

Allergic Bronchopulmonary Aspergillosis*

Lessons From 126 Patients Attending a Chest Clinic in North India

Ritesh Agarwal, MD, DM, FCCP; Dheeraj Gupta, MD, DM, FCCP;
Ashutosh N. Aggarwal, MD, DM; Digamber Behera, MD, FCCP; and
Surinder K. Jindal, MD, FCCP

Aims and objectives: To describe the experience of screening patients with asthma for allergic bronchopulmonary aspergillosis (ABPA) presenting to a chest clinic. The clinical, serologic, radiologic, and treatment aspects including outcome of ABPA are also described.

Methods: All consecutive patients with asthma presenting to the chest clinic over a period of 2 years were screened with an *Aspergillus* skin test. Patients who were found to be positive were further investigated for ABPA. Patients were also arbitrarily classified as ABPA-seropositive (ABPA-S), ABPA with central bronchiectasis (ABPA-CB), and ABPA-CB with other radiologic findings (ABPA-CB-ORF) based on the high-resolution CT findings.

Results: Five hundred sixty-four patients were screened using an *Aspergillus* skin test; 223 patients (39.5%) were found to be positive, and ABPA was diagnosed in 126 patients (27.2%). There were 34 patients (27%) with ABPA-S, 42 patients with ABPA-CB, and 50 patients with ABPA-CB-ORF. Fifty-nine patients (46.8%) had received antitubercular therapy in the past. The vast majority of patients had bronchiectasis at presentation to our hospital. High-attenuation mucous impaction was noted in 21 patients (16.7%). There was no significant difference between the stages of ABPA and the duration of illness, the severity of asthma, and the serologic findings (ie, absolute eosinophil count, IgE levels [total] and IgE levels [for *Aspergillus fumigatus*]). The median duration of follow-up was 13 months (range, 9 to 38 months). All patients went into "remission" at 6 weeks. Twenty-five patients had a "relapse" during the course of their treatment. One hundred nine patients had "complete remission," 17 patients were classified as having "glucocorticoid-dependent ABPA," and 7 patients were classified as having "end-stage ABPA."

Conclusions: There is a high prevalence of ABPA in asthmatic patients presenting at our hospital. The disease entity is still underrecognized in India; the vast majority of patients have bronchiectasis at presentation, and almost half are initially misdiagnosed as having pulmonary tuberculosis. There is a need to redefine the definitions of ABPA and the optimal dose/duration of glucocorticoid therapy. This study reinforces the need for the routine screening of asthmatic patients with an *Aspergillus* skin test. (CHEST 2006; 130:442–448)

Key words: allergic bronchopulmonary aspergillosis; CT scan; glucocorticoids; outcome; staging; steroids

Abbreviations: ABPA = allergic bronchopulmonary aspergillosis; ABPA-CB = allergic bronchopulmonary aspergillosis with central bronchiectasis; ABPA-CB-ORF = allergic bronchopulmonary aspergillosis with central bronchiectasis with other radiologic features; ABPA-S = allergic bronchopulmonary aspergillosis seropositive; HRCT = high-resolution CT; HU = Hounsfield units

A *Aspergillus* is a ubiquitous soil-dwelling organism. Because of its thermophilic nature, it has a propensity to cause a variety of clinical pulmonary syndromes (eg, invasive aspergillosis, aspergilloma, allergic rhinosinusitis and asthma, hypersensitivity

pneumonitis, chronic necrotizing aspergillosis, and allergic bronchopulmonary aspergillosis [ABPA]). ABPA is a pulmonary disorder that is caused by hypersensitivity to *Aspergillus fumigatus* with resultant systemic immune activation, chronic asthma,

recurrent pulmonary infiltrates, and bronchiectasis. First described by Hinson et al¹ in 1952, this disease occurs in 1 to 2% of patients with persistent asthma and in 2 to 15% of patients with cystic fibrosis.² In most cases, a lung biopsy is not required for diagnosis, and the diagnosis can be made on clinical, radiologic, and serologic grounds. Although the diagnostic criteria for ABPA have been laid down (and include bronchial asthma, immediate skin test reactivity to *A fumigatus*, elevated total serum Ig E level, pulmonary infiltrates, central bronchiectasis, peripheral blood eosinophilia, and positive serum precipitins [IgG] against Aspergillus antigen), none of these are specific for ABPA.³ There is still no consensus on the number of criteria needed for diagnosis, and patients in different stages of ABPA may not fulfill all these criteria.^{3,4}

