

Mild, Moderate, and Severe Forms of Allergic Bronchopulmonary Aspergillosis*

A Clinical and Serologic Evaluation

Raj Kumar, MD

Background: Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity disorder induced by *Aspergillus* species colonizing the bronchial tree. There are patients with asthma who fulfill the diagnostic criteria of ABPA by serologic evaluation (specific IgE/IgG to *Aspergillus fumigatus*), bronchography, CT, and or conventional linear tomography.

Objective: To identify different forms of ABPA based on various diagnostic criteria.

Methods: Eighteen patients with asthma fulfilling the criteria of ABPA were evaluated in the present study. Six patients each received a diagnosis of ABPA serologic positive (ABPA-S), ABPA with central bronchiectasis (ABPA-CB), and ABPA with central bronchiectasis and other radiologic features (ABPA-CB-ORF).

Results: The spirometric changes in the ABPA-S group (group 1) were mild, in the ABPA-CB group (group 2) were moderate, and in the ABPA-CB-ORF group (group 3) were severe. Absolute eosinophil count was raised in each group but was maximum (1,233 μ L) in severe form of disease (group 3). Specific IgE against *A fumigatus* was raised in each group, and the maximum was 47.91 IU/mL in ABPA-CB-ORF. CT scan findings of the ABPA-S group were normal without central bronchiectasis. The exacerbation in symptoms was maximum in group 3 compared to other groups.

Conclusion: The present observations suggest that ABPA includes mild (ABPA-S), moderate (ABPA-CB), and severe (ABPA-CB-ORF) forms of disease. It is recommended, therefore, that the disease should be diagnosed early, treated at the mild form of disease (ABPA-S), and prevented from leading to ABPA-CB or ABPA-CB-ORF. (CHEST 2003; 124:890–892)

Key words: allergic bronchopulmonary aspergillosis; enzyme-linked immunosorbent assay; specific IgE/IgG; type III hypersensitivity

Abbreviations: ABPA = allergic bronchopulmonary aspergillosis; ABPA-CB = allergic bronchopulmonary aspergillosis with central bronchiectasis; ABPA-CB-ORF = allergic bronchopulmonary aspergillosis with central bronchiectasis and other radiologic features; ABPA-S = allergic bronchopulmonary aspergillosis serologic positive; IgE-Af = specific IgE against *Aspergillus fumigatus*; IgG-Af = specific IgG against *Aspergillus fumigatus*

Allergic bronchopulmonary aspergillosis (ABPA) was first reported in England during 1952.¹ Since then, a number of cases have been diagnosed and reported from many countries.^{2,3} The incidence of ABPA in asthmatics varied from 3.7 to 11% in Western countries.^{3,4} In India, Chetty et al⁵ reported ABPA in 15% of cases in a group of children with perennial asthma. In a recent study by Kumar and

Gaur,⁶ the prevalence of ABPA in patients with chronic bronchial asthma has been reported as 16% (12% with central bronchiectasis, and 4% only serologic positive). It is very important to make a clinical and serologic evaluation of all patients with ABPA and to ascertain the severity of disease. The present study was planned to identify different forms of ABPA based on various diagnostic criteria.

*From the Department of Respiratory Medicine, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India. Manuscript received November 27, 2001; revision accepted January 23, 2003.

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Correspondence to: Raj Kumar, MD, 44/1, Probyn Rd, Dehli University Campus, Delhi-7, India; e-mail: rajneel44@rediffmail.com

MATERIALS AND METHODS

ABPA was diagnosed in 18 patients with chronic asthma who were receiving oral short courses of steroids approximately six to eight times per year. The diagnosis of ABPA was made using following criteria: asthma, immediate type cutaneous reactivity to *Aspergillus fumigatus*, elevated total IgE, specific IgE (enzyme-linked immunosorbent assay) against *A fumigatus* (IgE-Af), se-

Table 1—Clinical Characteristics of Patients With ABPA-S, ABPA-CB, and ABPA-CB-ORF*

