

◎総説

Type II (bronchiolar obstruction) asthma and number of neutrophils in bronchoalveolar lavage (BAL) fluid

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Abstract : Bronchial asthma is classified into three types ; type Ia (Ia-1 and Ia-2), type Ib, and type II, by clinical symptoms (clinical diagnosis). Asthma is also classified by clinical findings and examinations (score diagnosis). Both classification systems show that markedly increased proportion of BAL neutrophils and marked decrease in % \dot{V}_{25} value are characteristic of type II, bronchiolar obstruction, asthma. However, there are some type II asthma patients without BAL neutrophilia. In these patients, age is higher compared to those with BAL neutrophilia. Decrease in FEV1.0% value and decrease in the proportion of BAL lymphocytes and serum IgG level, are not so remarkable as decrease in those with BAL neutrophilia. It has been suggested that type II asthma with BAL neutrophilia correlates with suppression of humoral and cellular immunity, and same type of asthma without BAL neutrophilia is in part caused by aging.

Key words : Asthma classification, BAL lymphocytes, BAL neutrophils, % \dot{V}_{25} value

Introduction

It has been well known that airway inflammation is a common feature of bronchial asthma¹⁻⁷⁾. In the process of airway inflammation, lymphocytes, neutrophils, eosinophils and basophils migrate from peripheral blood into local allergic reaction sites. Among these

cells, roles of activated T cells and eosinophils have been noted in relation to late asthmatic redction^{8,9)}. Basophilic cells, mast cells and basophils, also play an important role in triggering events of asthma attacks. Furthermore, participation of neutrophils in the onset mechanisms of asthma has been reported in recent years^{10, 11)}.

Our studies have shown that asthma can be classified by clinical symptoms (clinical diagnosis)¹²⁻¹⁴⁾. We have also demonstrated that characteristic of each clinical asthma type is closely related to clinical examinations such as the proportion of cells in bronchoalveolar lavage (BAL) fluid. Thus, bronchial asthma is also classified by clinical findings and examinations (score diagnosis)¹⁵⁾. The results from these studies have revealed that type II, bronchiolar obstruction, asthma is closely associated with BAL neutrophilia. However, our recent studies of asthma have led to the results that there are some type II asthma patients without BAL neutrophilia¹⁶⁾. In the present article, we tried to clarify clinical features of type II asthma without BAL neutrophilia (BALn⁻), compared to type II asthma with BAL neutrophilia (BALn⁺), and to other asthma types.

Clinical diagnosis

Bronchial asthma is classified into three types; I a. simple bronchoconstriction type, I b. bronchoconstriction+hypersecretion type, and II. bronchiolar obstruction type, by clinical symptoms¹²⁻¹⁴⁾. Type I a is, furthermore, divided into two subtypes according to expectoration per day; type I a-1 (0-49 ml) and type I a-2 (50-99 ml) (Table 1)¹⁴⁾.

Different proportions of BAL cells are found in each asthma type. In I b. hypersecretion type, increased proportion of BAL eosinophils are often observed^{14, 17)}, as shown in Fig. 1. The proportion of BAL eosinophils tended to increase as dose of expectoration a day increased. A significant increase in BAL eosinophils was found in subjects with expectoration between 50 and 99 ml/

Table 1. Asthma classification by clinical symptoms and signs

Type	Clinical symptoms and signs
Ia. Simple bronchoconstriction:	Patients with symptoms such as wheezing and dyspnea which are mainly elicited by bronchoconstriction. This type is divided into two subtypes according to the amount of expectoration.
Ia-1:	0-49 ml/day
Ia-2:	50-99 ml/day
Ib. Bronchoconstriction +hypersecretion	Patients with symptoms due to hypersecretion (more than 100 ml/day), in addition to bronchoconstriction.
II. Bronchiolar obstruction	Patients with symptoms mainly elicited by bronchiolar obstruction

