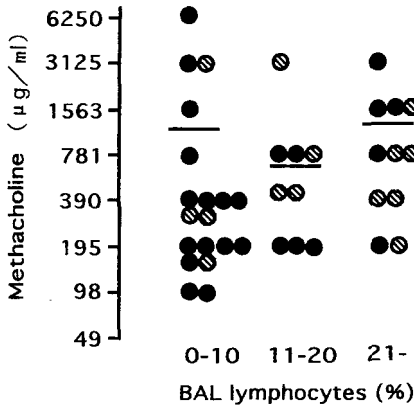


Fig. 4. The proportion of BAL lymphocytes and bronchial hyperresponsiveness in type Ia-1 (●) and type Ia-2 (⊗) asthma

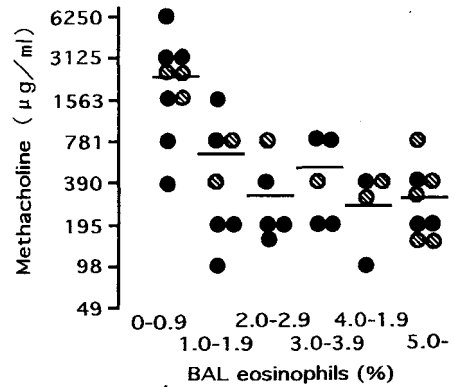


Fig. 6. The proportion of BAL eosinophils and bronchial hyperresponsiveness in type Ia-1 (●) and type Ia-2 (⊗) asthma

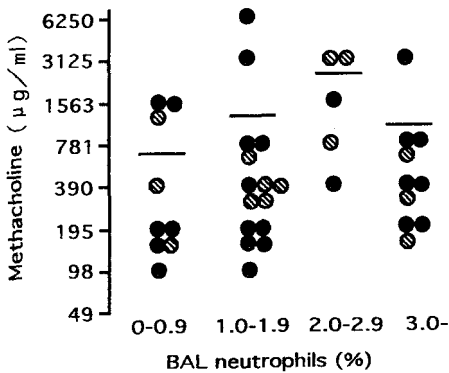


Fig. 5. The proportion of BAL neutrophils and bronchial hyperresponsiveness in type Ia-1 (●) and type Ia-2 (⊗) asthma

2 asthma. Bronchial reactivity to methacholine was higher as the proportion of BAL eosinophils was larger. The mean Cmin of methacholine was highest (22561  $\mu\text{g}/\text{ml}$ ) in patients with BAL eosinophils between 0 and 0.9%, and lowest (317  $\mu\text{g}/\text{ml}$ ) in patients with the proportion between 4.0 and 4.9% and over 5.0%.

## Discussion

Among three clinical types of asthma, type Ia (simple bronchoconstriction) shows representative symptoms, such as wheezing and transient dyspnea, of asthma. In many cases of asthma, these symptoms are mainly induced by bronchoconstriction, associated with and without IgE-mediated allergic reaction. In IgE-mediated reaction, bridging of IgE receptors on mast cell membranes caused by inhaled allergens, followed by release of chemical mediators such as histamine and leukotrienes<sup>14-17</sup>, which induce pathological changes of airways such as bronchoconstriction, mucus hypersecretion, and edema of mucous membrane (IAR; immediate asthmatic reaction). Following the IAR, airway inflammation, in which lymphocytes, neutrophils, eosinophils, and basophils migrate from peripheral blood into allergic reaction sites, is observed in late asthmatic reaction (LAR)<sup>18</sup>.

Attacks of type Ia-1 asthma seem to be mainly induced by release of chemical mediators during IAR, since any increase in the proportions of BAL cells except eosinophils in atopic asthma is not observed in many subjects with type Ia-1 asthma. In contrast, increased number of BAL eosinophils is often observed in type Ia-2 asthma, as in type Ib (hypersecretion)<sup>5, 13)</sup>. Furthermore, in type Ia-1 (and type Ia-2) asthma, ventilatory function does not markedly decreased<sup>19)</sup>, as in type II (bronchiolar obstruction)<sup>20)</sup>.

In the present study, bronchial hyperresponsiveness in type Ia-1 and Ia-2 asthma was examined in relation to patient age, ventilatory function, and the proportion of BAL cells. There was no significant difference in bronchial hyperresponsiveness between the two types of asthma, despite the difference in the proportion of BAL eosinophils between type Ia-1 and type Ia-2 asthma. The results obtained here revealed that bronchial reactivity to methacholine in type Ia asthma correlates with patient age and the proportion of BAL eosinophils; bronchial hyperresponsiveness is higher as patient age is younger, and as the proportion of BAL eosinophils is larger. However, any association of bronchial hyperresponsiveness with ventilatory function, and the proportions of BAL lymphocytes was not observed in this study. The proportions of BAL neutrophils did not correlate with bronchial hyperresponsiveness, although recent reports have suggested that there are some correlations between bronchial hyperresponsiveness and neutrophils<sup>21,22)</sup>.

### Conclusion

The proportion of BAL eosinophils was higher in type Ia-2 than in type Ia-1

asthma. Despite of the difference in BAL eosinophil count, there was no significant difference in bronchial hyperresponsiveness between type Ia-1 and type Ia-2 asthma. Bronchial hyperresponsiveness in both type Ia-1 and type Ia-2 asthma correlated with patient age and the proportion of BAL eosinophils.

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### Ia型(単純気管支れん縮型)喘息における気道過敏性について…年齢および気管支肺胞洗浄液中の細胞成分との関連について

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気管支喘息患者Ia型(単純気管支れん縮型)39人(Ia-1型25人, Ia-2型14人)の気道過敏性を年齢, 呼吸機能検査, 気管支肺胞洗浄液(BAL)中の細胞成分と関連で検討を行った。

1. BAL液中の好酸球の比率はIa-1型に比べIa-2型で優位に高値であった。2. メサコリンに対する過敏性はIa-1型とIa-2型とで差を認めなかった。3. 気道過敏性はどちらの病型においても年齢にともなって減弱する傾向にあったが, 一秒率及びBAL液中の好中球, リンパ球の比率とは相関しなかった。4. メサコリンに対する気道過敏性はIa-1型, Ia-2型ともにBAL液中の好酸球の比率が増加するにしたがって亢進した。

以上より単純気管支れん縮型(Ia型)の気管支喘息患者の気道過敏性はその年齢, BAL液中の好酸球の比率に相関することが示唆された。