Pictorial essay: Allergic bronchopulmonary aspergillosis

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Abstract

Allergic bronchopulmonary aspergillosis (ABPA) is the best-known allergic manifestation of Aspergillus-related hypersensitivity pulmonary disorders. Most patients present with poorly controlled asthma, and the diagnosis can be made on the basis of a combination of clinical, immunological, and radiological findings. The chest radiographic findings are generally nonspecific, although the manifestations of mucoid impaction of the bronchi suggest a diagnosis of ABPA. High-resolution CT scan (HRCT) of the chest has replaced bronchography as the initial investigation of choice in ABPA. HRCT of the chest can be normal in almost one-third of the patients, and at this stage it is referred to as serologic ABPA (ABPA-S). The importance of central bronchiectasis (CB) as a specific finding in ABPA is debatable, as almost 40% of the lobes are involved by peripheral bronchiectasis. High-attenuation mucus (HAM), encountered in 20% of patients with ABPA, is pathognomonic of ABPA. ABPA should be classified based on the presence or absence of HAM as ABPA-S (mild), ABPA-CB (moderate), and ABPA-CB-HAM (severe), as this classification not only reflects immunological severity but also predicts the risk of recurrent relapses.

Key words: Allergic bronchopulmonary aspergillosis; allergic bronchopulmonary aspergillosis; aspergillus; chest radiograph; computed tomography; High-resolution CT scan

Introduction

The clinical, radiological, and histological manifestations of bronchopulmonary aspergillosis depend not only on the number and virulence of the infective organism but also on the patient’s immune response.[1] Depending on these factors, the disease can be classified as saprophytic, allergic, and invasive [Table 1].[2,3] Allergic bronchopulmonary aspergillosis (ABPA), the most widely studied Aspergillus-related allergic phenomenon, is an immune-mediated inflammatory syndrome caused by hypersensitivity to a ubiquitous fungus, Aspergillus fumigatus.[4] On the other hand, allergic bronchopulmonary mycosis (ABPM) is an ABPA-like syndrome due to fungal organisms other than A. fumigatus. The frequency of ABPM is negligible compared to that of ABPA.[5]

ABPA most commonly complicates the course of bronchial asthma and cystic fibrosis (CF).[6] This review deals only with ABPA in bronchial asthma. The clinical presentation of ABPA is usually with poorly controlled asthma, hemoptysis, expectoration of mucus plugs, malaise, and fever. The diagnosis can be made on the basis of a combination of clinical, immunological, and radiological findings [Table 2],[7] which can easily be remembered using the mnemonic ARTSPICE (Asthma, Radiographic opacities, Type I skin test against Aspergillus antigen, Specific A. fumigatus IgG and IgE levels elevated, Precipitins against A. fumigatus, IgE levels raised, Central bronchiectasis, and Eosinophilia).[7] ABPA has also been classified into five stages, although the patient need not necessarily pass through these stages in a sequential fashion [Table 3].[8] The condition was first described in 1952 from the United Kingdom by Hinson et al.[9] Even after five decades of research the disorder is still underdiagnosed, with as many as one-third of cases being initially misdiagnosed as pulmonary tuberculosis in the developing countries.[10]
The fact is that the disorder is glucocorticoid-sensitive and early diagnosis and treatment can halt the development of bronchiectasis and end-stage fibrosis.

Most patients present with bronchiectasis, which is a manifestation of end-stage lung disease. Radiological investigations are used to establish the initial diagnosis of ABPA and to assess the pathologic sequel at different stages of the disease. This article reviews the chest radiographic and CT scan features of ABPA.

**Methodology**

For the purpose of this review, we performed a systematic search of the electronic databases PubMed and EmBase to identify relevant studies published literature from 1952 to 2011 using the free-text terms: “allergic bronchopulmonary aspergillosis” and “ABPA.” A total of 100 papers were identified and reviewed for this article.

