Background: Allergic bronchopulmonary aspergillosis (ABPA) is a disease that presents with diverse clinicoradiologic manifestations. High-attenuation mucus (HAM) is a characteristic radiologic finding seen in patients with ABPA; however, the clinical significance of the entity remains unknown.

Aims and objectives: To describe the outcome of patients with ABPA who were demonstrated to have HAM, and compare with the outcome of patients without HAM.

Methods: All consecutive patients with asthma presenting to the Chest Clinic of this institute over a 4-year period were screened with an Aspergillus skin test. Patients with positive findings were further investigated, and the diagnosis of ABPA was confirmed based on predefined criteria. The patients were further classified into two groups based on the presence of HAM on HRCT scan.

Results: During the study period, 755 patients were screened for ABPA using the Aspergillus skin test; 291 patients (38.5%) had positive findings, and ABPA was diagnosed in 155 patients (mean age, 33.98 years; 76 women). Twenty-nine patients (18.7%) with ABPA were identified to have HAM on HRCT scans at presentation. The baseline characteristics were similar between the two groups, but patients with HAM had higher mean eosinophil counts, higher mean serum total IgE, and higher Aspergillus fumigatus-specific IgE levels. On multivariate analysis, both the severity of bronchiectasis and HAM predicted relapse of ABPA (odds ratio [OR], 1.23; 95% confidence interval [CI], 1.13 to 1.42; and OR, 3.61; 95% CI, 1.23 to 10.61, respectively). Failure to achieve complete remission was influenced by the severity of bronchiectasis but not by HAM (OR, 1.55; 95% CI, 1.29 to 1.85; and OR, 3.41; 95% CI, 0.89 to 13.1, respectively).

Conclusions: HAM impaction in ABPA is associated with initial serologic severity and frequent relapses but does not seem to influence complete remission.

Key words: allergic bronchopulmonary aspergillosis; CT; high-attenuation mucus; hyperdense mucus; radiologic manifestations

Abbreviations: ABPA = allergic bronchopulmonary aspergillosis; ABPA-CB = allergic bronchopulmonary aspergillosis-central bronchiectasis; ABPA-S = allergic bronchopulmonary aspergillosis-serologic; CI = confidence interval; HAM = high-attenuation mucus; HRCT = high-resolution CT; HU = Hounsfield unit; OR = odds ratio
central bronchiectasis, peripheral blood eosinophilia, and presence of serum precipitins against Aspergillus antigen. However, none of these criteria are individually specific for ABPA. Progressive airflow obstruction and pulmonary fibrosis can complicate ABPA and lead to cor pulmonale and type II respiratory failure. Thus, it is important to diagnose the disease early and treat it aggressively to prevent end-stage lung disease. It is equally important to identify specific markers that portend a poor outcome. We have reported the baseline characteristics and outcome of 126 patients with ABPA and found no difference between the radiologic staging of ABPA and the duration of illness, the severity of asthma, and the serologic findings.

High-attenuation mucus (HAM) is a characteristic radiologic finding seen in patients with ABPA. However, apart from few case reports, only one series of four patients have been previously described in literature. Moreover, the clinical significance of the presence of absence of HAM is unknown to our knowledge. Also, there are no data on factors predicting outcome in patients with ABPA. In this study, we describe the clinical characteristics, radiology, and serologic findings of patients with ABPA who present with HAM impaction. We also evaluate whether this particular presentation is associated with poor outcomes.

**Materials and Methods**

The present study is a retrospective analysis of prospectively collected data, and includes 155 consecutive patients with ABPA (the clinical characteristics of 126 of these patients have been described) diagnosed between January 2002 and June 2006. We have been prospectively screening all consecutive patients with asthma presenting to the Chest Clinic of our institution since January 2002 with an Aspergillus skin test. Patients who were found to be Aspergillus skin test positive are further investigated. Briefly, the patients were considered to have ABPA if they met four of the following criteria: clinical diagnosis of asthma; elevated total IgE levels (>1,000 IU/mL); elevated IgE levels against *A. fumigatus* (>0.35 kU/L); presence of serum precipitating antibodies against *A. fumigatus*; radiographic pulmonary opacities (fixed/transient); and central bronchiectasis on HRCT.