This disorder is not uncommon in India.⁵ We have previously reported our retrospective analysis of 35 cases of ABPA during the period 1986 to 1990,⁶ and another 89 cases during the period 1991 to 1998.⁴ However, the disease is still underdiagnosed in India, and as many as one third of the cases are initially misdiagnosed as pulmonary tuberculosis.⁶ There is a need to diagnose ABPA early and treat it aggressively so as to prevent irreversible complications such as bronchiectasis and lung fibrosis. In this article, we describe our experience with screening patients with asthma presenting to a chest clinic for ABPA. The clinical, serologic, radiologic, and treatment aspects, including the outcome of ABPA, are also described.

MATERIALS AND METHODS

We screened all consecutive patients with asthma presenting to the chest clinic over 2 years (*ie*, from January 2002 onward) with an Aspergillus skin test. Patients who had received glucocorticoids for > 3 weeks in the preceding 6 months were excluded from the study. Patients who were found to be positive for Aspergillus were further investigated. They were considered to have ABPA if they met four of the following criteria: clinical diagnosis of asthma; elevated total IgE level (*ie*, > 1,000 IU/mL); presence of specific IgE against *A fumigatus* detected (by enzyme-linked immunosorbent assay; > 0.35 kU/L), serum pre-

cipitating antibodies against *A fumigatus*; radiographic pulmonary infiltrates (fixed/transient); and proximal or central bronchiectasis seen on high-resolution CT (HRCT) scan. A signed informed consent form was obtained from all patients as per protocol. None of the patients had been screened for cystic fibrosis.

The Aspergillus skin test was performed using *A fumigatus* antigen (Aspergillin; Hollister-Stier Laboratories; Spokane, WA). The test was read every 15 min for 1 h, and then after 6 to 8 h. For delayed-type reactions, the test was read after 24, 48, and 72 h. The reactions were classified as type I if a wheal and erythema developed within 1 min, reached a maximum after 10 to 20 min, and resolved within 1 to 2 h; a type III reaction was read after 6 h, and any amount of subcutaneous edema was considered to be a positive result; and a type IV reaction was read after 72 h, and an induration of > 5 mm was considered to be a positive result. *A fumigatus* precipitins were detected by the Ouchterlony gel diffusion techniques according to the method of Longbottom and Pepys.⁴ Levels of serum IgE (total) and IgE (for *A fumigatus*) were assayed with commercially available kits using the chemiluminescent enzyme assay (Diagnostic Products Corporation; Los Angeles, CA) and the fluorescent enzyme immunoassay (UniCap Systems; Pharmacia Upjohn; Stockholm, Sweden).

All patients underwent spirometry with bronchodilator reversibility (modal RS232; Morgan Scientific; Winchester, MA), and were categorized as mild, moderate, and severe obstructions as per the standardized practice in our laboratory.⁷ Bronchodilator reversibility was considered to be significant if, after inhaling 200 µg of salbutamol, the FEV₁ and/or FVC increased by > 12% and 200 mL.⁸ Patients were also categorized as having mild, moderate, and severe asthma based on the Indian guidelines.⁹

An HRCT scan of the thorax was performed (LightSpeed Plus CT scanner; GE Medical Systems; Little Chalfont, Buckinghamshire, UK) with a 512-matrix size. The scans (120 kV; 10 mA; window width, 1,500 Hounsfield units [HU]; and window level, -600 HU) were obtained with a scan time of 3 s with the patient in the supine position at full end-inspiration from lung apex to base with 1.25 mm contiguous slices using the high-spatial frequency algorithm. The scans were analyzed at the lobar level as well as the segmental level. Individual bronchopulmonary segments were identified by the anatomic division of the appropriate lobar bronchus, and its relationship with the major and minor fissures.¹⁰ All scans were assessed for radiologic abnormalities and were categorized as follows: (1) the presence or absence of bronchiectasis was noted, and the criteria described by Reiff et al¹¹ was used to classify bronchiectasis; it was deemed to be "central" when confined to the medial half of the lung, at a point midway between the hilum and the chest wall; (2) the presence of parenchymal abnormalities, which included the presence of centrilobular nodules and tree-in-bud appearance, consolidation, parenchymal scarring, bullae, atelectasis, and pneumothorax. The criteria used to define these appearances were described by Webb et al¹²; and (3) the presence or absence of high-attenuation mucus (defined as a mucous plug that is visually denser than normal skeletal muscle).¹³