**Chest Radiographic Findings**

Radiological findings are nonspecific or subtle in the early stages of the disease, and the diagnosis is often difficult.[12-15] There is preferential involvement of the upper lobes.

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**Table 1: Spectrum of pulmonary disorders caused by *Aspergillus* species**

<table>
<thead>
<tr>
<th>Category</th>
<th>Disorder</th>
</tr>
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<tbody>
<tr>
<td>Allergic</td>
<td>Allergic bronchopulmonary aspergillosis</td>
</tr>
<tr>
<td></td>
<td>Hypersensitivity pneumonitis</td>
</tr>
<tr>
<td>Saprophytic</td>
<td>Aspergiloma</td>
</tr>
<tr>
<td>Invasive</td>
<td>Chronic necrotizing pulmonary aspergillosis</td>
</tr>
<tr>
<td></td>
<td>Airway-invasive aspergillosis</td>
</tr>
<tr>
<td></td>
<td>Invasive pulmonary aspergillosis</td>
</tr>
</tbody>
</table>

**Table 2: Diagnostic criteria for allergic bronchopulmonary aspergillosis[7]**

- **Predisposing conditions**
  - Bronchial asthma, cystic fibrosis
- **Obligatory criteria**
  - Elevated serum total IgE levels (>1000 IU/ml)
  - Elevated serum IgG and/or IgE against *A. fumigatus*
- **Other criteria (at least three of five)**
  - Immediate type I reaction to *A. fumigatus* antigen
  - Presence of serum *A. fumigatus* precipitins
  - Transient and/or permanent chest radiographic opacities
  - Eosinophil count > 1000 cells/μl in peripheral blood
  - Central bronchiectasis on HRCT chest

**Table 3: Staging of ABPA with chest radiographic findings in different stages[8,16]**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Radiologic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Acute phase</td>
<td>Normal; pulmonary infiltrates and mucoid impaction, predominantly in the upper lobes</td>
</tr>
<tr>
<td>II</td>
<td>Remission</td>
<td>Significant resolution of pulmonary infiltrates and clearance of mucoid impaction</td>
</tr>
<tr>
<td>III</td>
<td>Exacerbation</td>
<td>Reappearance of infiltrates and/or mucoid impaction in previously involved, as well as new areas</td>
</tr>
<tr>
<td>IV</td>
<td>Glucocorticoid-dependent ABPA</td>
<td>Significant resolution of pulmonary infiltrates and mucoid impaction, although fixed pulmonary opacities may be encountered</td>
</tr>
<tr>
<td>V</td>
<td>End-stage (fibrotic) ABPA</td>
<td>Evidence of bronchiectasis, pulmonary fibrosis, pulmonary hypertension</td>
</tr>
</tbody>
</table>

**Table 4: Radiographic findings in the first chest radiograph in cases of ABPA**

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Normal</td>
<td>15</td>
</tr>
<tr>
<td>Transient</td>
<td></td>
</tr>
<tr>
<td>Consolidation</td>
<td>36</td>
</tr>
<tr>
<td>Nodular</td>
<td>11</td>
</tr>
<tr>
<td>Nonhomogenenous opacities</td>
<td>--</td>
</tr>
<tr>
<td>Tram lines</td>
<td>4</td>
</tr>
<tr>
<td>Toothpaste/finger-in-glove opacities</td>
<td>8</td>
</tr>
<tr>
<td>Fleeting opacities</td>
<td>NA</td>
</tr>
<tr>
<td>Extensive fibrosis</td>
<td>10</td>
</tr>
</tbody>
</table>

The fact is that the disorder is glucocorticoid-sensitive and early diagnosis and treatment can halt the development of bronchiectasis and end-stage fibrosis.[11] Most patients present with bronchiectasis, which is a manifestation of end-stage lung disease. Radiological investigations are used to establish the initial diagnosis of ABPA and to assess the pathologic sequel at different stages of the disease. This article reviews the chest radiographic and CT scan features of ABPA.