*From the Departments of Pulmonary Medicine (Drs. Agarwal, Gupta, Aggarwal, and Jindal), Radiodiagnosis (Dr. Saxena), and Medical Mycology (Dr. Chakrabarti), Postgraduate Institute of Medical Education and Research, Chandigarh, India. The authors have no conflicts of interest to disclose. Manuscript received March 31, 2007; revision accepted June 6, 2007. 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.07-0808*

Besides, all patients underwent spirometry with bronchodilator reversibility, and were categorized as having mild, moderate, and severe obstruction. Patients who had received glucocorticoids for >3 weeks in the preceding 6 months were excluded from screening. An informed consent was obtained from all patients as per protocol, and the study was cleared by the Institute Ethics Committee.

High-resolution CT (HRCT) of the thorax (IV contrast was not administered) was performed on a 16-row, multiple detector, CT scanner (LightSpeed Plus; GE Medical Systems; Slough, UK) with a 512 matrix size. The scans (120 kilovolts; 10 mA; window width, 1,500 Hounsfield units [HU]; and window level, −600 HU) were obtained with a scan time of 3 s in the supine position at full end-inspiration from lung apex to base. The image acquisition is contiguous and the images (1.25 mm at 10-mm intervals) were reconstructed using the high-spatial-frequency algorithm. Individual bronchopulmonary segments were identified by the anatomic division of the appropriate lobar bronchus, and their relationship with the major and minor fissures. Radiologic abnormalities were categorized for the presence and extent of bronchiectasis with the criteria described by Reiff et al used to classify bronchiectasis. Bronchiectasis 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. The presence of HAM was considered if the mucus plugs were visually denser than the normal skeletal muscle, and attenuation values were recorded wherever available.

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, and then tapered by 5 mg every 6 weeks to continue for a total duration of at least 6 to 12 months. The patients were followed up with history and physical examination, chest radiograph, and IgE levels (total) every 6 weeks. A repeat CT scan was not done unless a complication was suspected. Patients were classified as remission (if the IgE levels declined by >35% and there was clearance of chest radiographic lesions after 6 weeks of glucocorticoids); relapse (doubling of the baseline IgE levels irrespective of the patient’s symptoms or appearance of radiologic infiltrates); complete remission (no ABPA exacerbations over the next 3 months after stopping therapy); glucocorticoid-dependent ABPA (patient required oral prednisolone for persistent asthma or recurrent relapses of ABPA); and end-stage ABPA (extensive bronchiectasis with either cor pulmonale or type 2 respiratory failure).

**Statistical Analysis**

Statistical analysis was performed using statistical software (SPSS for MS Windows, version 10; SPSS; Chicago, IL, and StatsDirect, version 2.6.2 for MS-Windows; StatsDirect Ltd; Altrincham, UK; available at: http://www.statsdirect.com). Data are presented in a descriptive fashion (mean and 95% confidence interval [CI] or percentage and 95% CI). Categorical variables were compared using the χ² test, while Mann-Whitney U test was used as applicable in case of continuous variables. Multivariate logistic regression analysis was performed to derive adjusted odds ratios (ORs) and 95% CIs using the following variables: duration of asthma; lung function abnormality on spirometry; absolute eosinophil count; IgE levels (both total and *A. fumigatus* specific); extent of bronchiectasis based on the number of segments involved on HRCT; and the presence of hyperattenuating mucus to analyze the factors predicting poor outcome (ie, relapse and failure to achieve complete remission). Statistical significance was assumed at p < 0.05.
Results

During the study period, 755 patients were screened for ABPA using the Aspergillus skin test; 291 patients (38.5%) had positive findings, and ABPA was diagnosed in 155 patients (20.6%) [the baseline characteristics and outcome of 126 of these patients has been reported previously8]. There were 79 male patients and 76 female patients (mean age, 33.98 years; 95% CI, 32.1 to 35.9 years). Thirty-seven patients (23.9%) had normal HRCT findings (ABPA-serologic [ABPA-S]), and 118 patients (76.1%) had bronchiectasis (ABPA-central bronchiectasis [ABPA-CB]). Twenty-nine patients (18.7%) were identified to have HAM impaction at presentation (Fig 1, 2). The density measurements of the hyperattenuating mucus were available in 15 patients and ranged from 108 to 168 HU.

The baseline characteristics of the patients with and without HAM are shown in Table 1. Sixty-nine patients (44.5%; 95% CI, 36.9 to 52.4) had received antitubercular therapy in the past (median, one course of therapy; range, one to four courses) without any evidence of tuberculosis, and review of old records suggested that the diagnosis was ABPA. Serial chest radiographs showed pulmonary opacities in 62 patients (40%; 95% CI, 32.6 to 47.9). The baseline characteristics especially the age of presentation, duration, and severity of asthma were not different between patients with and without HAM except for the history of expectoration of brownish-black mucus plugs, which was seen more often in patients who had hyperattenuating mucus (Table 1). Patients with HAM had higher absolute eosinophil counts and serum IgE levels (both total and specific to Aspergillus); however, the severity of bronchiectasis (based on the number of lobes and segments affected by bronchiectasis on HRCT) was comparable to patients without HAM (Table 1).

