
◎原 著

Airway inflammation in elderly patients with bronchial asthma. Different airway inflammatory cell response related to disease severity.

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Abstract : Cellular composition of bronchoalveolar lavage (BAL) fluid was examined in 11 elderly asthmatics over the age of 70, and the results were compared with those of 11 younger asthmatics under the age of 50. In the subjects with mild asthma, the proportion of BAL cells in the elderly subjects was 86.2% macrophages, 11.0% lymphocytes, 1.9% neutrophils, 0.9% eosinophils and 0.08% basophilic cells. The proportion of neutrophils and eosinophils in the BAL fluid was slightly higher in younger subjects with mild asthma compared with that in elderly subjects, although no significant difference was found between the two groups. In subjects with severe asthma, the proportions of lymphocytes, neutrophils, eosinophils and basophilic cells were more increased in both younger and older patients compared to those with mild asthma, and a significant increase in the number of BAL eosinophils was found in younger subjects with severe asthma compared to those with mild asthma ($p < 0.05$). However, no significant difference was present in the proportion of BAL cells between younger and older patients with severe asthma.

The results reveal that BAL cells are more increased in subjects with severe asthma than in those with mild asthma in both younger and older subjects, and show the possibility that this increase is more predominant in neutrophils in older subjects and in eosinophils in younger subjects.

Key words : Neutrophils, Eosinophils, Bronchoalveolar lavage, asthma severity.

Introduction

In recent years, it has been widely accepted that airway inflammation is a common feature of bronchial asthma (1–6). The inflammatory process in the airways of asthma has been observed even in mild asthma (7–9). The inflammatory cells including lymphocytes, neutrophils, eosinophils and basophils have been examined by analyzing the cellular composition in bronchoalveolar lavage (BAL) fluid (10–18). The role of inflammatory cells in the airways has been also studied by estimating mediators and lymphokines released from these cells (19–22). Thus, the traditional concept that asthma is a disease characterized by transient bronchoconstriction, which is mainly caused by release of chemical mediators from tissue mast cells has been changing.

Number of elderly patients with bronchial asthma has been increasing. It has been speculated that asthma in the elderly patients is different from that in younger patients. The difference may be due to changes in allergic reaction and in the structure of airways with aging.

In the present study, airway inflammation was examined in elderly patients with bronchial asthma, by analyzing cellular composition in BAL fluid.

Subjects and Methods

To examine characteristics of airway inflammation in elderly patients with bronchial asthma, 11 asthmatics (4 females and 7 males) over the age of 70 were selected in this study. Their mean age was 71.4 years. The mean level of serum IgE was 276 IU/ml (range 14–1150 IU/ml). Of these, 5 were patients with mild asthma, and 6 were those

with severe intractable asthma. Eleven asthmatics under the age of 50 were selected as control subjects. Their mean age was 33.5 years (range 21–48 years). The mean level of serum IgE was 458 IU/ml (range 87–2430 IU/ml). Of these, 5 were patients with mild asthma and 6 were those with severe intractable asthma. All subjects were non-smokers.

The subjects were divided into two groups: patients with mild asthma and those with severe intractable asthma. Patients whose asthma attacks can be well controlled with conventional antiasthma drugs were evaluated as having mild asthma, and those whose attacks often require a large dose of glucocorticoids and can not be controlled without glucocorticoids were assessed as having severe intractable asthma.

Bronchoalveolar lavage (BAL) was performed by a method previously described (5, 6). The BAL examination for patients with severe intractable asthma was carried out when their asthma was stable with prednisolone of the dose of 5mg or less/day. Informed consent was obtained from all subjects. Cell differentiation was carried out by observing 500 cells excluding epithelial cells on smear preparations which were made from BAL cell suspension and stained with May Giemsa.

Serum IgE levels were estimated by radioimmunosorbent test (RIST). IgE antibodies to inhalant allergens were measured by radioallergosorbent test (RAST).