Mendelson *et al.* described the chest radiographic findings in various stages of ABPA [Table 3].[14] The chest radiographic appearances of ABPA are myriad, and can be broadly classified as transient and permanent [Table 4]. In our experience, the chest radiograph is normal in almost 50% of the cases.

**Transient Changes**

The active stage is characterized radiographically by transient and recurrent infiltrates that may clear with or without glucocorticoid therapy, although steroid therapy does hasten the clearing of opacities [Figure 1]. Consolidation is believed to be one of the most common findings, and the occurrence of eosinophilic pneumonia has also been pathologically demonstrated.[12] Massive consolidation was present in 71% of the 111 cases of ABPA described by McCarthy *et al.*[12] However, this report is from the pre-CT scan era. In our experience, while consolidation does occur in patients with acute exacerbation, it is not as common as mucoid impaction of the bronchi. Pulmonary...
masses in ABPA can occur via three mechanisms, namely, mucus plugging of bronchi with distal accumulation of secretions, formation of large bronchoceles (mucus-filled dilated bronchi) without any proximal obstruction, and eosinophilic parenchymal consolidation without endobronchial involvement.\textsuperscript{[17]} In fact, many cases of consolidation are revealed to be large areas of mucus-filled bronchi on the CT chest [Figure 2].\textsuperscript{[17]}

Tram-line shadows\textsuperscript{[12]}, band-like (toothpaste) shadows\textsuperscript{[12,14,15]} showing sometimes ‘‘V,’’ inverted ‘‘V,’’ or ‘‘Y’’ shaped shadows [Figure 3].\textsuperscript{[14]} and finger-in-glove opacities [Figure 4] may occur. They are the most characteristic finding of ABPA and represent mucoid impaction in dilated bronchi with occlusion of the distal end. These shadows are often transient, disappearing with the expulsion of secretions either spontaneously or following treatment. Transient air-fluid levels may be seen in dilated bronchi. In some instances, the dilated bronchus is filled completely with allergic mucin and appears as a circular shadow. Atelectasis is identified as a homogeneous shadow with fissure displacement. It is usually segmental and occasionally lobar [Figure 5].

Perihilar opacities simulating hilar/mediastinal lymphadenopathy (also referred to as pseudohilar opacities) occur due to the presence of mucus-filled, dilated, central bronchi close to the hilum or mediastinum [Figure 6].\textsuperscript{[15,18,21]} Rarely, true hilar adenopathy (which resolves on therapy) has also been reported in ABPA.\textsuperscript{[22,23]} This lymphadenopathy is probably reactive hyperplasia of the lymphoid tissue, which disappears following therapy. We have also recently reported a rare occurrence of miliary nodular opacities in a case of ABPA, which responded to steroid therapy.\textsuperscript{[24]}

Permanent Changes

Parallel-line shadows are similar to tram-line shadows but the width of the zone between the lines is more than that of a normal bronchus and represent a dilated bronchus [Figure 7]. Transient toothpaste shadows can disappear due to expectoration of the sputum plug within the bronchi and leave behind a parallel-line shadow. Ring shadows are circular hair-line shadows about 1–2 cm in diameter that represent dilated bronchi. Occasionally numerous ring shadows representing multiple dilated bronchi can be observed [Figure 8]. Patients with end-stage disease may present with secondary spontaneous pneumothorax [Figure 9].

CT Scan Findings

Plain chest radiography is not sufficiently sensitive to assess the extent of bronchiectasis.\textsuperscript{[25]} Bronchography has been traditionally considered the investigation of choice for the diagnosis of bronchiectasis. On the bronchogram, a characteristic pattern of proximal bronchial dilatation with normal peripheral filling is observed in ABPA.\textsuperscript{[14,15,26]} However, bronchography is invasive, relatively contraindicated in asthma, and may be associated with...
Figure 3: Chest radiograph shows a “Y-shaped” opacity (circle) that represent mucus-filled bronchi.

Figure 4: Chest radiograph shows mucoid impaction with the classic finger-in-glove pattern (arrow).