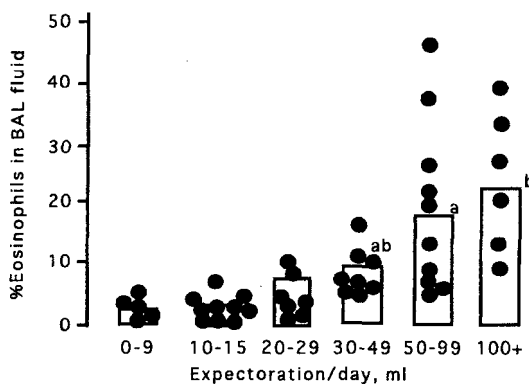


Fig. 1. Relationship of amount of expectoration to proportion of eosinophils in BAL fluid in patients with bronchial asthma. a and b: $p < 0.01$.

day ($p < 0.05$) and in those with expectoration over 100 ml/day ($p < 0.01$) compared with those expectoration between 30 and 49 ml/day. The proportion of BAL lymphocytes was the highest in patients with type I a-1 and lowest in those with type II. There was, however, no significant difference in the number of BAL lymphocytes between the clinical asthma types. The proportion of BAL neutrophils was significantly higher in patients with type II compared to those with type I a-1 ($P < 0.001$), type I a-2

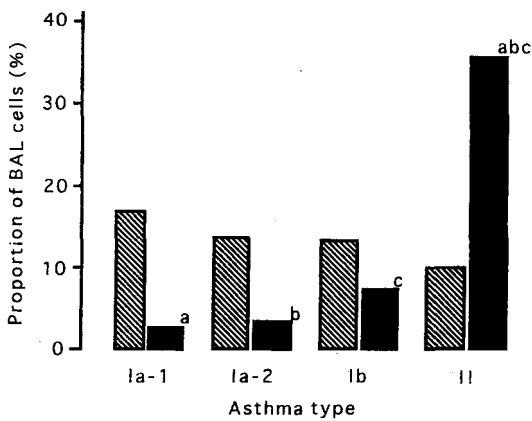


Fig. 2. Proportion of BAL lymphocytes (▨) and neutrophils (■) in each clinical asthma type. a, b, c : $p < 0.001$.

($p < 0.001$), and type Ib ($p < 0.001$), as shown in Fig. 2. Decreased proportion of BAL lymphocytes and increased proportion of BAL neutrophils, which are often observed in asthma patients with long-term glucocorticoid therapy, are found in type II asthma.

Ventilatory function is also related to clinical asthma type. The values of parameters such as FEV_{1.0} % and % \dot{V}_{25} showing obstructive ventilatory dysfunction markedly decrease in type II asthma, particularly, marked decrease in % \dot{V}_{25} value representing ventilatory dysfunction of small airways. This is characteristic of type II asthma with BAL neutrophilia (Fig. 3).

These results demonstrate that increased number of BAL neutrophils and marked decrease in % \dot{V}_{25} value closely correlates with pathophysiological changes of the airways of type II asthma.

Score diagnosis

Asthma classification can be performed by a score calculated from clinical findings and

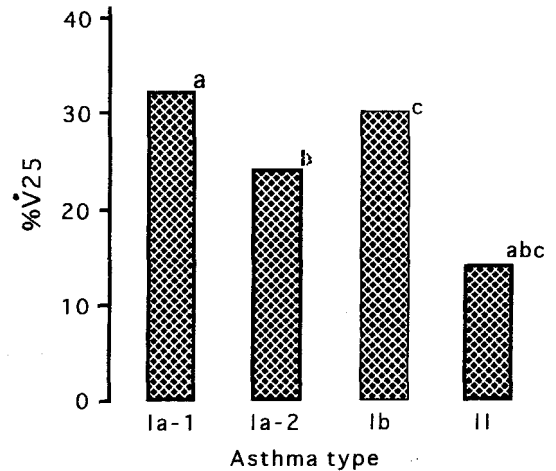


Fig. 3. % \dot{V}_{25} value in each clinical asthma type. a : $p < 0.001$, b : $p < 0.02$, c : $p < 0.01$.