Patients at the time of diagnosis were classified based on the HRCT findings^{14,15} as follows: (1) ABPA-seropositive (ABPA-S), those with ABPA who had normal HRCT findings; (2) ABPA with central bronchiectasis (ABPA-CB), those who had central bronchiectasis with no other manifestation described; and (3) ABPA-CB with other radiologic features (ABPA-CB-ORF) such as centrilobular nodules, tree-in-bud appearance, parenchymal scarring, bullae, atelectasis, and pneumothorax. The patients were treated with glucocorticoids with the following regimen: prednisolone, 0.75 mg/kg for 6 weeks, 0.5 mg/kg for 6 weeks, then tapered by 5 mg every 6 weeks to continue for a total

*From the Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Sector-12, Chandigarh, India.

The authors report that they have no conflicts of interest related to this paper.

Manuscript received November 30, 2005; revision accepted February 2, 2006.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Surinder K. Jindal, MD, FCCP, Professor & Head, Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Sector-12, Chandigarh-160012, India; e-mail: skjindal@indiachest.org

DOI: 10.1378/chest.130.2.442

duration of at least 6 to 12 months. The patients were followed up with a medical history and physical examination, chest radiograph, and measurement of IgE levels (total) every 6 weeks. Patients were classified as follows:

1. Remission: The patients were said to be “in remission” if the IgE levels declined by > 35% and there was clearance of chest radiographic lesions after 6 weeks of therapy with glucocorticoids.
2. Relapse or exacerbation: A doubling of the baseline IgE levels was taken as an indicator of “relapse” irrespective of the patient’s symptoms or the appearance of radiologic infiltrates.
3. Complete remission: If the patient did not have any additional ABPA exacerbations (100% rise in total serum IgE concentration with or without new pulmonary infiltrates) over the next 3 months after stopping therapy, the patient was said to be “in complete remission.” Patients who are in complete remission are followed up by measuring IgE levels every 6 months for the first year and then annually.
4. Glucocorticoid-dependent ABPA: If the patient required oral prednisolone therapy for the treatment of persistent asthma or recurrent relapses of ABPA, then the patient was said to have “glucocorticoid-dependent ABPA.”
5. End-stage ABPA: Patients who had extensive bronchiectasis or fibrobullous disease with either cor pulmonale or type 2 respiratory failure were classified as “end-stage ABPA.”

Statistical Analysis

Statistical analysis was performed using a statistical software package (SPSS for Microsoft Windows, package version 10; SPSS Inc; Chicago, IL). The data are presented in a descriptive fashion as the mean (SD) or the median (range). Categorical variables were compared using the χ^2 test, while continuous variables were compared using the Mann-Whitney *U* test or Kruskal-Wallis tests, as applicable. Statistical significance was assumed at a *p* value of < 0.05.

RESULTS

During the study period, 564 patients were screened for ABPA using the Aspergillus skin test; 223 patients (39.5%) were found to be positive, and ABPA was diagnosed in 126 patients (27.2%). There were 64 male patients and 62 female patients, with a mean age of 34.4 years (SD, 12.7 years). The baseline characteristics of these patients are shown in Table 1. The recognition of ABPA was generally delayed, and 59 patients (46.8%) had received antitubercular therapy in the past (median, one course of therapy; range, one to three courses). Chest radiographs showed fleeting pulmonary shadows in 46 patients (36.5%).

Of the 126 patients, 34 had normal HRCT findings (ABPA-S patients); thus, in total, there were 92 patients with a total of 460 lobes and 1,656 lung segments (number of lobes per patient, 5; number of segments per patient, 18). However, for final analysis, there were 431 lobes and 1,621 segments evaluable as 15 patients had other parenchymal abnormal-

