◎原 著

Difference in small airway inflammation between type II (bronchiolar obstruction) asthma and obstructive bronchiolitis

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Abstract : Ventilatory function and inflammatory cells in airways were compared between patients with type II (bronchiolar obstruction) asthma and those with obstructive bronchiolitis. 1. Age and age at onset were higher in patients with type II asthma than in those with obstructive bronchiolitis. IgE-mediated allergic reaction was observed in patients with type II asthma, but not in those with obstructive bronchiolitis. 2. In ventilatory function tests, all ventilatory parameters examined were lower in patients with type II asthma compared to those with obstructive bronchiolitis, and the differences were significant in FEV1.0% ($p<0.001$), %MMF ($p<0.02$), and $\dot{V}50$ ($p<0.01$). 3. The proportion of BAL neutrophils was very high in type II asthma (55.7%) and obstructive bronchiolitis (74.4%), however, this was not significant. 4. Absolute numbers/BAL fluid of total cells, BAL macrophages and BAL neutrophils were significantly higher in patients with obstructive bronchiolitis than in those with type II asthma. 5. The results on absolute number/mℓ of BAL cells demonstrated that number of BAL neutrophils markedly larger in patients with obstructive bronchiolitis compared to those with type II asthma.

These results show that high proportion of BAL neutrophils was observed in the two respiratory diseases, however, the degree of inflammation in airways was markedly greater in obstructive bronchiolitis.

Key words : Type II asthma, Obstructive bronchiolitis, Ventilatory function, BAL neutrophils, IgE-mediated allergy

Introduction

Inhalation of a relevant allergen induces immediate bronchoconstriction, and late asthmatic reaction[1-3], and then airway hyperresponsiveness[4,5]. Allergen-induced airway hyperresponsiveness is associated with

migration of inflammatory cells, lymphocytes[6-8], neutrophils[9,10], eosinophils[11-13], and basophils[14]. Thus, airway inflammation is a common feature of bronchial asthma[15].

Among three clinical types of asthma (type Ia. simple bronchoconstriction, type Ib. Bronchoconstriction+hypersecretion, and type II. bronchiolar obstruction), type II asthma is characterized by increased number of neutrophils in bronchoalveolar lavage (BAL) fluid and marked decrease in values of FEV1.0 and $\dot{V}25$[16-18]. In contrast, obstructive bronchiolitis, which is increasing in recent years as the number of aged-patients increases, is also characterized by BAL neutrophilia and obstructive ventilatory dysfunction in small airways.

In the present study, difference in inflammation of small airways between type II asthma and obstructive bronchiolitis was examined by analyzing ventilatory function, and the proportion and number of BAL cells.

Subjects and Methods

The subjects of this study were 7 patients (1 female and 6 males) with type II (bronchiolar obstruction) asthma, and 9 patients (4 females and 5 males) with obstructive bronchiolitis. Type II asthma was assessed according to a asthma classification method by clinical symptoms (clinical diagnosis)[16-18]. The subjects were reevaluated by a score calculated from clinical findings and examinations (score diagnosis)[19]. Obstructive bronchiolitis was diagnosed by chest X ray finding, clinical findings and examinations.

BAL was performed according to a previously described method[16-20] when the subjects were attack-free. Informed consent for this BAL procedure was obtained from all study subjects. The cell pellet obtained by centrifugation of BAL fluid was resuspended in Tris ACM. BAL cytology was performed by observing 500 cells, excluding epithelial cells, on smear preparations which were made from BAL cell suspensions and stained with May-Giemsa. The results were expressed as percentages of the total cells, and absolute number ($\times 10^6$/BAL fluid and $\times 10^4$/ml).

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

The level of serum IgE was measured by the radioimmunosorbent test (RIST) and IgE antibodies to inhalant allergens were evaluated by the redioallergosorbent test (RAST).

Statistically significant differences of the mean were estimated using the unpaired Student' t test. A p value of <0.05 was regarded as significant.

Results

Table 1 shows characteristics of patients with type II asthma and those with obstructive bronchiolitis. Age and age at onset of the disease were higher in patients with type II asthma than in those with obstructive bronchiolitis. The mean level of serum IgE was higher in type II asthma patients compared to those with obstructive bronchiolitis.

