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Neutrophils in the airways of patients with bronchial asthma. Relationship to ventilatory function

Yoshiro Tanizaki, Hikaru Kitani, Morihiro Okazaki, Takashi Mifune, Fumihiro Mitsunobu, Masakuni Tanimizu, Naoko Honke, Yasuharu Kusaura and Ikuro Kimura¹⁾

Division of Medicine, Misasa Medical Branch, ¹⁾Second Department of Medicine, Okayama University Medical School

Abstract : Ventilatory function was compared between two age-matched asthma groups : group A (study group) consists of 8 patients with bronchial asthma with marked neutrophilia (20% or more) in the BAL fluid and group B (control group) of 8 patients with neutrophils (less than 5% of total BAL cells). The values of six ventilatory parameters were lower in group A than in group B, and a significant difference was found in FEV_{1.0%}, %MMF, % \dot{V}_{50} and % \dot{V}_{25} between groups A and B. Of these parameters, the value of % \dot{V}_{25} was markedly decreased in group A compared with group B. The results show that ventilatory dysfunction in airways, especially in small airways, is closely correlated to increased number of neutrophils in BAL fluid.

Key words : ventilatory function, neutrophils in BAL fluid, small airways, bronchial asthma

Introduction

Bronchial asthma is one of the chronic obstructive lung diseases (COLD). The clinical features of asthma, wheezing and dyspnea, are caused by narrowing or obstruction of the airways, which are due to bronchoconstriction, bronchial wall edema and mucus hypersecretion. In addition to these pathophysiological changes of airways, bronchiolar obstruction during asthma attacks is observed in some adult patients with asthma^{1, 2)}. The ventilatory function in asthma patients show obstructive

ventilatory dysfunction, characterized by decreased value of FEV_{1.0%}.

Bronchial challenge with an allergen produces two kinds of airway responses, immediate asthmatic reaction (IAR) and late asthmatic reaction (LAR), in asthma patients. It has been suggested that humoral factor including chemical mediators such as histamine and leukotrienes mainly participates in the IAR and cellular components in the LAR. Analysis of cellular composition in bronchoalveolar lavage (BAL) fluid has demonstrated that cells infiltrating into local allergic reac-

tion site play an important role in the LAR³⁻⁵. Thus, airway inflammation is a common feature in bronchial asthma⁶⁻⁹, even in mild asthma^{10, 11}.

In the present study, a correlation between the proportion of neutrophils in BAL fluid and ventilatory function was discussed in patients with bronchial asthma.

Subjects and methods

Eight patients with bronchial asthma, whose proportion of neutrophils in BAL fluid was 20% or more (group A), were selected for this study. Of these, 2 were females and 6 were males. The mean age was 58.8 years (range, 46–71 years). The mean serum IgE level was 326 IU/ml (range, 65–1280 IU/ml). Four cases out of the eight subjects showed a positive PAST score of 2+ or more to allergens. Eight age-matched patients with asthma, whose proportion of neutrophils in BAL fluid was less than 5% (group B), were selected as control group. The mean age was 59.4 years (range, 49–70 years). The mean serum IgE level was 351 IU/ml. Four cases out of the eight subjects were sensitive to inhalant allergens. All subjects in groups A and B were admitted at our hospital because of their severe asthma attacks. They were all non-smokers.

The BAL examination was performed in all subjects by the method previously described when they were attack free^{1, 2}. Informed consent for the BAL examination was obtained from all of the subjects. The BAL cytology was performed on smear preparations stained with May-Giemsa, by observing 500 cells excluding epithelial cells. The results were expressed as a percentage of total cells.

Ventilatory function test was carried out in all subjects using a Box Spiro 81-S

(Chest Co) when they were asymptomatic. The values of six ventilatory parameters, %FVC, FEV_{1.0%}, %PEFR, %MMF, % \dot{V}_{50} and % \dot{V}_{25} , were compared between group A (study group) and group B (control group).

The total IgE level was measured by radioimmunosorbent test (RIST). Specific IgE antibodies for allergen were estimated by radioallergosorbent test (RAST).

Results

Table 1 shows the characteristics of group A (proportion of neutrophils in the BAL fluid of 20% or more) and group B (proportion of neutrophils less than 5%). The amount of expectoration/day was higher in group B than in group A. The proportion of neutrophils in the BAL fluid was markedly higher in group A compared with group B (Table 1).

Table 1. Characteristics of patients with bronchial asthma classified by the proportion of neutrophils in BAL fluid

Asthma group	No of cases	Age, years	Amount of expectoration * ml/day	%Neutrophils in BAL fluid
A	8	58.8	37.1±40.4**	51.4±20.9
B	8	59.4	75.3±100.2	2.3± 1.5

A: cases with BAL neutrophils of 20% or more; B: cases with BAL neutrophils less than 5%. * ml/day, ** mean±sd

The values of six parameters were in general lower in group A than in group B. The difference was, however, not significant in the values of %FVC and %PEFR between groups A and B. The values of FEV_{1.0%}, %MMF, % \dot{V}_{50} and % \dot{V}_{25} were significantly lower in group A compared with group B (FEV_{1.0%}, $p < 0.001$; %MMF, $p < 0.01$; % \dot{V}_{50} , $p < 0.01$; % \dot{V}_{25} , $p < 0.001$) (Fig. 1).

