
◎原 著

Clinical significance of airway inflammation in bronchial asthma. Comparison with chronic obstructive bronchiolitis.

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Abstract : Clinical significance of airway inflammation was assessed in 28 patients with bronchial asthma, and the results were compared with those in 9 patients with chronic obstructive bronchiolitis (COB). 1. Total cell number in bronchoalveolar lavage (BAL) fluid was markedly increased in patients with COB (51.0×10^6), which was significantly greater than that in those with bronchial asthma (9.6×10^6). 2. The proportion of BAL macrophages was significantly higher in patients with bronchial asthma than in those with COB. However, the absolute number of BAL macrophages was not significantly different between them. 3. The proportion of BAL lymphocytes was higher in patients with bronchial asthma than in those with COB, but this difference was not significant. In contrast, the absolute number of BAL lymphocytes was significantly greater in patients with COB than in those with bronchial asthma. 4. The proportion and the number of BAL neutrophils were markedly increased in patients with COB compared to those with bronchial asthma. 5. The proportion and the number of BAL eosinophils were higher in patients with bronchial asthma than in those with COB, although these differences were not significant. The results suggest that airway inflammation in bronchial asthma is not so intensive as that in COB.

Key words : airway inflammation, bronchial asthma, chronic obstructive bronchiolitis, lymphocytes, neutrophils.

Introduction

IgE-mediated allergy, in which chemical

mediators are released from tissue mast cells by bridging of IgE receptors on the cell membranes, has been evaluated as a major

reaction participating in the mechanism of onset of bronchial asthma (1-5). However, recently, attention has been focused on airway inflammation in the pathogenesis of bronchial asthma (6-8). Inflammatory cell infiltration in the airways of asthma has been found by analyzing humoral and cellular components in bronchoalveolar lavage (BAL) fluid (9-12): lymphocytes, neutrophils, eosinophils and basophils are assessed as inflammatory cells in the airways of asthma. These findings suggest that airway inflammation is assessed as a major mechanism related to asthma attack.

There are many kinds of respiratory diseases with airway inflammation. Of these respiratory diseases, chronic obstructive bronchiolitis (or diffuse panbronchiolitis: DPB) is one of the chronic obstructive pulmonary diseases (COPD), which is clearly caused by airway inflammation.

In the present study, airway inflammation is evaluated in patients with bronchial asthma and chronic obstructive bronchiolitis (COB) by analyzing the proportions and the numbers of bronchoalveolar lavage (BAL) cells such as macrophages, lymphocytes, neutrophils and eosinophils.

Subjects and Methods

The subjects of this study were 28 patients with bronchial asthma (18 females and 10 males, age 52.6 years, range 24-72 years). Nine patients with chronic obstructive bronchiolitis (COB) (5 females and 4 males, mean age 48.9 years, range 21-73) were selected as controls. To compare the numbers of bronchoalveolar lavage (BAL) cells between patients with asthma and those with COB, asthma patients whose recovery rate at BAL examination was more than 30% were

selected in this study, since recovery rate at BAL examination was sometimes very low in patients with asthma (this may be due to bronchoconstriction induced by BAL examination). All patients were admitted to our hospital, and all of them were non-smokers. Bronchial asthma was diagnosed according to the criteria of American Thoracic Society (13). Chronic obstructive bronchiolitis (COB) was diagnosed by clinical symptom, finding on auscultation and micronodular shadow on chest X-ray films.

Bronchoalveolar lavage (BAL) was performed by a previously reported method (14, 15) in all the patients when their symptoms were stable. Informed consent for the BAL examination was obtained from all study subjects. The aspirates obtained by a bronchofiberscope were filtered through a sterile steel mesh and centrifuged at 1200 rpm for 10 min at 4°C. The cell pellet was resuspended in Tris ACM which comprises 1ml of 0.1 M Ca, 0.5ml of 0.1 M Mg and 98.5ml of Tris A buffer (TRIZMA pre-set crystal, pH 7.7, Sigma Chemical Co., 0.3275 g + NaCl 0.7015 g + KCl 0.0372 g + 3% albumin 5ml + H₂O 100ml). After the number of cells was calculated, smear preparations were made from the cell suspension, and stained with May Giemsa. BAL cytology was performed by observing 500 cells, excluding epithelial cells. The absolute numbers of total cells and each BAL cell, and the proportions of each BAL cell were compared in patients with bronchial asthma and those with COB.

Results

Total cell number

Total cell number in BAL fluid was 9.6×10^6 in patients with bronchial asthma, and 51×10^6 in those with COB. The number of

total cells in BAL fluid was markedly different between the two obstructive respiratory diseases, and the number was significantly greater in patients with COB than in those with asthma ($P < 0.001$) (Fig. 1). Recovery rate at BAL examination was similar between patients with asthma (42.6%) and those with COB (41.4%).