Table 1—Baseline Characteristics of 126 Patients With ABPA*

Clinical Characteristics	Results
Age, yr	
Mean (SD)	34.4 (12.7)
Median (range)	34 (13–70)
Sex	
Male	64
Female	62
Duration of asthma, yr	
Mean (SD)	8.8 (7.6)
Median (range)	6 (0–40)
History of hemoptysis	56 (44.4)
History of expectoration of brownish-black mucous plugs	60 (47.6)
History of prescription of antituberculous therapy	59 (46.8)
Cigarette smoking	10 (8.1)
Crackles on physical examination	18 (14.3)
Presence of clubbing	22 (17.5)
Spirometry findings	
Normal	18 (14.3)
Mild obstruction	33 (26.2)
Moderate obstruction	45 (35.7)
Severe obstruction	30 (23.8)
Bronchodilator reversibility	63 (50)
Aspergillus skin test	
Type 1	126 (100)
Type 3	95 (75.4)
Type 4	10 (7.9)
Absolute eosinophil count, cells/ μ L	
Mean (SD)	1,191 (1,247)
Median (range)	800 (180–8,200)
Aspergillus precipitins	108 (85.7)
IgE levels	
Total, IU/mL	
Mean (SD)	6,265.6 (5,140.7)
Median (range)	4,688.5 (1,134–24,000)
Specific to <i>A fumigatus</i> , kU/L	
Mean (SD)	7.96 (10.2)
Median (range)	3.0 (0.43–48.2)

*Values are given as No. (%), unless otherwise indicated.

ities (fibrosis, 10 patients; consolidation, 6 patients; collapse, 3 patients; bullae, 7 patients). Of these, 59.2% of lobes (255 of 431 lobes) and 40.9% of segments (664 of 1,621 segments) were involved with bronchiectasis. The median number of lobes was 2 (range, 0 to 5 lobes), and the median number of segments was 5 (range, 0 to 16 segments). Of these 255 lobes, 156 (61.2%) had central bronchiectasis (Fig 1), whereas the remaining 99 (38.8%) lobes had bronchiectasis extending to the periphery (Fig 2). The HRCT findings are shown in Table 3. Interestingly, 21 patients (16.7%) had high-attenuation mucous impaction (Fig 3), which is supposed to be a highly characteristic HRCT finding for ABPA. No patient had any evidence of pleural involvement at presentation, but spontaneous pneumothorax developed in four patients during the course of their

Table 2—HRCT Findings in 126 Patients With ABPA*

HRCT Scan Appearance	Results
Normal	34 (26.9)
Bronchiectasis	92 (73.1)
Lobes†	2 (0–5)
Segments†	5 (0–18)
Centrilobular nodules/tree-in-bud appearance	40 (31.7)
Consolidation/mass	6 (4.8)
Fibrosis	10 (7.9)
Collapse	3 (2.4)
Bullae	7 (5.6)
High-attenuation mucus	21 (16.7)

*Values are given as the No. (%), unless otherwise indicated.

†Values are given as the median (range).

therapy, and they underwent chemical pleurodesis. Five patients had evidence of pulmonary hypertension at presentation, whereas two patients were detected to have pulmonary hypertension on follow-up. All of these patients also had type 2 respiratory failure (PaO_2 , < 60 mm Hg; PaCO_2 , > 45 mm Hg).

There were 34 patients (27%) with ABPA-S, 42 patients with ABPA-CB (Fig 4), and 50 patients with ABPA-CB-ORF (Fig 4). There was no significant difference between the stages of ABPA (Kumar¹⁴ and Patterson et al¹⁵), and the severity of asthma, the duration of illness, and the serologic findings (*ie*, absolute eosinophil count and IgE levels [total and for *A fumigatus*]) [Table 3].

The median duration of follow-up was 13 months (range, 9 to 38 months). All the patients went into remission at 6 weeks. Twenty-five patients had a relapse during the course of their treatment; importantly, only 8 of these patients had infiltrates visible on their chest radiographs. All of these patients were restarted therapy with prednisolone (10 patients also



FIGURE 1. HRCT scan showing central bronchiectasis. The patient was a 42-year-old man who had asthma since childhood. Spirometry showed mild obstruction with significant bronchodilator reversibility.

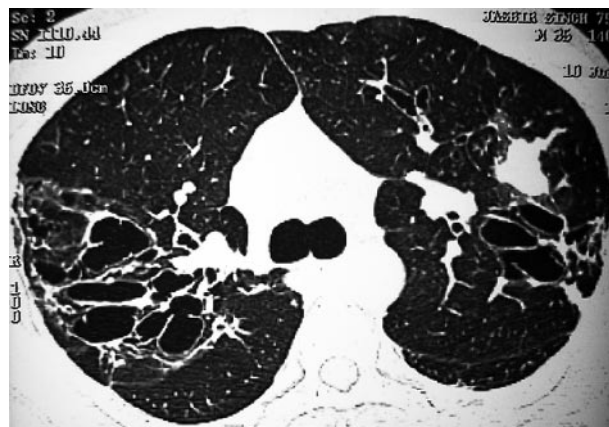


FIGURE 2. HRCT scan showing bronchiectasis extending to the periphery. Spirometry showed moderate obstruction with significant bronchodilator reversibility. The patient was a 35-year-old man with known asthma since the age of 10 years who had received antituberculous therapy twice before ABPA was diagnosed.