Clinical Profile	Group 1, ABPA-S	Group 2, ABPA-CB	Group 3, ABPA-CB-ORF
Mean age of presentation, yr	30	22.5	36
Mean duration of illness, yr	11	11	10
Male/female sex, No.	1/5	3/3	5/1
History of asthma	6 (100)	6 (100)	6 (100)
Passage of brownish plugs in sputum	2 (33)	2 (33)	3 (50)
Hemoptysis	2 (33)		3 (50)
History of antituberculous drugs		2 (33)	4 (66)
Spirometry (airway obstruction)			
Normal	2 (33)	0	0
Mild	2 (33)	2 (33)	0
Moderate	2 (33)	3 (50)	1 (16)
Severe	0	1 (16)	5 (84)

*Data are presented as No. (%) unless otherwise indicated.

rum precipitating antibodies IgG against *A fumigatus* (IgG-Af), radiographic pulmonary infiltrates (fixed/transient), and proximal or central bronchiectasis on CT. The patients with all the criteria except central bronchiectasis were labeled as ABPA serologic positive (ABPA-S) [group 1; n = 6]. A second category of patients was labeled as ABPA with central bronchiectasis (ABPA-CB) [group 2; n = 6]. A third category (group 3; n = 6) of patients, who apart from central bronchiectasis had other radiologic features such as pulmonary fibrosis, bleb, bullae, pneumothorax, parenchymal scarring, emphysematous change, multiple cyst, fibrocavitary lesions, aspergilloma, ground-glass appearance, collapse, mediastinal lymph node, pleural effusion and pleural thickening, were labeled as ABPA with central bronchiectasis and other radiologic features (ABPA-CB-ORF).

RESULTS

The 18 patients evaluated were nonsmokers and between the ages of 12 years and 54 years. The duration of illness was 4 to 20 years. The clinical details of these patients are summarized in Table 1. It is evident from the results that the severity of the disease is maximum in group 3 (ABPA-CB-ORF). It is the severe form of ABPA in comparison to

ABPA-S (normal CT findings) and ABPA-CB. It has been observed that two patients in group 2 (ABPA-CB) and four patients in group 3 (ABPA-CB-ORF) had earlier received antituberculous drugs due to wrong diagnosis. The clinical and radiologic features suggest ABPA-S as mild, ABPA-CB as moderate, and ABPA-CB-ORF as the severe form. This is further supported by serological data presented in Table 2. Total IgE was 597 IU/mL, 2,571 IU/mL, and 3,435 IU/mL in ABPA-S, ABPA-CB, and ABPA-CB-ORF groups, respectively. IgE-Af was raised in each group (ABPA-S, 9.88 IU/mL; ABPA-CB, 23.12 IU/mL; and ABPA-CB-ORF, 47.91 IU/mL), but was maximum in ABPA-CB-ORF. Serum precipitins and IgG-Af (enzyme-linked immunosorbent assay) were positive in 50% and 100% in ABPA-S, 66% and 66% in ABPA-CB, and 100% and 66% in ABPA-CB-ORF, respectively. The evaluation of chest CT also showed that ABPA-S is mild, ABPA-CB is moderate, and ABPA-CB-ORF is the severe form of disease. The exacerbation of symptoms was at a minimum in ABPA-S.

DISCUSSION

The patients included in the present study were followed up for a 2-year period. It was observed that ABPA-S did not progress to severe form of disease, ie, ABPA-CB or ABPA-CB-ORF. Even ABPA-CB did not progress to ABPA-CB-ORF. This may be due to the early diagnosis of the disease and the regular treatment administered. Patterson et al^{7,8} reported that early treatment prevents the progress of disease into the severe form. It is evident from the results that ABPA-S lacks demonstrable lung damage and represents a mild clinical form of the disease. The apparent decrease of frequency with which disease exacerbation and pulmonary infiltrates occur in patients with ABPA-S may be due to less intense inflammatory obstructive response and absence of bronchiectasis. Similar observations have been recorded by other workers.⁹