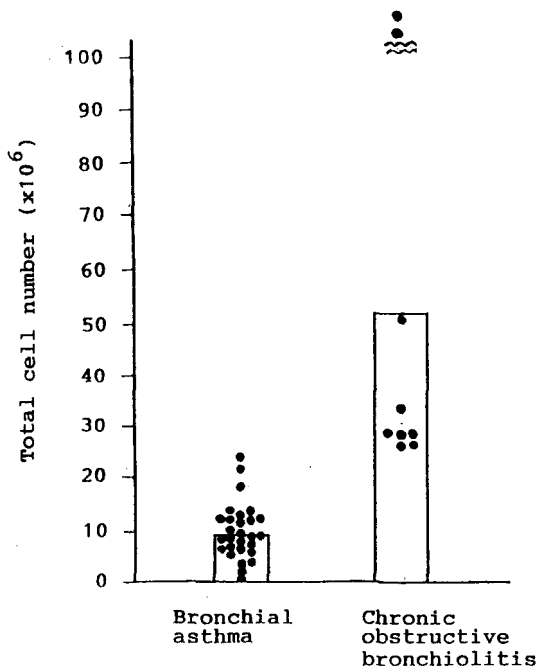


Fig. 1. Total cell number in bronchoalveolar lavage (BAL) fluid of patients with asthma and of those with chronic obstructive bronchiolitis (COB). The mean total cell number was significantly higher in patients with COB than in those with asthma.

Proportions of each BAL cell

The proportion of each BAL cell in patients with asthma was 74.8% macrophages, 15.0% lymphocytes, 2.6% neutrophils and 7.6% eosinophils. In contrast, the mean proportion

of each BAL cell in patients with COB was 21.2% macrophages, 9.4% lymphocytes, 68.7% neutrophils and 0.7% eosinophils. The proportion of BAL macrophages was significantly higher in patients with asthma than in those with COB ($p < 0.001$). In contrast, the proportion of BAL neutrophils was significantly higher in patients with COB than in those with asthma ($p < 0.001$). The proportions of lymphocytes and eosinophils in BAL fluid were higher in patients with asthma than in those with COB, however, these differences were not significant (Fig. 2).

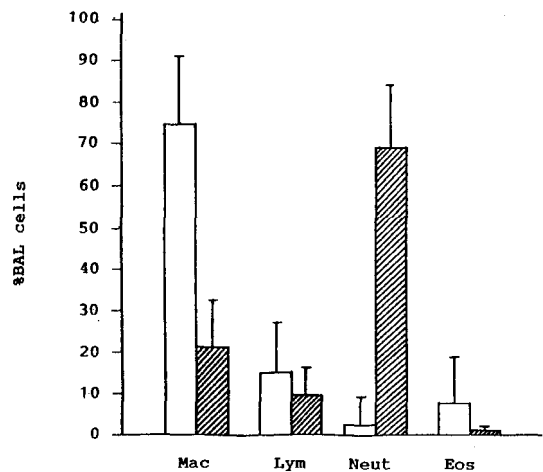


Fig. 2. Proportions of each bronchoalveolar lavage (BAL) cell in patients with asthma (□) and in those with chronic obstructive bronchiolitis (COB) (▨). The proportion of BAL macrophages was significantly higher in patients with asthma than in those with COB. In contrast, the proportion of BAL neutrophils was significantly higher in patients with COB than in those with asthma. Mac, macrophages; Lym, lymphocytes; Neut, neutrophils; Eos, eosinophils.

Numbers of each BAL cell

The absolute number of BAL lymphocytes was significantly greater in patients with COB than in those with asthma ($p < 0.05$). The absolute number of BAL neutrophils was markedly increased in patients with COB, which was significantly greater than that in those with asthma ($p < 0.001$). The absolute numbers of macrophages and eosinophils in BAL fluid were not significantly different between the two obstructive respiratory diseases, although the number of BAL eosinophils was greater in patients with asthma compared to those with COB (Table 1).

Table 1. Absolute number of bronchoalveolar lavage (BAL) cells in patients with asthma and those with chronic obstructive bronchiolitis

Disease	No of patients	Number of BAL cells ($\times 10^4$)			
		Mac	Lym	Neut	Eos
Bronchial asthma	28	712 ± 379	171 ^a ± 265	17 ^b ± 25	62 ± 114
Chronic obstructive bronchiolitis	9	872	495 ^{a'} ± 585	3702 ^{b'} ± 3004	32 ± 37

Mac, macrophages; Lym, lymphocytes; Neut, neutrophils; Eos, eosinophils. A significant difference between a and a' at $p < 0.05$, and between b and b' at $p < 0.001$.

