
◎原 著

Age-related changes of IgE-mediated allergic reaction in patients with late onset asthma.

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Abstract : Age-related changes in IgE-mediated allergic reaction were examined in patients with late onset asthma, whose asthma occurred over the age at onset of 40.

1. The number of patients with a high serum IgE level over 300IU/ml was larger in those between the ages at onset of 40 and 49 and over age at onset 60 than in those between the ages at onset 50 and 59. 2. A positive RAST score to Hdm and cockroach allergens was more frequently found in patients between 40 and 49 and over age 60 at onset compared to those between 50 and 59 at onset. In contrast, the number of patients with a positive RAST to *Candida* was larger in those between 50 and 59 at onset than in those of between 40 and 49 and over 60 at onset. 3. Severe asthma was more frequently and slight asthma was less frequently observed in patients between 50 and 59 at onset than in those of the other age at onset groups.

These results suggest that IgE-mediated allergic reaction in patients between the ages at onset of 50 and 59 is different from that in those with early onset asthma, and that the reaction in patients between the ages at onset 40 and 49 and over 60 resembles to the reaction in those with early onset asthma.

Key words : IgE, RAST, inhalant Allergen, Bronchial asthma, aging

Introduction

IgE antibodies are involved in allergen-induced allergic reactions, which are observed at immediate phase and late phase after allergen challenge. Chemical mediators such as histamine¹⁻³⁾ and leukotrienes⁴⁻⁶⁾ play major roles in the immediate phase of

allergic reaction, and airway inflammation in the late phase⁷⁻¹⁰⁾. The IgE-mediated allergic reactions, closely associated with the mechanism of the onset of asthma, has been recognized to change qualitatively and quantitatively with aging¹¹⁻¹³⁾.

Our previous studies showed that reaction of basophils in patients with late onset

asthma was different from that in patients with early onset asthma¹⁴⁾. The subjects whose skin reaction was positive to *Candida* alone were clearly divided into two groups, one showed a significantly increased release when anti-IgE was added and the other showed little histamine release.

Pathophysiology of asthma¹⁵⁻¹⁸⁾ is also affected by aging. Severe intractable asthma might be caused by bronchospasm in patients under the age of 30, by bronchospasm + hypersecretion in those between the ages of 31 and 40, and by bronchiolar obstruction in those over age 40¹⁹⁾.

The frequency of patients with bronchospasm + hypersecretion (type Ib) showed a peak between the ages of 51 and 60, and the number of patients with bronchiolar obstruction (type II) increased with aging.²⁰⁾ Furthermore, bronchial hyperresponsiveness showed a tendency to decrease with aging.

In the present study, age-related changes in IgE-mediated allergic reactions were examined in patients with late onset asthma.

Subjects and Methods

The subjects of this study were 54 outpatients (23 females and 31 males, mean age 57.3 years, range 15-82 years) with late onset asthma, whose asthma occurred over the age of 40. The subjects were divided into 4 groups according to age at onset: 0-39, 40-49, 50-59, and 60+. Three inhalant allergens, house dust mite (Hdm), cockroach and *Candida albicans*, were estimated by a radioallergosorbent test (RAST). Asthma severity was evaluated according to their symptoms and dose of glucocorticoids used a day. Patients with asthma attacks despite glucocorticoid regimen, and with maintenance dose of prednisolone over 5 mg/day were

evaluated as having severe asthma. In contrast, patients who have sometimes slight attacks without necessity of any medications or no attacks for a long time (more than 2 months) were assessed as having slight asthma. The level of serum IgE was measured by a radioimmunosorbent test (RIST).

Statistical difference was evaluated by χ^2 analysis. A p value of <0.05 was assessed as significant.

Results

Characteristics of patients studied

The characteristics of patients with asthma studied are shown in Table 1. The mean level of serum IgE was higher in patients between the ages at onset 40 and 49 than in those of other ages at onset however there were no significant differences among the four groups. Difference of serum levels of

Table 1. Characteristics of patients with asthma studied

| Age at onset (years) | No of subjects | Mean age (years) | Serum IgE (IU/ml) |
|----------------------|----------------|------------------|-------------------|
| 0-40 | 13 | 41.1 | 345 (50-1043) |
| 40-49 | 17 | 55.8 | 616 (9-3220) |
| 50-59 | 11 | 61.7 | 345 (16-929) |
| 60- | 13 | 73.2 | 399 (5-859) |

IgE in relation to age at onset.