Table 1. Cgaracteristics of patients with type II asthma and those with obstructive bronchiolitis

Disease	No of patients	Age (years)	Age at onset (years)	Serum IgE (IU/ml)	RAST to HDm
Type II asthma	7	58.9	45.1	389 (105-1820)	2/7
Obstructive bronchiolitis	9	48.8	41.7	115 (45-309)	0/9

HDm, house dust mite

RAST to house dust mite (HDm) was positive in 2 of 7 patients with type II asthma, however, no patients with obstructive bronchiolitis showed a positive RAST to HDm and other inhalant allergens.

In ventilatory function tests, 6 ventilatory parameters were applied to evaluate difference between the two respiratory diseases. The values of all ventilatory parameters were lower in patients with type II asthma than in those with obstructive bronchiolitis. The differences were significant in FEV1.0% ($p<0.001$), %MMF ($p<0.02$) and $\%\dot{V}50$ ($p<0.01$), as shown in Fig. 1.

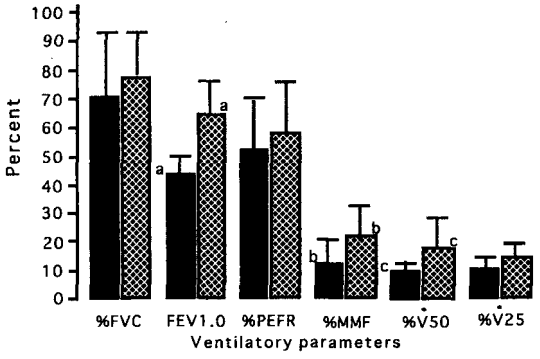

Fig. 1. Difference in ventilatory function between patients with type II asthma (■) and those with obstructive bronchiolitis (▩). a,$p<0.001$, b, $p<0.02$, c,$p<0.01$.

The proportion of BAL cells was compared in the two diseases. The proportion of BAL macrophages (Mac) was higher in patients with type II asthma, however, this was not significant. The proportion of BAL neutrophils (Neut) was very high in both respiratory diseases, and the proportion was higher in patients with obstructive bronchiolitis (74.4%) compared to those with type II asthma (55.7%). However, this was not significant. The proportions of BAL lymphocytes (Lymph) and eosinophils (Eos) were not different between the two diseases (Fig. 2).

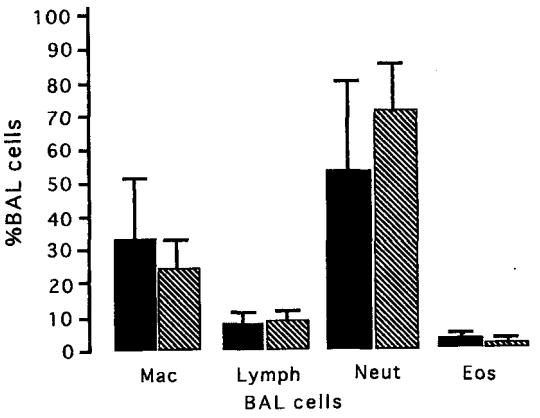

Fig. 2. Difference in BAL cells between patients with type II asthma(■) and those with obstructive bronchiolitis (▩).

Comparison of absolute number/BAL fluid obtained of BAL cells is demonstrated in Table 2. The recovery rate of BAL fluid was significantly larger in patients with obstructive bronchiolitis than in those with type II asthma. The absolute numbers/BAL fluid of total cells ($p<0.01$), BAL macrophages ($p<0.02$), and BAL neutrophils ($p<0.05$) were significantly higher in patients with obstructive bronchiolitis than in those with type II asthma. Figure 3 reveals absolute numbers/$m\ell$ of BAL cells. The number of BAL neutrophils was markedly larger ($88.3 \times 10^4/m\ell$) in patients with obstructive bronchiolitis compared to the number ($10.8 \times 10^4/m\ell$) in those with type II asthma.

Discussion

Clinical symptoms of patients with type II (bronchiolar obstruction) asthma are

Table 2. Absolute number of BAL cells in patients with type II asthma and obstructive bronchiolitis

Disease	Recovery rate (%)	No of cells ($\times 10^6$)	BAL cells ($\times 10^6$) Mac	Lymph	Neut	Eos
Type II asthma	18.6[a] ±8.9	4.8[b] ±3.1	177[c] ±105	29 ±35	249[d] ±218	20 ±26
Obstructive bronchiolitis	39.2[a] ±19.3	50.2[b] ±40.1	775[c] ±537	420 ±630	3787[d] ±3123	26 ±40

a,p<0.05, b,p<0.01, c,p<0.02, d.p<0.05.