began therapy with itraconazole). Of the 25 patients who relapsed, all went into remission at 6 weeks; however, the steroid dosage could be tapered and then therapy stopped only in 8 patients (3 patients in the itraconazole group [*ie*, complete remission]). One hundred nine patients had complete remission; the dosage of steroids was tapered, and then therapy was stopped at a median duration of 8 months (range, 7 to 16 months) in these patients. All patients who underwent complete remission showed no evidence of radiologic worsening and are on close follow-up with measurement of IgE levels and chest radiographs. Relapse, glucocorticoid-dependent ABPA, or end-stage ABPA has developed in none of the patients. Seventeen patients (13.5%; repeated exacerbations, 7 patients; persistent asthma, 10 patients) were maintained on long-term treatment with steroids and were classified as having glucocorticoid-dependent ABPA; 7 patients had extensive bronchiectasis and evidence of cor pulmonale and type II respiratory failure, and were classified as having end-stage ABPA.

DISCUSSION

Despite the description of ABPA in India as early as 1971,¹⁶ this disease entity is still underrecognized,^{4,6} and this study highlights its continued underrecognition. This series, which represents one of the largest reported experiences of managing patients with ABPA, showed a prevalence rate of 27.2% in the population screened. This high rate does not reflect the prevalence in the general community but probably represents referral bias to pulmonary med-

Table 3—Clinical, Spirometric, and Serologic Findings in the Various Stages of ABPA*

Stages of ABPA	Kumar ¹⁴			Patterson et al ¹⁵		P Value
	ABPA-S (n = 34)	ABPA-CB (n = 42)	ABPA-CB-ORF (n = 50)	ABPA-S (n = 34)	ABPA-CB (n = 92)	
Sex						NS
Male	14	23	27	14	50	
Female	20	19	23	20	42	
Duration of asthma, yr	7 (2–25)	8 (1–40)	5 (1–40)	7 (2–25)	6 (1–40)	NS
Stage of asthma						
Mild	14 (11.1)	17 (13.5)	20 (15.8)	14 (11.1)	34	NS
Moderate	14 (11.1)	14 (11.1)	17 (13.5)	14 (11.1)	31	NS
Severe	6 (4.8)	11 (8.7)	13 (10.3)	6 (4.8)	24	NS
Absolute eosinophil count, cells/mL	660 (180–3,250)	990 (310–8,200)	800 (240–2,560)	660 (180–3,250)	825 (180–8,200)	NS
IgE levels						
Total, IU/mL	3,264.5 (1,160–21,340)	3,887.5 (1,134–22,120)	5,711.5 (1,280–24,000)	3,264.5 (1,160–21,340)	5,060 (1,134–24,000)	NS
Specific to <i>A. fumigatus</i> , kU/L	2.14 (0.44–48.2)	2.8 (0.43–45.4)	3.8 (1.1–29.9)	2.14 (0.44–48.2)	3.4 (0.43–45.4)	NS

*Values are given as No. (%) or median (range), unless otherwise indicated. NS = not significant ($P \geq 0.05$)

icine specialists. In fact, in one study¹⁷ the prevalence of ABPA was found to be as high as 25 to 40% in an asthma clinic. Almost half of the patients (46.8%) had been misdiagnosed as having pulmonary tuberculosis, and they had been treated with antitubercular therapy before a diagnosis of ABPA could be made. Thus, even though pulmonary tuberculosis is common in India, other diagnostic possibilities should also be considered in patients with respiratory symptoms.