Table 2. Clinical score for classification of asthma

	No of points
1. Expectoration more than 100 ml a day	5
2. Expectoration between 50-99 ml a day	4
3. Presence of sputum in many areas of the airways on auscultation	1
4. Day-long difficulty of expectoration	1
5. Transient bubbling rales in both lower lung fields on auscultation	4
6. Alveolar breath sounds in both lower lung fields markedly decreased or disappeared on auscultation	4
7. Value for % \dot{V}_{25} less than 10%	4
8. Proportion of BAL neutrophils more than 20%	4
9. Proportion of BAL eosinophils more than 10%	1

Clinical score: from 0 to 4 (type Ia), from 5 to 11 (type Ib, of 12 or more (type II)

examinations¹⁵). The criteria for this classification system is shown in Table 2. Asthma classification by a score is almost same to classification by clinical symptoms, since a score calculated from each finding and examination is specific for each clinical asthma type; marked increase of BAL eosinophils is specific for I b. bronchoconstriction+hypersecretion type, and BAL neutro-

philia^{18, 19}) and marked decrease in % \dot{V}_{25} value for type II, bronchiolar obstruction type of asthma.

Type II asthma with BAL neutrophilia

As shown in Fig. 2, BAL neutrophilia is often found in type II asthma. In this type of asthma, marked decrease in number of BAL lymphocytes is also observed²⁰. The increased number of BAL neutrophils related to decreased number of BAL lymphocytes is observed in some of patients with long-term glucocorticoid therapy^{18, 19, 21}), in whom, in addition to decrease in number of BAL and peripheral lymphocytes, suppressed humoral and cellular immunity is found. Thus, it has been suggested that suppressed immunity leads to BAL neutrophilia, which is major feature of type II asthma.

Type II asthma without BAL neutrophilia

It has been shown that BAL neutrophilia is a common feature of type II asthma¹²⁻¹⁵). However, our recent studies have demonstrated that type II asthma without BAL neutrophilia is present when classification is performed by clinical symptoms (clinical diagnosis), not by clinical findings and examinations (score diagnosis)¹⁶). This type of asthma is not related to suppressed immunity, and severity of their symptoms is not so marked as that of same type with BAL neutrophilia. The onset mechanisms of type II asthma without BAL neutrophilia is not clear. However, it has been speculated that one of factors leading to this type of asthma is aging, since mean age of this type of asthma is higher than age of same type with BAL neutrophilia. Other causes inducing type

II asthma without BAL neutrophilia should be analyzed by further studies of asthma.

Conclusion

It has been suggested that there are two kinds of type II, bronchiolar obstruction, asthma with and without BAL neutrophilia when asthma is classified by clinical symptoms. The pathogenesis of type II asthma with BAL neutrophilia is closely related to suppressed immunity. In contrast, pathogenesis inducing type II asthma without BAL neutrophilia is not clear. It has been speculated that one of factors causing this type of asthma is aging.

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II型喘息（細気管支閉塞型）と気管支肺胞洗浄液の好中球数

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気管支喘息は, その臨床症状より, I a型 (I a-1およびI a-2), I b型およびII型の3つの病型に分けることができる(臨床分類)。また, 同時に臨床所見および検査により分類することができる(スコア分類)。いずれの分類においても, BAL液中の好中球の著増および高度な

%V₂₅値の低下がII細気管支閉塞型の特徴的所見である。しかしながら, BAL液中の好中球の増加をともなわないII型喘息が存在することが明らかにされている。これらの症例では, BAL液中好中球増加をともなう症例に比べ平均年齢が高い。しかし, FEV₁0%値, BAL液中リンパ球頻度や血清IgG値などは, 好中球増加をともなう症例ほどの低下傾向は見られない。これらの結果はBAL液中好中球増加をともなうII型喘息の発症機序には, 液性および細胞性免疫能の低下が, また, BAL液中好中球増加をともなわないII型喘息では, 加齢がある程度関連していることを示している。

キーワード; 喘息分類, II型喘息, BALリンパ球, BAL好中球, %V₂₅