A high serum IgE level (over 300 IU/ml) was more frequently observed in patients between the ages of 40 and 49, and in those over the age of 60 at onset. In contrast, regarding a low level of serum IgE (under 100 IU/ml), there were no significant differences among these groups (Fig. 1).

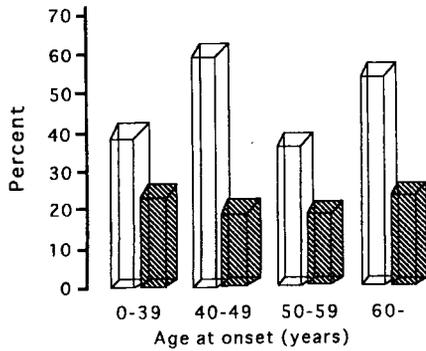


Fig. 1. Frequency of asthma patients with serum IgE levels over 300IU/ml (□) and less 100IU/ml (▨)

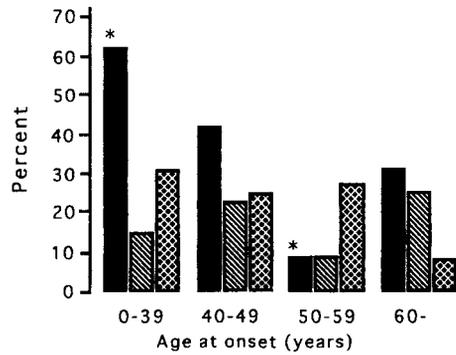


Fig. 2. Frequency of asthma patients with positive RAST to HDm (■), cockroach (▨) and Candida (⊠), and age at onset *P<0.05

Difference of specific IgE antibodies in relation to age at onset.

The frequency of positive RAST to house dust mite (HDm) was relatively high in patients between the ages of 40 and 49, and in those over age 60 at onset. However, the frequency was significantly lower in the patients between ages 50 and 59 at onset than in those under age 39 at onset ($p < 0.05$). The frequency of positive RAST to cockroach was relatively high in patients between ages 40 and 49 at onset, and in those over age 60 at onset, although the frequency was low in patients between ages 50 and 59 at onset. The frequency with positive RAST to *Candida albicans* was relatively high in patients between ages 40 and 49 at onset, and in those between ages 50 and 59 at onset. The frequency was low in the patients over age 60 at onset (Fig. 2).

The frequency with positive RAST either to HDm, cockroach, or *Candida*, seemed to be low in patients between ages 50 and 59 at onset, but relatively high in those between ages 40 and 49, and over age 60 at onset (Fig. 3). Frequency of asthma patients with family history of allergic diseases and age at

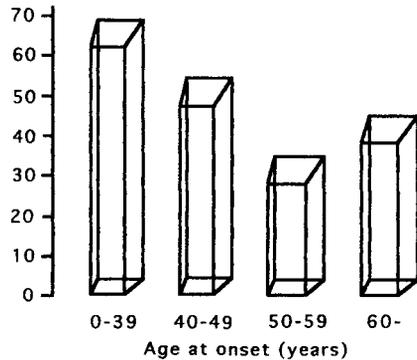


Fig. 3. Frequency of asthma patients with positive RAST either to HDm, cockroach or *Candida* and age at onset

onset.

Family history of allergic diseases was more frequently observed in those between ages 50 and 59 at onset, but relatively low in those between ages 40 and 49, and over age 60 at onset (Fig. 4). Asthma severity in relation to patient age at onset.

In late onset asthma patients, severe asthma was more frequently observed in patients between ages 50 and 59 at onset, than in those between ages 40 and 49, and

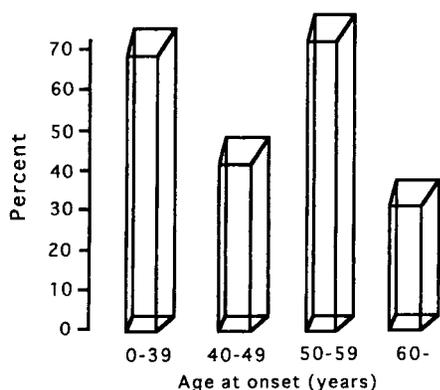


Fig. 4. Frequency of asthma patients with family history of allergic diseases and age at onset