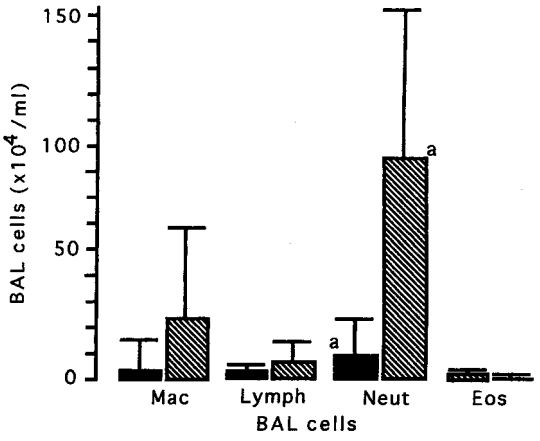

Fig. 3. Absolute number ($\times 10^4$/mℓ) of BAL cells in patients with type II asthma (■) and obstructive bronchiolitis (▨). a,p<0.02.

resemble to that of those with obstructive bronchiolitis. The pathophysiological changes in airways in the two kinds of respiratory diseases are inflammation in small airways, resulting in ventilatory dysfunction in these airways. It is well known that airway inflammation is a major pathogenesis of bronchial asthma[15]. Among inflammatory cells, activated T lymphocytes and eosinophils play an important role in triggering events of asthma attacks[7, 21]. However, a role of neutrophils in onset mechanisms of asthma attacks has been also noted in recent years[22, 23].

Our previous studies have shown that type II, bronchiolar obstruction, asthma is charcterized by an increase in number of BAL neutrophils and marked decrease in the value of ventilatory parameters such as FEV1.0 and $\%\dot{V}25$[16–18]. BAL neutrophilia in type II asthma might be associated with suppressed humoral and cellular immunity[24, 25], which is mainly caused by long-term glucocorticoid therapy.

In this study, the two respiratory diseases, which have resemble pathophysiological changes in airways were compared in relation to ventilatory function and proportions and numbers of BAL cells. In ventilatory function tests, the values of all parameters measured were lower in patients with type II asthma than in those with obstructive bronchiolitis, and the differences were significant in %FEV1.0, %MMF, and $\%\dot{V}50$, which represent airway narrowing. The results suggest that airway narrowing is stronger in patients with type II asthma compared to those with obstructive bronchiolitis.

Regarding airway inflammation, a high proportion of BAL neutrophils was observed in both respiratory diseases, however, the difference between the two diseases was not significant. Absolute numbers per BAL fluid and per mℓ of BAL neutrophils were markedly and significantly larger in patients with obstructive bronchiolitis than in those with type II asthma. Furthermore, the numbers/BAL fluid of total cells and macrophages were also significantly higher in patients with obstructive bronchiolitis. These results demonstrate that airway inflammation is markedly stronger in patients with obstructive bronchiolitis compared to that in

those with type II asthma.

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Ⅱ型（細気管支閉塞）喘息と閉塞性細気管支炎における細気管支領域の炎症反応の差

御舩尚志，光延文裕，保崎泰弘，芦田耕三，横田　聡，柘野浩史，竹内一昭，名和由一郎，谷崎勝朗，多田慎也[1)]，原田実根[1)]

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Ⅱ型喘息と閉塞性細気管支炎の臨床的特徴について，換気機能および気道炎症反応を中心に検討を加えた。１．年齢，および発症年齢とも閉塞性細気管支炎に比べⅡ型喘息において高い傾向が見られた。IgE系反応はⅡ型喘息では観察されたが，閉塞性細気管支炎では見られなかった。２．換気機能では，測定された全ての換気パラメーターにおいて，その値は閉塞性細気管支炎に比べⅡ型喘息でより低い値を示し，FEV1.0%，%MMFおよび%$\dot{V}$50では有意の差が見られた。３．BAL液中好中球頻度は，Ⅱ型喘息（55.7%），閉塞性細気管支炎（74.4%）いずれにおいても高い値を示したが，両者間に有意の差は見られなかった。４．一方，BAL液中の絶対数では，Ⅱ型喘息に比べ，閉塞性細気管支炎において，総細胞数，マクロファージおよび好中球数が有意の高値を示した。５．また，１mℓあたりの細胞数の比較でも，閉塞性細気管支炎で好中球数が著明な高値を示した。

これらの結果より，この２疾患では気道内好中球増多は同様に見られるものの，その気道炎症の程度は明らかに閉塞性細気管支炎でより高度であることが示された。

索引用語：Ⅱ型喘息，閉塞性細気管支炎，換気機能，BAL好中球，IgE系反応