The mean duration of follow-up was 17.7 months (95% CI, 16.7 to 18.8 months). All the patients went into remission at 6 weeks (Table 2). Thirty-five patients had a relapse during the course of their treatment, and relapses were higher in the HAM group (41.4% vs 18.3%, p = 0.007). All patients were restarted on therapy with prednisolone (14 patients also began therapy with itraconazole). Of the 35 patients who relapsed, all went into remission at 6 weeks; however, therapy could be stopped only in 10 patients (ie, complete remission). One hundred thirty patients finally were determined to have undergone complete remission. The number of patients who went into complete remission was lower albeit not statistically significant (p = 0.63) in the HAM group (72.4% vs 86.5%). The dosage of steroids was tapered, and therapy was stopped at a mean duration of 10.4 months (95% CI, 9.6 to 11.1 months) in these patients. All patients who had complete remission showed no evidence of radiologic worsening and are receiving follow-up with measurement of IgE levels and chest radiographs. Twenty-five patients (16.1%; repeated exacerbations, 18 patients; persistent asthma, 7 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.

Multivariate logistic regression analysis was performed to identify the factors predicting relapse and failure to achieve complete remission. We used two models: in one model, all patients were included; in another model, patients with normal HRCT scans

Figure 1. Mediastinal window of HRCT scan (left) shows HAM impaction in a 70-year-old man with ABPA (arrow); the corresponding section on the lung window (right) shows the bronchocele (arrow). In addition, there is extensive bilateral bronchiectasis. The patient was a long-standing asthmatic who presented with poorly controlled asthma and hemoptysis. Spirometry revealed moderate obstruction with significant bronchodilator reversibility. The absolute eosinophil count was 700/μL, and total and A fumigatus-specific IgE levels were 3,400 IU/mL and 3.4 kU/L, respectively.
were excluded to remove the residual confounding effect of bronchiectasis on the results, as only patients with bronchiectasis would have HAM impaction. After adjustment (for duration of asthma, abnormal lung function, absolute eosinophil count, IgE levels [total and \textit{A fumigatus} specific]), the factors that predicted relapse were the severity of bronchiectasis and the presence of HAM whether patients with normal HRCT were excluded or not (Table 3). Similarly, after adjustment (for duration of asthma, abnormal lung function, absolute eosinophil count, IgE levels [total and \textit{A fumigatus} specific]), only the severity of bronchiectasis predicted failure to complete remission whether or not patients with normal

![Figure 2](https://via.placeholder.com/150.png)

**Figure 2.** Mediastinal window of HRCT scan (left) shows HAM impaction in a 30-year old woman with ABPA (arrow); the corresponding section on the lung window (right) shows the mucus-filled dilated bronchi (arrow) and extensive bronchiectasis. The patient presented with massive hemoptysis. Spirometry revealed severe obstruction with significant bronchodilator reversibility, the absolute eosinophil count was 3100/μL, and total and \textit{A fumigatus}-specific IgE levels were 38,800 IU/mL and 7.6 kU/L, respectively.

