

Allergic bronchopulmonary aspergillosis: Lessons for the busy radiologist

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Abstract

The probability of a radiologist interpreting a disease correctly is not only influenced by their training and experience but also on the knowledge of a particular entity. This editorial reviews certain myths and realities associated with radiological manifestations of allergic bronchopulmonary aspergillosis (ABPA). ABPA is a hypersensitivity disorder against the antigens of *Aspergillus fumigatus*. Although commonly manifesting with central bronchiectasis (CB), the disorder can present without any abnormalities on high-resolution computed tomography (HRCT) of the chest, so-called serologic ABPA (ABPA-S). HRCT of the chest should not be used in screening or in the initial diagnostic work up of asthmatics, as asthma without ABPA can manifest with findings of CB. High-attenuation mucus (HAM) is the pathognomonic sign of ABPA and is very helpful in the diagnosis of ABPA complicating asthma and cystic fibrosis. Instead of classifying ABPA based on the presence and absence of CB into ABPA-CB and ABPA-S respectively, ABPA should be classified as ABPA-S, ABPA-CB and ABPA-CB-HAM. The classification scheme based on HAM not only identifies an immunologically severe disease but also predicts a patient with increased risk of recurrent relapses.

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is an inflammatory pulmonary syndrome complicating the course of various pulmonary disorders including bronchial asthma and cystic fibrosis (CF)^[1]. The disorder occurs secondary to the immune response against antigens released by *Aspergillus fumigatus* (*A. fumigatus*), which colonize the airways of these patients^[2]. The clinical presentation is usually with uncontrolled asthma, expectoration of mucus plugs, hemoptysis, fever and weight loss^[3]. The major reason for the interest in this condition is due to the fact that it responds remarkably well to glucocorticoid therapy. In fact, early detection and treatment can eliminate the risk of progression to bronchiectasis, a manifestation of end-stage fibrotic lung disease^[4]. The diagnosis can be made using a combination of clinical, immunological and radiological findings (Table 1)^[5].

The chest radiographic findings depend on the clinical presentation of the disease. During acute exacerbations of the disease, transient and fleeting opacities are characteristically found, whereas fixed abnormalities are encountered in chronic stages of the disease (Table 2). Common findings include consolidation, mucoid impaction of

bronchi, and areas of atelectasis, whereas rare findings include pleural effusion, perihilar bronchoceles mimicking adenopathy miliary nodules and unilateral lung collapse^[6-9]. Chest radiographic findings are non-specific and high-resolution computed tomography (HRCT) of the chest is the radiological investigation of choice in ABPA. The findings on HRCT chest include central bronchiectasis (CB, defined as bronchiectasis limited to the medial half of the lung, at a point midway between the hilum and the chest wall), mucus plugging with bronchocele formation and others (Table 3)^[10]. Since its first description in 1952, numerous advances have taken place, and the remaining portion of the article will discuss the recent radiological advances associated with this condition.

ABPA CAN PRESENT WITH NORMAL HRCT CHEST

It is the usual belief of clinicians and radiologists that all patients with ABPA should manifest with CB on HRCT chest (Figure 1). However, ABPA is primarily a serological diagnosis and lung biopsy is rarely, if ever, needed in the diagnostic work up. Moreover, the earliest stage of ABPA is serologic ABPA (ABPA-S) in which the patients fulfill all other diagnostic criteria but do manifest with CT abnormalities^[11]. In fact, in Chest or Asthma clinics where there is an active screening program in asthmatics for ABPA, almost 25% of ABPA will be diagnosed in the serological stage, even in developing countries^[12].

ROLE OF CT IN THE DIAGNOSIS OF ABPA

While CB is believed to be a characteristic finding of ABPA, HRCT chest by itself has a poor specificity in distinguishing between various causes of bronchiectasis^[13]. In fact, in one study the sensitivity of CB in the diagnosis of ABPA was only 37%^[14]. Moreover, patients with ABPA can have central as well as peripheral bronchiectasis. In our study, we found that almost 40% of patients with ABPA have concomitant peripheral bronchiectasis^[10]. To add to the confusion, patients with asthma can also develop bronchiectasis^[15,16]. Although in asthmatic patients, bronchiectasis affecting three or more lobes, centrilobular nodules, and mucoid impaction on HRCT are believed to be suggestive of ABPA^[17], a recent paper noted all these findings in patients with asthma with *Aspergillus* sensitization without ABPA^[18]. CT has also been proposed as a tool in the routine diagnostic work up of asthmatics with minimal diagnostic criteria (asthma, *Aspergillus* skin test positivity and CB) used for the diagnosis of ABPA^[19]. However, the occurrence of bronchiectasis in asthmatics without ABPA limits the utility of this approach. Rather, minimal diagnostic criteria for ABPA should include all of the following: asthma, *Aspergillus* skin test positivity, raised serum total and *A. fumigatus* specific IgE levels.