Figure 5 (A, B): Chest radiograph at presentation (A) shows left upper lobe collapse (arrow) that cleared (B) after treatment with glucocorticoids.

Figure 6 (A, B): Chest radiograph (A) of a proven case of ABPA shows a left paratracheal opacity (arrow). Axial contrast-enhanced CT scan confirmed this opacity to be a bronchocele with high attenuation mucus in the left suprahilar region.

Figure 7: Chest radiograph shows the presence of tram-line (thick arrow) and parallel-line (thin arrow) shadows.

Utility of CT Scan in Diagnosis of Bronchiectasis

The diagnostic utility of CT scan depends on the protocol followed for image acquisition. Conventional CT scan used in the past is neither as sensitive as bronchography,[28-31] nor does it demonstrate all forms of bronchiectasis.[32,33] As compared to bronchography, HRCT (1–1.5 × 5–15 mm) of the chest has a sensitivity and specificity of 96%–98% and 93%–99%, respectively, in the diagnosis of bronchiectasis.[34,35] Helical scanning (3-mm collimation) can improve CT detection of bronchiectasis compared to conventional HRCT (1.5 × 10 mm).[36] Finally, multidetector CT (MDCT; 1-mm...
slices) has been shown to be superior to HRCT (1 × 10 mm) in demonstrating the presence and extent of bronchiectasis.\textsuperscript{[37,38]}

The only problem with the newer helical and MDCT scans is the increase in radiation dose to the patient.\textsuperscript{[36,39]}

In one study, with a tube current setting of 70 mA, MDCT provided acceptable quality images for the evaluation of bronchiectasis, but the radiation dose was five times higher with MDCT (10.54 mGy) versus conventional HRCT (2.17 mGy; at settings of 120 kVp, 170 mA, 1-mm collimation, and 10-mm intervals).\textsuperscript{[39]}

**Table 5: HRCT chest findings in ABPA**

<table>
<thead>
<tr>
<th>Condition</th>
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<tr>
<td>Central bronchiectasis: extensive, usually involving three or more lobes</td>
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<tr>
<td>Mucus plugging, usually hypodense</td>
</tr>
<tr>
<td>High-attenuation mucus, seen in up to 20% of patients</td>
</tr>
<tr>
<td>Centrilobular nodules with or without tree-in-bud opacities</td>
</tr>
<tr>
<td>Atelectasis</td>
</tr>
<tr>
<td>Areas of consolidation</td>
</tr>
<tr>
<td>Mosaic attenuation due to air trapping</td>
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</table>

**HRCT Findings in ABPA**

HRCT findings encountered in ABPA are shown in Table 5. Bronchiectasis is the most common finding.\textsuperscript{[40]}

On HRCT of the chest, a bronchus is considered to be dilated if the broncho-arterial ratio (internal diameter of the bronchus divided by the external diameter of its accompanying artery) is > 1.\textsuperscript{[41]}

Based on the appearance of the dilated bronchi, bronchiectasis is further classified into: (a) **cylindrical bronchiectasis** (the mildest form of which appears as tram-track or signet-ring depending on the orientation of bronchi relative to the scan plane); (b) **varicose bronchiectasis** (suggested by irregular bronchial walls with a beaded appearance); and (c) **cystic bronchiectasis** (which appears as a cluster of air-filled cysts) [Figure 10].\textsuperscript{[42]}

**Central bronchiectasis** (CB) is believed to be a characteristic finding in ABPA although there are no uniform criteria for the diagnosis of CB. Depending on the proximity of the dilated bronchi from the hilum at a point midway between the hilum and the chest wall, bronchiectasis is arbitrarily defined as central if confined to the medial two-thirds or the medial half of the lung [Figure 11].\textsuperscript{[43]}

Bronchiectasis can however extend to the periphery as well [Figure 12], and peripheral bronchiectasis has been described in 26%–39% of the lobes involved by bronchiectasis.\textsuperscript{[44,45]}

The bronchiectasis in ABPA usually involves the upper lobes although, rarely, there may be involvement of the lower zones without involvement of the upper lobes [Figure 13].