An HRCT scan is presently the investigation of choice for the diagnosis of bronchiectasis in patients with ABPA.¹⁸ The characteristic radiologic findings

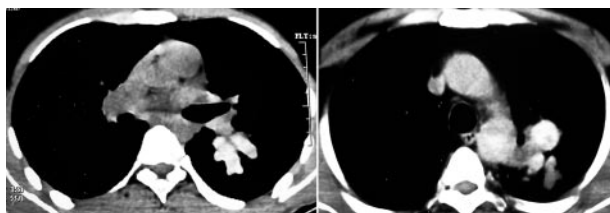


FIGURE 3. HRCT scan showing hyperdense mucus in two different patients (Note: the attenuation of the mucus is higher than the skeletal muscle). The HRCT scan on the left depicts a 40-year-old male patient in whom asthma had been diagnosed 20 years previously. Spirometry showed mild obstruction without any bronchodilator reversibility. The HRCT scan on the right depicts a 50-year-old male patient who had known asthma since childhood. Lung cancer had been diagnosed at another center, where he underwent bronchoscopy for the condition. A skin test for *A. fumigatus* was positive, the total IgE count was 12,000 IU/mL, the IgE count specific to *A. fumigatus* was 14 kU/L, the absolute eosinophil count was 2,000 cells/ μ L, and Aspergillus precipitins were present.

described for ABPA in the literature were also seen in this study.^{18–21} However, we did not find any evidence of pleural involvement as reported in different studies,^{20,21} although secondary spontaneous pneumothorax requiring treatment with chemical pleurodesis did develop in four of our patients. In this study, most of the patients had fairly advanced bronchiectasis, and seven patients also were found to have cor pulmonale and type 2 respiratory failure. Central bronchiectasis (*ie*, bronchiectasis confined to the medial half of the lung) with normal peripheral bronchi is a characteristic feature of ABPA; this was seen in approximately 60% of patients in the present study, but almost 40% of patients had peripheral lung involvement. In another study, almost 30% of the patients had peripheral lung involvement.²¹ This implies that there is a need to exclude ABPA even in patients without central bronchiectasis. Also, HRCT scanning has limited value in distinguishing between

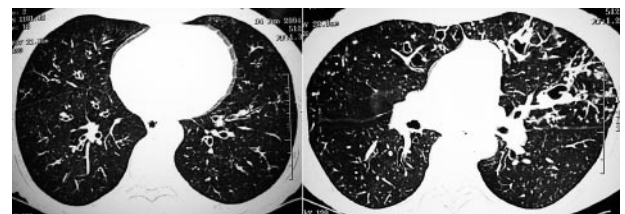


FIGURE 4. HRCT scan showing a patient with ABPA-CB (left) and another patient in the ABPA-CB-ORF (right). Spirometry showed severe obstruction with no significant bronchodilator reversibility in the patient with ABPA-CB and mild obstruction with significant reversibility in the patient with ABPA-CB-ORF.

idiopathic and specific types of bronchiectasis²² unless there are specific findings. In this context, high-attenuation mucus, which is the most characteristic (if not pathognomonic) finding of ABPA, was seen in almost 17% of the patients. This finding has been reported¹³ to occur in as high as 28% of patients, but that study had only 14 patients. The term *high attenuation mucus* is applied if the plug is visually denser than the normal skeletal muscle or if the mucous plug density measurements are of 72 to 102 HU.¹³ The hyperdense mucous plugging seen on CT scans is thought to be attributable to contained calcium salts, metals (the ions of iron and manganese), and/or hemorrhagic products,^{13,23} and has a basis that is similar to that seen in patients with fungal sinusitis.²⁴

Over the past few years, ABPA has been arbitrarily classified into ABPA-S; ABPA-CB; and ABPA-CB-ORF based on the radiologic findings, with both the severity of the radiologic and serologic findings increasing from patients with ABPA-S to those with ABPA-CB-ORF; however, this study had only six patients in each group.¹⁴ Previously, Patterson et al¹⁵ have divided ABPA into two stages (ABPA-S and ABPA-CB), with ABPA-S representing patients with ABPA without pulmonary damage. Greenberger et al²⁵ found that the antibody levels and concentrations were higher in patients with ABPA-CB than in those with ABPA-S and concluded that ABPA-S represents the earliest stage or apparently a less aggressive form of ABPA. We found no difference between the radiologic staging of ABPA and the duration of illness, the severity of asthma, and the serologic findings. Thus, it may not be important to stage ABPA into categories, but it remains prudent to diagnose and treat ABPA early before bronchiectasis, which is irreversible lung damage, sets in.