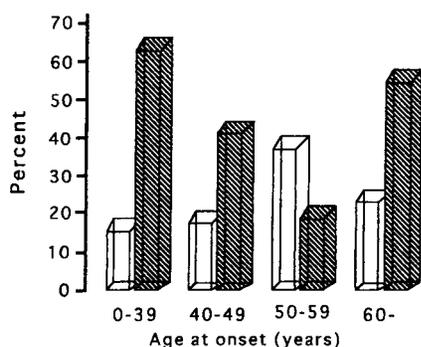


Fig. 5. Frequency of patients with severe (□) and slight asthma (▨) in relation to patient age

over age 60 at onset. On the other hand, slight asthma was frequently found in those between ages 40 and 49, and over age 60 at onset. The tendency in those age groups resembled to that in early onset asthma patients (Fig. 5).

Discussion

Bronchial asthma is characterized by bronchial hyperresponsiveness to various stimuli, which seems to be affected by pathophysiological changes in the airways

associated with allergic reactions.

One of main factors in the onset mechanism of asthma is IgE antibodies-induced allergic reactions, which are observed at immediate phase¹⁻³⁾ and late phase⁷⁻¹⁰⁾ after allergen challenge. The IgE-mediated allergic reactions has been suggested to change qualitatively and quantitatively with aging.^{4, 11-13, 20)}

Pathophysiology of asthma patients is also affected by aging.^{15, 20)} In this study, we examined changes in IgE-mediated allergic reactions in patients with late onset asthma. In late onset asthma patients (over age 40 at onset), a high serum IgE level was more frequently observed in patients between ages 40 and 49 at onset, however, it was less frequently found in those between ages 50 and 59 at onset than in those over age 60 at onset.

The frequency of positive RAST to Hdm and cockroach in patients between ages 40 and 49, and over age 60 at onset seems to resemble to that in early onset asthma patients. However, the frequency of positive RAST to Hdm was low, and that to *Candida albicans* was high in patients between ages 50 and 59 at onset.

In patients between ages 50 and 59 at onset, serum IgE level was low, and frequency of positive RAST to Hdm and cockroach allergens seemed to be relatively low. This might suggest that IgE-related allergic reaction is less involved. However, family history of allergic diseases was more frequently found in these patients between ages 50 and 59 at onset, it is still unclear why IgE-related allergic reaction is less involved in these patients despite a high frequency of family history of allergic diseases. Furthermore, in these patients between ages

50 and 59 at onset, severe asthma with glucocorticoid therapy was more frequently observed.

Patient age, when asthma often begin to occur has two peaks, 0–9 and 50–59 years. Many of patients between ages 0 and 9, and between 50 and 59 at onset have family history of allergic diseases. However, participation of IgE-mediated allergic reaction in the onset mechanism of asthma is markedly different between the two age at onset groups, one has a close correlation with IgE-mediated reactions, and another has less relationship to the reactions. It was not clear from the present study that the difference in IgE-related reaction is caused by aging.

Our previous studies showed that characteristics of patients with late onset asthma (over age 40 at onset) were differed from those with early onset asthma.^{14,19)} However, in this study, it was suggested that IgE-mediated allergic reaction in patients between the ages of 50 and 59 at onset, but not in those between ages 40 and 49 at onset, was different from that in those with early onset asthma, and that the reaction in patients between the ages 40 and 49, and over 60 at onset resembles to the reaction those with early onset asthma.

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中高年発症型喘息患者におけるIgE系アレルギー反応の加齢による変化

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発症年齢が40才以上の中高年発症型喘息患者におけるIgE系アレルギー反応の加齢による変化について検討を加えた。

1. 発症年齢が40から49才と60才以上の患者では、50から59才の患者に比して血清IgE値が300IU/ml以上の高値を示す頻度が高い傾向が見られた。
2. ダニ、ゴキブリに対するRAST陽性率は発症

年齢が50から59才の患者に比して、40から49才と60才以上の患者で高値を示した。一方、カンジダに対するRAST陽性率は、発症年齢が40から49才と60才以上の患者に比して、50から59才の患者で高値を示した。

3. 発症年齢が50から59才の患者では、他の発症年齢の患者に比べて、重症例が多く、軽症例が少ない傾向が見られた。

以上の結果から、発症年齢が50から59才の患者のIgE系アレルギー反応は若年発症型喘息患者と異なり、発症年齢が40から49才と60才以上の患者のIgE系アレルギー反応は若年発症型喘息患者と類似することが示唆された。

索引用語：IgE, RAST, 吸入抗原, 気管支喘息, 加齢