The pathogenesis of ABPA remains unclear since it has multiple components. Passive transfer of serum containing isotopic antibodies IgE-Af and

Table 2—Skin Tests and Serologic Values in ABPA-S, ABPA-CB, and ABPA-CB-ORF*

Variables	Skin Tests		ABPA-S Absolute Eosinophil Counts	ABPA-CB Total IgE, ng/mL	ABPA-CB-ORF IgE-Af, IU/mL	IgG-Af (Positive)	Precipitating Antibodies (Positive)
	Type I (Positive)	Type III (Positive)					
ABPA-S	6 (100)	2 (33)	935	597 ± 330.22	9.88 ± 7.45	6 (100)	3 (50)
ABPA-CB	6 (100)	3 (50)	1,008	2,571 ± 1,492.14	43.12 ± 38.02	4 (66)	4 (66)
ABPA-CB-ORF	6 (100)	1 (16)	1,233	3,435 ± 3,948.7	47.91 ± 33.00	4 (66)	6 (100)

*Data are presented as No. (%) or mean ± SD unless otherwise indicated.

IgG-Af from patients with ABPA to a monkey resulted in the development of pulmonary lesions when *Aspergillus* was inhaled.¹⁰ IgE-Af and IgG-Af has been demonstrated essential for the development of biopsy lesion consistent with ABPA following *A fumigatus* aerosol challenge.¹¹ Isotypic antibodies to *A fumigatus* in the lung likely mediate immunologic injury. Mast cell activation by intersection of IgE and *A fumigatus* results in mediator release and cytokine production, which contribute to lung damage. Lymphocyte and eosinophil activation may participate in immunologic reaction also. In patients with ABPA and previous infiltrates, bronchiectasis develops and chronic colonization by *A fumigatus* results in continuing bronchial wall damage. In the case of ABPA-S, there is less intense inflammatory destructive response and hence absence of bronchiectasis. The continuous intense inflammation that results in bronchiectasis or bronchiolitis obliterans as occurs in ABPA-CB has not been identified in ABPA-S. Patients with ABPA-S represent the early stage of the disease or a less aggressive mild form of the disease. In two of the ABPA-S group patients, sputum contained *A fumigatus*. This shows that spores are able to colonize the bronchial mucosa in this subset of patients, but the absence of bronchiectasis in these patients (ABPA-S) is difficult to understand.

The host response to Aspergilli in the bronchial mucosa may be an important factor in determining why some patients acquire bronchiectasis (ABPA-CB) and others acquire ABPA-S. Robertson and coworkers¹² demonstrated that spores of *A fumigatus* were resistant to phagocytosis by human macrophages in contrast to *Penicillium* spores that were readily ingested. The *Aspergillus* spores apparently released a substance that inhibited their ingestion by macrophages. Proteolytic enzymes from *Aspergillus* spores result in additional bronchial antigenic exposure and consequent immunologic response.¹³ An exaggerated host response including cytokine release, lymphocyte sensitization, and complement activation is thought to mediate in bronchial wall damage leading to bronchiectasis and later fibrosis of the lung. ABPA is frequently misdiagnosed as pulmonary tuberculosis^{14,15} and ends up in the severe form of ABPA (*ie*, ABPA-CB-ORF). This may be due to lack of awareness or requisite diagnostic facilities (especially serologic investigations).

In conclusion, a high index of suspicion of ABPA should be made in all patients with chronic asthma and immediate-type cutaneous reactivity to *A fu-*

migatus. It is better to diagnose the disease in the early phase (mild form) of disease (*ie*, ABPA-S) and start the necessary treatment that may prevent the progression of the disease. ABPA-CB-ORF is clinically and serologically a severe form of ABPA; hence, prevention of this stage should always be attempted by early treatment and longer or life-long follow-up of the patient.

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