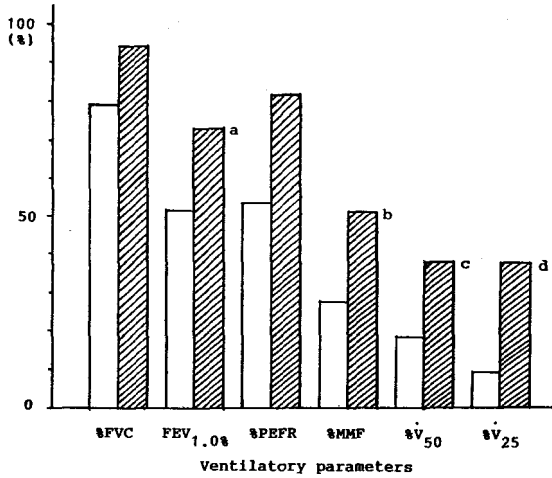


Fig. 1. Ventilatory function in group A (BAL neutrophils of 20% or more) (\square) and group B (BAL neutrophils less than 5%) subjects (hatched). Significant difference from group A at : a, $p < 0.001$; b and c, $p < 0.01$; d, $p < 0.001$

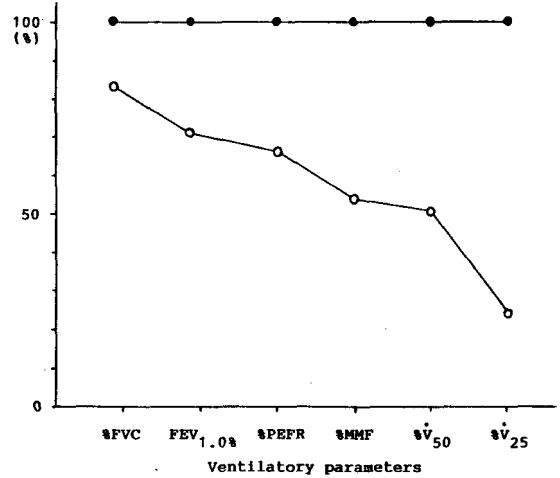


Fig. 2. Comparison of the values of ventilatory parameters between group A (BAL neutrophils of 20% or more) (\circ) and group B (BAL neutrophils less than 5%) (\bullet). The values of group B were calculated as 100%.

When the value of each ventilatory parameter in group B was calculated as 100%, the value of each parameter in group A was 83.8% in %FVC, 70.8% in FEV_{1.0%}, 65.7% in %PEFR, 54.8% in %MMF, 50.2% in % \dot{V}_{50} and 24.9% in % \dot{V}_{25} , respectively (Fig. 2). Thus, the value of ventilatory parameters in group A was considerably lower in %MMF and % \dot{V}_{50} , and lowest in % \dot{V}_{25} compared with the value of group B. These results reveal that ventilatory dysfunction in airways, particularly in small airways represented by markedly decreased value of % \dot{V}_{25} , is related to neutrophilia in BAL fluid.

Discussion

Recently, airway inflammation in bronchial asthma has been noted mainly in relation to LAR³⁻⁵, which is elicited 6 to 8 hours after bronchial challenge with an allergen. Inflammatory cells such as lymphocytes, neutrophils and eosinophils have been found in BAL fluid of asthma patients after bronchial inhalation with an allergen³⁻⁵ and during non-attack stages^{10, 11}. Regarding lymphocytes and eosinophils, several investigators have observed changes in the number and population of subtypes of the cells in BAL fluid and hypothesized the function of these cells¹²⁻¹⁴. There are, however, little reports about neutrophils in BAL fluid.

In the present study, ventilatory function was compared between two age-matched groups of asthma; group A showing marked

neutrophilia (20% or more) in the BAL fluid and group B whose proportion of BAL neutrophils was less than 5%. The values of ventilatory parameters such as FEV_{1,0%}, %MMF, % \dot{V}_{50} and % \dot{V}_{25} representing obstructive ventilatory dysfunction was significantly lower in group A than in group B. Furthermore, marked decrease in the % \dot{V}_{25} value showing ventilatory dysfunction in small airways was found in group A. The results reveal that markedly decreased value of % \dot{V}_{25} associated with increased number of neutrophils in BAL fluid is observed in group A.

Increased number of neutrophils in BAL fluid has been observed in the asthmatic patients whose symptoms are mainly due to bronchiolar obstruction^{1,2)} and in asthmatics with long-term corticosteroid therapy¹⁵⁾. Although the precise reason why neutrophils increase in BAL fluid of some asthmatics is not clear and there are many factors causing ventilatory dysfunction in asthma, it is speculated that neutrophilia in BAL fluid is one of the factors inducing ventilatory dysfunction, particularly in small airways, of patients with asthma.

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気管支喘息における気道内への好中球の出現とその意義 換気機能と関連して

谷崎勝朗, 貴谷 光, 岡崎守宏, 御船尚志, 光延文裕, 谷水将邦, 本家尚子, 草浦康浩, 木村郁郎¹⁾

岡山大学医学部附属病院三朝分院内科, ¹⁾医学部第二内科

気管支喘息を対象に, 年齢をmatchさせた2つのグループ, すなわち, 気管支肺胞洗浄液(BALF)中の好中球の出現頻度が20%以上の8症例(グループA)と, BALF中の好中球の出現頻度が5%以下の8症例(グループB)における換気

機能について比較検討を行った。6つの換気パラメーターは, 全般的にグループAにおいてグループBに比べ低い傾向が見られ, FEV_{1.0%}, %MMF, % \dot{V}_{50} および% \dot{V}_{25} 値は, いずれもグループAにおいて有意に低い値が示された。これらのパラメーターのうち, % \dot{V}_{25} 値はグループBに比べグループAにおいて著明に低い値が示された。

これらの結果は, 気道における換気障害, 特に小さい細気管支領域の換気障害は, BALF中の好中球の出現頻度とある程度関連していることを示すものと考えられた。

キーワード : 好中球, 換気機能, BAL, 細気管支, 気管支喘息