**Atelectasis and mucoid impaction:** Atelectasis is usually subsegmental or segmental, occasionally lobar, and rarely can involve an entire lung [Figure 14]. Mucoid impaction is a common finding and is described as filling of the airways by mucoid secretions. The bronchial mucus plugging in ABPA is generally hypodense, but may also have high CT attenuation values [Figure 15].\textsuperscript{[46]} High-attenuation mucus (HAM) is said to be present if the mucus plug is visually denser than the paraspinal skeletal muscle. Goyal et al.
Figure 10 (A-C): Axial HRCTs (lung window) show the various types of bronchiectasis in three different patients with ABPA: cylindrical bronchiectatic cavities (thin arrow) of various sizes with the characteristic signet-ring appearance (thick arrow) (A), varicose bronchiectasis (arrows in B), and cystic bronchiectasis.

Figure 11: Axial HRCT (lung window) shows the classic presentation of central bronchiectasis (arrow), with sparing of the periphery.

Figure 12: Axial HRCT (lung window) shows bronchiectasis (arrow) extending till the periphery.

Figure 13 (A, B): Axial HRCT (lung window) through the upper lobes (A) and lower lobes (B) demonstrates predominant lower zone involvement by bronchiectasis (arrows) in a proven case of ABPA.

Figure 14 (A-E): Atelectasis in ABPA in four different patients. Axial HRCT (lung window) (A) shows subsegmental atelectasis. Axial noncontrast CT scan (soft tissue window) (B) shows hyperattenuated mucus (arrow) with segmental collapse (arrowhead). Axial contrast-enhanced CT scan (soft tissue window) (C) shows high attenuation mucus (arrow) within a collapsed left upper lobe and lingula (arrowhead). Chest radiograph (D) shows left lung collapse which is due to hyperdense mucus (arrow) within the collapsed lung, seen on this axial contrast-enhanced CT scan (E).

Figure 15 (A, B): Axial HRCTs with soft tissue (A) and lung (B) windows show mucoid impaction with both hypo- (bold arrow) and hyper-dense (thin arrow) characteristics.
was the first to describe HAM in ABPA. Although this radiological diagnosis was missed for long periods before and probably even after the description of this finding, numerous reports have since described the finding of HAM in ABPA. Currently, the presence of HAM is considered pathognomonic of ABPA. The constituents of HAM are not entirely clear. The reason for the hyperattenuating mucus is probably similar to that in patients with allergic fungal sinusitis, and is currently attributed to the presence of calcium salts and metals (the ions of iron and manganese) or desiccated mucus.

Other findings: In ABPA, centrilobular nodules are often seen as branching opacities, the so-called “tree-in-bud” pattern. The finding of centrilobular nodules is more common in CB associated with ABPA than in CB associated with asthma. Mosaic pattern presents on HRCT as patchy areas of differential attenuation within the lung. In patients with ABPA, the mosaic pattern is due to the concomitant small airways disease.

Pleural involvement in ABPA has been reported in the form of pleural effusion. However, the most common pleural finding encountered in our patients was secondary spontaneous pneumothorax. If ABPA is left untreated, there is progression of the disease, with development of extensive bronchiectasis and pulmonary fibrosis. Eventually, type 2 respiratory failure, cor pulmonale, and right heart failure develop in end-stage fibrotic ABPA, with extensive bronchiectasis and fibrosis on HRCT of the chest.

The presence of aspergilloma in dilated bronchiectatic cavities has also been documented. Rarely, invasive aspergillosis can complicate the course of ABPA due to lowering of immunity, either because of chronic steroid therapy or due to occurrence of other immune suppressive illnesses. The radiological picture is usually characterized by diffuse consolidation.