Results

The mean proportion of each BAL cell in 11 elderly subjects over the age of 70 was $77.5 \pm 12.9\%$ (\pm SD) macrophages, $12.7 \pm 8.6\%$ lymphocytes, $5.7 \pm 10.7\%$ neutrophils, 3.8

$\pm 6.0\%$ eosinophils and $0.06 \pm 0.2\%$ basophilic cells. In contrast, the mean proportion in 11 younger subjects under the age of 50 was $71.3 \pm 17.0\%$ macrophages, $12.9 \pm 9.0\%$ lymphocytes, $4.3 \pm 5.3\%$ neutrophils, $11.3 \pm 14.7\%$ eosinophils and $0.22 \pm 0.32\%$ basophilic cells. The proportion of BAL eosinophils was higher in younger subjects than in elderly subjects, although no significant difference was present between the two groups. The proportion of the other BAL cells was not different between younger and older subjects (Fig. 1).

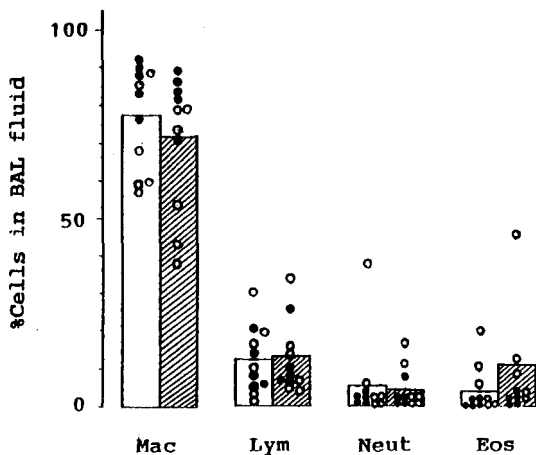


Fig. 1. Cellular composition in bronchoalveolar lavage (BAL) fluid of older (\square) and younger patients with asthma (hatched) in relation to asthma severity: mild asthma (\bullet) and severe asthma (\circ). Mac, macrophages; Lym, lymphocytes; Neut, neutrophils; Eos, eosinophils.

To examine a correlation between cellular composition of BAL fluid and asthma severity, analysis of BAL cells was compared between subjects with mild and severe intractable asthma. The proportions of lymphocytes, eosinophils and basophilic cells were

generally low in elderly subjects with mild asthma, as shown in Table 1. The proportions of neutrophils and eosinophils were higher in younger subjects than in elderly subjects in mild asthma, although these differences were not significant (Table 1, Fig. 1).

Table 1. Comparison of the proportions of BAL cells between younger and older subjects with mild asthma

Asthma group	No of patients	BAL cells				
		Mac	Lym	Neut	Eos	Bas
Older subjects	5	86.2* ± 5.3	11.0 ± 6.0	1.9 ± 0.9	0.9 ± 0.1	0.08 ± 0.10
Younger subjects	5	83.2 ± 6.4	11.8 ± 2.3	2.8 ± 3.1	2.2 ± 1.4	0.14 ± 0.20

* Mean \pm SD. Mac, macrophages; Lym, lymphocytes; Neut, neutrophils; Eos, eosinophils; Bas, basophilic cells

In subjects with severe asthma, the proportions of lymphocytes, neutrophils, eosinophils, and basophilic cells were increased in both younger and older subjects compared with those with mild asthma. Of these cells, the proportions of neutrophils and eosinophils were predominant in the two groups with severe asthma, and a significant difference was found in the proportion of BAL eosinophils between younger subjects with mild and severe asthma. These results show that the proportions of lymphocytes, neutrophils, eosinophils and basophilic cells are increased in subjects with severe asthma compared with those with mild asthma. In comparison of the proportions of BAL cells between younger and older subjects with severe asthma, the proportion of BAL neutrophils was higher in older subjects than in younger subjects, while the proportion of BAL eosinophils was higher in younger subjects than in older subjects. However, there was no significant difference in the proportions of BAL cells between younger and older

subjects with severe asthma (Table 2, Fig. 1).