Table 1 Diagnostic criteria for allergic bronchopulmonary aspergillosis^[5]

Predisposing conditions
Bronchial asthma, cystic fibrosis, chronic obstructive lung disease
Obligatory criteria
Elevated total IgE levels (> 1000 IU/mL)
Elevated IgG and/or IgE against <i>A. fumigatus</i>
Other criteria (at least three of five)
Immediate cutaneous hypersensitivity to <i>A. fumigatus</i> antigen (type I reaction)
Presence of serum precipitins against <i>A. fumigatus</i>
Fixed/transient pulmonary opacities on chest radiograph
Peripheral blood eosinophil count > 1000 cells/ μ L
Bronchiectasis on HRCT chest
Please retain HRCT chest

A. fumigatus: *Aspergillus fumigatus*; HRCT: High-resolution computed tomography.

Table 2 Chest radiographic findings encountered in patients with allergic bronchopulmonary aspergillosis

Transient changes
Consolidation
Mucoid impaction - "finger-in-glove" and toothpaste shadows
Atelectasis
Bronchial wall thickening - tramline shadows
Nodular opacities
Rare: Pleural effusion, air-fluid levels due to fluid filled bronchiectatic cavities, perihilar bronchoceles simulating adenopathy, unilateral lung collapse, miliary nodules
Fixed changes
Bronchiectatic cavities
Rare: Pulmonary fibrosis and scars, pleural thickening, pneumothorax

Table 3 High-resolution computed tomography chest findings in allergic bronchopulmonary aspergillosis

Central bronchiectasis, extensive and involving more than three lobes
Mucus plugging, usually hypodense
High attenuation mucus, seen in up to 20% of patients
Centrilobular nodules with or without tree-in-bud opacities
Atelectasis, generally subsegmental or segmental
Areas of consolidation
Mosaic attenuation due to air trapping

HIGH-ATTENUATION MUCUS IS THE PATHOGNOMONIC SIGN OF ABPA

High-attenuation mucus (HAM) remains an important radiological sign in differentiating ABPA from asthma or other causes of bronchiectasis. The bronchial mucus plugging in ABPA is generally hypodense; however, mucus secretions can also have high attenuation CT values^[10]. HAM is defined as the presence of mucus, which is denser than normal paraspinal skeletal muscle (Figure 2)^[20-22]. Although present in only about 20% of ABPA complicating bronchial asthma^[12], it is a characteristic finding and can be very useful in differential diagnosis. The presence of HAM in patients with bronchiectasis confirms ABPA

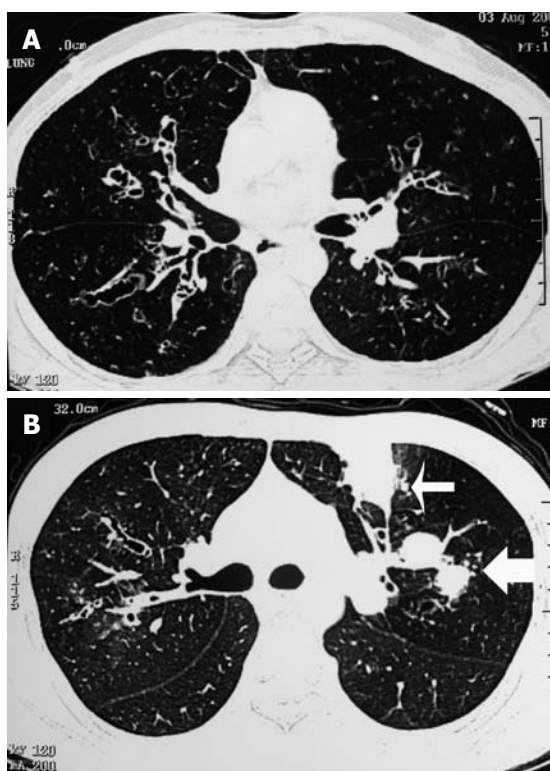


Figure 1 High-resolution computed tomography of the chest from two different patients showing typical central bronchiectasis (panel A). Mucus plugging within dilated bronchi (bronchoceles, thick arrow) and subsegmental atelectasis (thin arrow) are other common findings (panel B).

as the cause of the underlying bronchiectasis. The diagnosis of HAM is also very important in patients with CF. Unlike asthma, the diagnosis of ABPA complicating CF is difficult, as ABPA shares many clinical features with CF-related lung disease without ABPA. Wheezing, fleeting pulmonary infiltrates, bronchiectasis and mucus plugging are common manifestations of CF-related pulmonary disease with or without ABPA^[4]. The finding of HAM suggests that the lung disease is due to ABPA rather than CF *per se*^[23].