ABPA with allergic Aspergillus sinusitis (AAS): Mucoid impaction akin to that seen in ABPA occurs in the paranasal sinuses of patients with AAS, which can be considered as the upper airway analogue of ABPA. The contemporaneous occurrence of both AAS and ABPA represents an extension of the allergic response to the presence of fungi within the sinus cavity.

Clinical Significance of HRCT Findings

ABPA has been classified by Patterson et al. on the basis of HRCT chest findings as ABPA-CB and ABPA-S, depending on the presence or absence of bronchiectasis. It was hypothesized by Greenberger et al. that ABPA-S is the earliest stage of ABPA, with less severe immunologic findings.

Figure 16: Axial HRCT (lung window) shows a mosaic pattern. There is central bronchiectasis with mucoid impaction in many of the bronchiectatic cavities (thin arrow). Also seen are centrilobular nodules in a tree-in-bud pattern (bold arrow).

Figure 17: Axial HRCT (lung window) in a patient of ABPA who presented with a left-sided spontaneous pneumothorax (arrow). Extensive central and peripheral bronchiectasis is seen involving the right lung (arrowheads).

Figure 18: Axial HRCT (lung window) shows extensive bronchiectatic cavities (arrows), with pleural (arrowhead) and pulmonary fibrosis (curved arrow).
Utility of CT Scan in Diagnosis of ABPA

CT scan has been proposed as a diagnostic tool in the workup of asthmatic patients with minimal diagnostic criteria (asthma, *Aspergillus* skin test positivity, and CB) for the diagnosis of ABPA.[78] However, patients with asthma but without ABPA can also develop bronchiectasis.[79,80] In asthmatic patients, the presence of bronchiectasis affecting three or more lobes, with centrilobular nodules and mucoid impaction on HRCT, suggests ABPA.[81] However, a recent paper noted all these findings in *Aspergillus*-sensitized asthma without ABPA.[81] Hence, HRCT cannot be used in the initial workup of ABPA because of its poor positive predictive value.[82] Although HRCT findings in ABPA have been well described, there has been no uniformity in the reporting of various findings.[44,45,46,59,83-87] Moreover, there is no consistent criterion for defining CB, with some authors using the medial half[45,46,80] and others using the medial two-thirds as the distance from the hilum to the chest wall for the diagnosis.[44,45,79,83,86] The significance of CB as a specific diagnostic marker for ABPA is also controversial as it has been shown that almost 40% of involved lobes have bronchiectasis extending to the periphery.[44,45,87] HRCT of the chest by itself has a poor specificity in differentiating between the various etiologies of bronchiectasis.[89] While there is a good inter-observer agreement for the presence or absence of bronchiectasis in each lobe, the agreement between observers for the correct diagnosis is only moderate.[89] Reiff et al. reported that, by itself, the presence of CB had a sensitivity of only 37% for the diagnosis of ABPA.[88]

Although present in only about 20% of cases of ABPA,[79] HAM remains an important radiological sign for differentiating ABPA from asthma or other causes of bronchiectasis. The presence of HAM in patients with bronchiectasis confirms ABPA as the cause of the underlying bronchiectasis. The diagnosis of ABPA in CF is difficult as ABPA shares many clinical features with CF-lung disease without ABPA. Wheezing, fleeting pulmonary infiltrates, bronchiectasis, and mucus plugging are common manifestations of CF-pulmonary disease with or without ABPA.[81] Here, the diagnosis of HAM has important implications as its presence suggests that the lung disease is due to ABPA rather than CF per se.[55]

Conclusions

In summary, ABPA can present with diverse radiologic
manifestations. Patients with ABPA can present with central as well as peripheral bronchiectasis. The sensitivity of CB as a predictor of ABPA is poor. HAM is a characteristic CT finding in ABPA and should be actively sought as its presence confirms the diagnosis of ABPA in patients with bronchiectasis. ABPA should be classified based on the presence or absence of HAM as ABPA-S, ABPA-CB, and ABPA-CB-HAM. The clinical significance of HRCT findings lies in the fact that the presence of CB or HAM at diagnosis predicts the risk for frequent relapses.

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