The number of each BAL cell per ml was compared between the two respiratory diseases. The number of BAL lymphocytes was significantly greater in patients with COB ($5.39 \pm 5.2 \times 10^4 / \text{ml}$) than in those with asthma ($2.0 \pm 2.6 \times 10^4 / \text{ml}$) ($p < 0.02$). The BAL neutrophil number in patients with COB was markedly increased ($54.8 \pm 44.7 \times 10^4 / \text{ml}$), and this was significantly greater than that in those with asthma ($0.22 \pm 0.34 \times$

$10^4 / \text{ml}$) ($p < 0.001$). The numbers of macrophages and eosinophils in BAL fluid were not significantly different between the two diseases (Fig. 3).

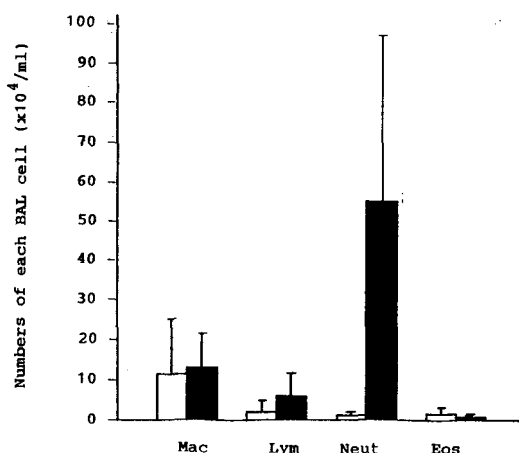


Fig. 3. Numbers of each bronchoalveolar lavage (BAL) cell in patients with asthma (□) and in those with chronic obstructive bronchiolitis (COB) (■). The number of lymphocytes and neutrophils were significantly greater in patients with COB than in those with asthma. Mac, macrophages; Lym, lymphocytes; Neut, neutrophils; Eos, eosinophils.

Discussion

It is well known that bronchial response to allergen is divided into two phases: immediate asthmatic reaction (IAR) and late asthmatic reaction (LAR). The IAR is mainly induced by the release of chemical mediators from tissue mast cells (1-5). In contrast, the LAR has been clarified to be related to inflammatory cell infiltration (16). Thus, airway inflammation is a common feature of asthma (9-12, 17, 18).

In the present study, clinical significance of airway inflammation in bronchial asthma was evaluated in relation to inflammatory process in chronic obstructive bronchiolitis (COB). The total cell number in the BAL fluid was considerably small in patients with asthma compared to the number in those with COB. The results suggest that airway inflammation in bronchial asthma is not so intensive as that in COB. Regarding the proportion of BAL cells, the proportion of BAL macrophages was significantly higher in patients with asthma than in those with COB. However, the absolute number of BAL macrophages was not significantly different between the two obstructive respiratory diseases. The proportion of BAL lymphocytes was higher in patients with asthma than in those with COB, although this difference was not significant. In contrast, the absolute number of BAL lymphocytes was significantly greater in patients with COB than in those with asthma. The proportion and the number of BAL neutrophils were markedly increased in patients with COB, and this increase was significantly higher than that in patients with asthma.

An increase in eosinophil number in the peripheral blood and local allergic reaction site is one of the characteristics of bronchial asthma. In this study, the proportion and the number of BAL eosinophils were greater in patients with asthma than in those with COB. However, the difference was not significant between them: this may be due to the reason that BAL examination was performed in asthma patients when they were free of attacks.

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気管支喘息における気道炎症反応の臨床的意義。 慢性閉塞性細気管支炎との比較検討

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気管支喘息28例および慢性閉塞性細気管支炎9例を対象に, 気道炎症反応の臨床的意義について検討を加えた。

1. 気管支肺胞洗浄 (BAL) 液中の総細胞数は, 慢性閉塞性細気管支炎において著明に増加しており (51.0×10^6), 気管支喘息 (9.6×10^6) との間に有意の差が見られた。
2. BAL液中マクロファージの頻度は気管支喘息において, 慢性閉塞性細気管支炎に比べ有意

に高い値を示したが, 絶対数での比較では両疾患群間に有意の差は見られなかった。

3. BAL液中リンパ球の頻度は, 気管支喘息においてやや高い傾向が見られたが, 絶対数の比較では慢性閉塞性細気管支炎において有意に高い値であった。
 4. BAL液中の好中球は, その頻度および絶対数とも慢性閉塞性細気管支炎において著明に増加しており, これは気管支喘息と比べ有意に高い値であった。
 5. BAL液中好酸球の頻度および絶対数は, 気管支喘息においてやや高い値であったが, 両疾患群間に有意の差は見られなかった。
- 以上の結果より, 気管支喘息における気道炎症反応は, 慢性閉塞性細気管支炎ほど高度ではないことが明らかにされた。

キーワード: 気道炎症反応, 気管支喘息, 慢性閉塞性細気管支炎, リンパ球, 好中球