### Table 1—Baseline Characteristics of 155 Patients With ABPA With and Without HAM Impaction*

<table>
<thead>
<tr>
<th>Variables</th>
<th>HAM (n = 29)</th>
<th>No HAM (n = 126)</th>
<th>Total (n = 155)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>35.4 (30.5–40.2)</td>
<td>33.7 (31.5–35.8)</td>
<td>34.0 (32.1–35.9)</td>
</tr>
<tr>
<td>Female gender</td>
<td>16 (55.2,37.5–71.6)</td>
<td>60 (47.6,39.1–56.3)</td>
<td>76 (49.0,41.3–56.8)</td>
</tr>
<tr>
<td>Duration of asthma, yr</td>
<td>8.2 (4.8–11.6)</td>
<td>9.1 (7.7–10.4)</td>
<td>8.9 (7.7–10.1)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>2 (6.9,19–22.0)</td>
<td>9 (7.1,33–13.1)</td>
<td>11 (7.1,40–12.3)</td>
</tr>
<tr>
<td>Prescription of antituberculous therapy</td>
<td>13 (44.8,25–62.5)</td>
<td>56 (44.4,35–53.2)</td>
<td>69 (44.5,35–62.4)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>15 (51.7,34–68.6)</td>
<td>52 (49.4,38–60.0)</td>
<td>67 (43.2,35–51.1)</td>
</tr>
<tr>
<td>Expectoration of brownish-black mucous plugs</td>
<td>20 (69.0,58–82.7)†</td>
<td>52 (41.3,33–50.0)</td>
<td>72 (46.8,38–54.3)</td>
</tr>
<tr>
<td>Crackles</td>
<td>4 (13.8,5–30.6)</td>
<td>19 (15.1,9–22.4)</td>
<td>23 (14.8,10–21.3)</td>
</tr>
<tr>
<td>Clubbing</td>
<td>3 (10.3,3–26.4)</td>
<td>22 (17.5,11–25.0)</td>
<td>25 (16.1,11–22.7)</td>
</tr>
<tr>
<td><strong>Spirometry findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>8 (27,6,14–45.7)</td>
<td>21 (16.7,11,2–24.1)</td>
<td>29 (18.7,13.4–25.6)</td>
</tr>
<tr>
<td>Mild obstruction</td>
<td>8 (27.6,14–45.7)</td>
<td>32 (25.4,18–33.6)</td>
<td>40 (25.8,19–33.2)</td>
</tr>
<tr>
<td>Moderate obstruction</td>
<td>11 (37.9,22–56)</td>
<td>41 (32.5,25–41.1)</td>
<td>52 (33.5,26–41.3)</td>
</tr>
<tr>
<td>Severe obstruction</td>
<td>2 (6.9,19–22.0)</td>
<td>32 (25.4,18–33.6)†</td>
<td>34 (21.9,16.1–29.1)</td>
</tr>
<tr>
<td>Bronchodilator reversibility</td>
<td>8 (27.6,14–45.7)</td>
<td>63 (50.0,41.4–58.6)†</td>
<td>71 (45.8,38–53.7)</td>
</tr>
<tr>
<td><strong>Immunologic findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>29 (100,88–100)</td>
<td>126 (100,97–100)</td>
<td>155 (100,97–100)</td>
</tr>
<tr>
<td>Type 3</td>
<td>24 (82.8,65–92.4)</td>
<td>105 (83.3,75–88.8)</td>
<td>129 (83.2,76–88.3)</td>
</tr>
<tr>
<td>Absolute eosinophil count, cells/μL</td>
<td>1,856 (1,138–2,574)†</td>
<td>1,127 (873–1,381)</td>
<td>1,264 (1,017–1,510)</td>
</tr>
<tr>
<td>Aspergillus precipitins</td>
<td>25 (86,2,69–94.5)</td>
<td>109 (86,5,79–91.4)</td>
<td>134 (86.5,80–91.0)</td>
</tr>
<tr>
<td>IgE levels (total), IU/mL</td>
<td>11,099 (7,822–14,195)†</td>
<td>5,522.7 (4,681.6–6,363.8)</td>
<td>6,434.2 (5,523.9–7,344.6)</td>
</tr>
<tr>
<td>IgE levels (\textit{A fumigatus}), kU/L</td>
<td>11.7 (7.7–15.8)†</td>
<td>7.6 (6.5–9.7)</td>
<td>8.4 (6.5–10.3)</td>
</tr>
<tr>
<td><strong>HRCT extent of bronchiectasis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobes</td>
<td>2.1 (1.8–2.3)</td>
<td>2.8 (2.3–3.2)</td>
<td>2.2 (2.0–2.4)</td>
</tr>
<tr>
<td>Segments</td>
<td>7.0 (5.7–8.3)†</td>
<td>5.2 (4.4–5.0)</td>
<td>5.6 (4.9–6.2)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (95% CI) and No. (%, 95% CI) unless otherwise stated. †p < 0.05.
HRCT findings were excluded (Table 4). Although patients with HAM impaction showed a trend toward poor outcome, this was not statistically significant (Table 4).