RADIOLOGICAL CLASSIFICATION OF ABPA SHOULD BE BASED ON HAM

ABPA is radiologically classified as ABPA-CB or ABPA-S, respectively, depending on the presence or absence of bronchiectasis^[24]. It was hypothesized that ABPA-S represents the earliest stage of ABPA with less severe immunologic findings compared to ABPA-CB^[25]. However, in this study only the *A. fumigatus* specific IgG levels and precipitins were higher in patients with ABPA-CB, whereas the other immunologic parameters (total and *A. fumigatus* specific IgE values) were similar in the two groups^[25]. One author has also classified the disease into three groups: ABPA-S (mild), ABPA-CB (moderate) and ABPA-CB-other radiologic findings (ORF)^[26]. However, this study included only 18 patients, and the HRCT findings in ORF included pulmonary fibrosis, bleb, bullae,

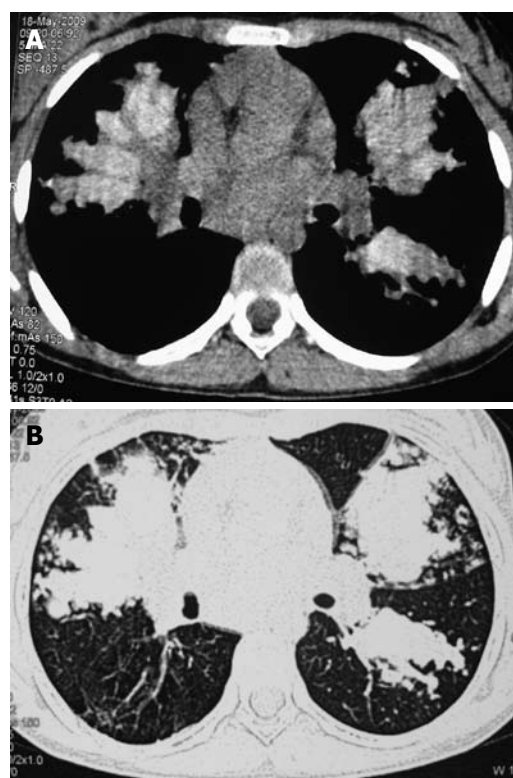


Figure 2 High-resolution computed tomography of the chest showing high-attenuation mucus in a patient with allergic bronchopulmonary aspergillosis (mediastinal window, right panel). The corresponding lung window is also shown on the left panel.

pneumothorax, parenchymal scarring, emphysematous changes, multiple cysts, fibrocavitary lesions and pleural thickening, all findings representing the fibrotic, immunologically inactive disease. In the largest study published on ABPA to date, we not only assessed the immunological parameters in both the earlier classifications but also suggested a new classification scheme based on HAM. We propose that ABPA should be classified as ABPA-S, ABPA-CB and ABPA-CB-HAM. In a study involving 234 patients with ABPA, we found that the classification scheme of Patterson *et al*^[24] and Greenberger *et al*^[25] showed immunological severity only in some parameters (eosinophil count and *A. fumigatus* specific IgE levels) but not in others (total IgE levels). Moreover, on excluding patients with HAM, the immunological severity was restricted only to eosinophil counts. Interestingly, in the Kumar classification^[26], the immunological markers were most severe in patients with ABPA-CB and not ABPA-CB-ORF. This suggests that ORF do not determine serological severity and probably represents the burnt out phase of the disease^[12].

The presence of HAM at diagnosis not only represents immunologically severe disease but also identifies a patient who is at risk of recurrent relapses. In a multivariate analysis, both CB and HAM were independent predictors of frequent relapses of ABPA (OR 3.41; 95% CI: 1.45-8.01 and OR 3.61; 95% CI: 1.23-10.61, respectively)^[12].

CONCLUSION

All patients with bronchial asthma should be routinely screened with an *Aspergillus* skin test with the aim of diagnosing ABPA before the development of bronchiectasis as bronchiectasis is a poor prognostic marker in the natural history of this disease. HRCT findings not only help in the diagnosis of ABPA but can also predict outcome. HAM is a pathognomonic sign of ABPA. ABPA should be classified based on HRCT findings as ABPA-S, ABPA-CB and ABPA-CB-HAM as the presence of HAM at diagnosis represents immunologically severe disease and identifies patients at risk for recurrent relapses.

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