Oral glucocorticoids are currently the drug treatment of choice for ABPA as they suppress both immune function and inflammation.^{26,27} However, there have been no well-defined trials of glucocorticoid therapy in patients with ABPA, with different doses of glucocorticoids used in different studies and reviews (*ie*, from 0.5 mg/kg/d for 14 days, then on alternate days for 3 months, and discontinue^{15,26,28} to 0.75 mg/kg/d for 4 weeks, taper, and stop over 5 to 6 months²⁷), and such therapy is associated with frequent relapses or corticosteroid dependence (45%).^{15,28} In our study, the dose of glucocorticoids used and the duration of therapy were generally more than previously recommended, but the remission rates were also higher, and the prevalence of glucocorticoid-dependent ABPA was only 13.5%. This raises the possibility of a higher dose and longer duration for corticosteroid therapy being associated with better outcomes; however, further randomized

controlled studies are required to settle this issue. Antifungal agents, especially itraconazole, have been suggested to modify the immunologic activation associated with ABPA and to improve clinical outcome.^{29,30} We were not able to use it widely because of the expensive nature of the drug; however, in the limited numbers of patients in whom we used the drug, there was no observable advantage.

Finally, there is a need to redefine certain definitions of ABPA. For example, there are differences in definitions used in this study vis-à-vis the definitions used in the literature. Remission has been defined as the absence of pulmonary infiltrates for 6 months after therapy with oral steroids has been discontinued.¹⁵ However, we have mainly used the serologic criteria for defining relapse and remission, especially in light of the fact that serologic changes predate pulmonary damage. The relapse of patients with ABPA has been variably defined as a doubling of the baseline IgE levels with clinical symptoms or radiologic worsening^{15,27} or without them.²⁶ In our study, we defined relapse as a doubling of serum IgE levels with or without worsening of symptoms or chest radiograph findings. In fact, 25 patients fulfilled the serologic criteria for relapse, but only 8 patients had radiologic infiltrates. Similarly, it does not clinically matter if therapy with glucocorticoids is continually required for the control of asthma or ABPA; hence, we grouped both of these entities together. Also, there is no well-accepted definition of end-stage ABPA; it has been defined variably based on the symptoms, the severity of pulmonary function abnormalities, and the extent of pulmonary fibrosis.^{31,32} We defined end-stage ABPA as occurring in a patient who had either pulmonary hypertension or type 2 respiratory failure.

CONCLUSIONS

This study indicates a high proportion of ABPA in the population attending the chest clinic of this hospital, and thus active screening with an *Aspergillus* skin test is advocated for all asthmatic patients. There is a need for better recognition of ABPA as the disease entity is still underrecognized in India, with the majority of patients presenting with features of permanent lung damage, and almost half initially misdiagnosed as having pulmonary tuberculosis.

The currently used staging system, based on HRCT criteria, and the definitions of ABPA need further clarification. However, it is important to diagnose the disease early and to treat it aggressively so as to prevent the stage of central bronchiectasis. Finally, there is a need to conduct randomized trials to adequately define the optimal dose and duration of steroid therapy for patients with ABPA.