**DISCUSSION**

HRCT is presently the investigation of choice for the diagnosis of bronchiectasis in patients with ABPA.18 Bronchial mucous plugging when present in ABPA is usually low attenuation or hypodense on thoracic CT.10 High-attenuation bronchial mucous plugging in patients with ABPA on thoracic CT has been rarely described in the literature mainly as case reports,9,10,12 with only one series14 reporting an incidence of 28% but consisted only of 14 patients overall and four patients with HAM. Also, the clinical significance of this entity remains unknown. Described as the most characteristic finding of ABPA, the term HAM is applied if the plug is visually denser than the normal skeletal muscle.11 The hyperattenuating mucus probably has a basis similar to that seen in patients with allergic fungal sinusitis.19,20 An initial theory proposed the role of hemosiderin occurring within inspissated mucin is responsible for the areas of increased signal intensity. This was disputed by Zinreich et al,21 who were unable to identify increased hemosiderin within typical allergic fungal mucin. The hyperattenuating mucus plugging seen on CT scans is currently attributed to the presence of calcium salts and metals (the ions of iron and manganese)22 or desiccated mucus.23 In our study, the presence of HAM was documented in 18% of patients with a diagnosis of ABPA. In contrast to the previous series14 of HAM that suggested that this radiologic presentation may be more common in...
patients with unilobar plugging, in our study most patients with hyperattenuating mucus had multilobar involvement. In a previous study, the density of the mucus was noted to be 72 to 102 HU, whereas in our study the density recorded was from 108 to 168 HU.

There are few studies that have described the factors predicting outcome in patients with ABPA. Patterson et al divided ABPA into two stages: ABPA-S and ABPA-CB, with ABPA-S representing the earliest stage or an apparently less aggressive form of ABPA. Kumar included that ABPA-S represents the earliest stage or a factor that can be used to predict relapses (and trend toward failure to complete remission) in patients with ABPA. Unlike bronchiectasis, HAM is also a marker of initial severity, although in this study the initial severity of serologic markers (like eosinophil count, serum IgE levels [total and A fumigatus specific]) did not predict poor outcome. Thus, it remains prudent to diagnose and treat ABPA early before bronchiectasis (which is irreversible lung damage) sets in. The present study also suggests that the presence of bronchiectasis is a marker associated with frequent relapses and failure to achieve complete remission. Thus, it is of paramount importance to diagnose ABPA before bronchiectasis sets in (ie, in the ABPA-S stage).

The exact reason why hyperattenuating mucus is associated with poorer outcomes remains unclear, but one reason may be that the mucus is more impacted, and the higher attenuation points to a more inspissated type of mucus. It may also be hypothesized that patients with hyperattenuating mucus have specific genetic alterations associated with genetic susceptibility to ABPA. Kumar arbitrarily classified cases of ABPA into ABPA-S, ABPA-CB, and ABPA-CB with other radiologic findings based on radiologic findings, with both the severity of the radiologic and serologic findings increasing from patients with ABPA-S to those with ABPA-CB with other radiologic findings, but this study had only six patients in each group. In contrast, in our previous study, we found no difference between the radiologic staging of ABPA and the duration of illness, the severity of asthma, and serologic findings. In this study, besides the extent of bronchiectasis on HRCT (which showed the strongest association with poor outcomes [relapses and failure to have complete remission]); HAM is also a factor that can be used to predict relapses (and trend toward failure to complete remission) in patients with ABPA.
may argue that we have not used cutoffs of twice the upper limit of normal of Aspergillus-specific IgE and IgG levels in the diagnostic criteria for ABPA, and that this may lead to an overdiagnosis of ABPA. Unfortunately, we do not have quantitative IgG levels against *A. fumigatus*, nor do we have any study from India that has evaluated the normal levels of Aspergillus-specific IgG and IgE in non-ABPA asthmatic patients. However, this has not led to any overdiagnosis of ABPA because a majority of our patients met six or more criteria. The high incidence of ABPA in our outpatient clinic probably represents referral bias of patients with uncontrolled asthma because our hospital is a tertiary care center that caters to a very large population of patients. Secondly, all patients with asthma are screened with an Aspergillus skin test, and this may be another reason for the high proportion of ABPA in our asthma clinic. In fact, in one study,29 the prevalence of ABPA was found to be as high as 25 to 40% in an asthma clinic.

The limitations of this study include the small number of patients in the hyperattenuating mucus group, and the fact that the proportion of patients who had poorer outcomes was also small. Hence, many of the conclusions regarding outcome in our study have limitations because of the small numbers of patients in each group because our data set did not allow for a valid assessment of whether some of these conditions in the study population may or may not be a contributing factor. Hence, more studies with larger number of patients are required to confirm our findings.

**CONCLUSION**

In conclusion, HAM impaction in patients with ABPA is associated with initial serologic severity and frequent relapses but does not seem to influence complete remission.

**REFERENCES**