Table 2. Comparison of the proportions of BAL cells between younger and older subjects with severe asthma

Asthma group	No of patients	Mac	Lym	Neut	Eos	Bas
Older subjects	6	70.3* ±12.9	14.2 ±10.1	8.9 ±13.6	6.2 ±7.2	0.12 ±0.26
Younger subjects	6	61.4 ±16.7	13.8 ±10.1	5.6 ±6.3	18.9 ±16.4	0.36 ±0.38

* Mean ± SD. Mac, macrophages; Lym, lymphocytes; neut, neutrophils; Eos, eosinophils; Bas, basophilic cells.

Discussion

Recently, airway inflammation has been noted in relation to the pathophysiology of bronchial asthma (1-8). It has been reported that increased numbers of lymphocytes (14-17), neutrophils (13), and eosinophils (9-12) are observed in BAL fluid of patients with bronchial asthma. Furthermore, many investigations have been performed to examine the pathophysiology of asthma by observing mediators released from activated cells found in BAL fluid (19-22).

In the present study, airway inflammation in elderly asthmatics over the age of 70 was examined by analyzing cellular composition of BAL fluid. In all subjects, the proportion of BAL eosinophils was lower in older subjects than in younger subjects, but there was no significant difference between the two groups. In subjects with mild asthma, the proportion of BAL lymphocytes in older subjects was within a normal with a mean of 11.0% (14, 16). The proportions of neutrophils and eosinophils in BAL fluid of older subjects were 1.9% and 0.9%, respectively, which were slightly increased compared with those in healthy subjects (23). In

comparison of the proportions of BAL cells between younger and older subjects, the proportions of neutrophils and eosinophils were slightly higher in younger subjects than in older subjects, but there was no significant difference between the two groups.

In subjects with severe asthma, the proportions of lymphocytes and neutrophils, eosinophils, and basophilic cells were more increased in both younger and older subjects compared to those with mild asthma. There was a significant difference in the proportion of BAL eosinophils between younger subjects with mild and severe asthma. These results reveal the proportions of inflammatory cells such as lymphocytes, neutrophils, eosinophils, and basophilic cells are more increased in subjects with severe asthma compared to those with mild asthma. This increase in BAL cells of patients with severe asthma seems to be predominant in neutrophils in older subjects and in eosinophils in younger subjects.

Regarding BAL eosinophils, it has been shown that the numbers of activated T cells and eosinophils in BAL fluid are related to the severity of asthma, as measured by impairment of FEV1.0 and increased methacholine bronchial responsiveness (18). Our results are in agreement with those previously reported. Further studies are necessary to confirm results about a correlation between numbers of BAL cells and asthma severity.

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老年者気管支喘息における気道炎症細胞、喘息重症度と関連した気道細胞反応の特徴

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70才以上の老年者気管支喘息11例(平均年齢71.4才)を対象に、重症度と気道細胞反応との関連について検討を加えた。なお、対照として50才以下の喘息症例11例(平均年齢33.5才)を選んだ。

1. 老年者の軽症型喘息における気管支肺胞洗浄(BAL)液中の出現細胞の頻度は、マクロファ-

ジが86.2%, リンパ球が11.0%, 好中球が1.9%, 好酸球が0.9%, 好塩基性細胞が0.08%であった。BAL液中の好中球, 好酸球の頻度は若青年症例でやや高い傾向が見られたが、両群間に有意の差は見られなかった。重症例では、老年症例, 若青年症例とも、軽症例に比べリンパ球, 好中球, 好酸球などのBAL細胞の出現頻度が増加しており、特に好酸球では若青年症例の重症例で軽症例に比べ有意に高い頻度が観察された。

これらの結果は、リンパ球, 好中球, 好酸球などのBAL細胞は、軽症例に比べ重症例で増加してくること、そして、その増加は老年症例では好中球, 若青年症例では好酸球の増加が特徴的であることを示唆しているものと考えられた。

キーワード：好中球, 好酸球, 気管支肺胞洗浄, 喘息重症度