REFERENCES

- 1 Hinson KF, Moon AJ, Plummer NS. Broncho-pulmonary aspergillosis: a review and a report of eight new cases. *Thorax* 1952; 7:317–333
- 2 Greenberger PA. Clinical aspects of allergic bronchopulmonary aspergillosis. *Front Biosci* 2003; 8:s119–s127
- 3 Greenberger PA. Allergic bronchopulmonary aspergillosis. In: Grammer LC, Greenberger PA, eds. *Patterson's allergic diseases*. Philadelphia, PA: Lippincott, Williams and Wilkins, 2002; 529–554
- 4 Chakrabarti A, Sethi S, Raman DS, et al. Eight-year study of allergic bronchopulmonary aspergillosis in an Indian teaching hospital. *Mycoses* 2002; 45:295–299
- 5 Shah A, Panjabi C. Allergic bronchopulmonary aspergillosis: a review of a disease with a worldwide distribution. *J Asthma* 2002; 39:273–289
- 6 Behera D, Guleria R, Jindal SK, et al. Allergic bronchopulmonary aspergillosis: a retrospective study of 35 cases. *Indian J Chest Dis Allied Sci* 1994; 36:173–179
- 7 Aggarwal AN, Gupta D, Jindal SK. Development of a simple computer program for spirometry interpretation. *J Assoc Physicians India* 2002; 50:567–570
- 8 American Thoracic Society. Standardization of spirometry: 1994 update. *Am J Respir Crit Care Med* 1995; 152:1107–1136
- 9 Jindal SK, Gupta D, Aggarwal AN, et al. Guidelines for management of asthma at primary and secondary levels of health care in India (2005). *Indian J Chest Dis Allied Sci* 2005; 47:309–343
- 10 Osborne D, Vock P, Godwin JD, et al. CT identification of bronchopulmonary segments in 50 normal subjects. *AJR Am J Roentgenol* 1984; 142:47–52
- 11 Reiff DB, Wells AU, Carr DH, et al. CT findings in bronchiectasis: limited value in distinguishing between idiopathic and specific types. *AJR Am J Roentgenol* 1995; 165:261–267
- 12 Webb WR, Muller NL, Naidich DP. *High-resolution CT of the lung*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2001
- 13 Logan PM, Muller NL. High-attenuation mucous plugging in allergic bronchopulmonary aspergillosis. *Can Assoc Radiol J* 1996; 47:374–377
- 14 Kumar R. Mild, moderate, and severe forms of allergic bronchopulmonary aspergillosis: a clinical and serologic evaluation. *Chest* 2003; 124:890–892
- 15 Patterson R, Greenberger PA, Halwig JM, et al. Allergic bronchopulmonary aspergillosis: natural history and classification of early disease by serologic and roentgenographic studies. *Arch Intern Med* 1986; 146:916–918
- 16 Shah JR. Allergic bronchopulmonary aspergillosis. *J Assoc Physicians India* 1971; 19:835–841
- 17 Eaton T, Garrett J, Milne D, et al. Allergic bronchopulmonary aspergillosis in the asthma clinic: a prospective evaluation of CT in the diagnostic algorithm. *Chest* 2000; 118:66–72
- 18 Shah A. Allergic bronchopulmonary and sinus aspergillosis: the roentgenologic spectrum. *Front Biosci* 2003; 8:e138–e146
- 19 Neeld DA, Goodman LR, Gurney JW, et al. Computerized tomography in the evaluation of allergic bronchopulmonary aspergillosis. *Am Rev Respir Dis* 1990; 142:1200–1205
- 20 Angus RM, Davies ML, Cowan MD, et al. Computed tomographic scanning of the lung in patients with allergic bronchopulmonary aspergillosis and in asthmatic patients with a positive skin test to *Aspergillus fumigatus*. *Thorax* 1994; 49:586–589
- 21 Panchal N, Bhagat R, Pant C, et al. Allergic bronchopulmonary aspergillosis: the spectrum of computed tomography appearances. *Respir Med* 1997; 91:213–219
- 22 Reiff D, Wells A, Carr D, et al. CT findings in bronchiectasis: limited value in distinguishing between idiopathic and specific types. *AJR Am J Roentgenol* 1995; 165:216–267
- 23 Goyal R, White CS, Templeton PA, et al. High attenuation mucous plugs in allergic bronchopulmonary aspergillosis: CT appearance. *J Comput Assist Tomogr* 1992; 16:649–650
- 24 Manning SC, Merkel M, Kriesel K, et al. Computed tomography and magnetic resonance imaging diagnosis of allergic fungal sinusitis. *Laryngoscope* 1997; 107:170–177
- 25 Greenberger PA, Miller TP, Roberts M, et al. Allergic bronchopulmonary aspergillosis in patients with and without evidence of bronchiectasis. *Ann Allergy* 1993; 70:333–338
- 26 Greenberger PA. Allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol* 2002; 110:685–692
- 27 Vlahakis NE, Aksamit TR. Diagnosis and treatment of allergic bronchopulmonary aspergillosis. *Mayo Clin Proc* 2001; 76:930–938
- 28 Tillie-Leblond I, Tonnel AB. Allergic bronchopulmonary aspergillosis. *Allergy* 2005; 60:1004–1013
- 29 Wark PA, Hensley MJ, Saltos N, et al. Anti-inflammatory effect of itraconazole in stable allergic bronchopulmonary aspergillosis: a randomized controlled trial. *J Allergy Clin Immunol* 2003; 111:952–957
- 30 Wark PA, Gibson PG, Wilson AJ. Azoles for allergic bronchopulmonary aspergillosis associated with asthma. *Cochrane Database Syst Rev* Issue 3, 2004
- 31 Greenberger PA, Patterson R, Ghory A, et al. Late sequelae of allergic bronchopulmonary aspergillosis. *J Allergy Clin Immunol* 1980; 66:327–335
- 32 Lee TM, Greenberger PA, Patterson R, et al. Stage V (fibrotic) allergic bronchopulmonary aspergillosis: a review of 17 cases followed from diagnosis. *Arch Intern Med* 1987; 147:319–323