ALLERGIC BRONCHOPULMONARY AND SINUS ASPERGILLOSIS: THE ROENTGENOLOGIC SPECTRUM

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1. ABSTRACT

Allergic bronchopulmonary aspergillosis (ABPA) and allergic *Aspergillus* sinusitis (AAS) are the best recognized manifestations of *Aspergillus*-associated hypersensitivity respiratory disorders. These conditions occur predominantly in atopic individuals. Roentgenologic techniques play a pivotal role in the diagnosis of these two conditions. ABPA, on imaging, is characterized by fleeting pulmonary infiltrates often confused with pulmonary tuberculosis. However, central bronchiectasis on computed tomography (CT) is considered to be the hallmark of the disease. Though the diagnosis of AAS is primarily based on histopathology, roentgenology is essential for the diagnosis. Haziness of one or more paranasal sinuses is almost always seen on plain roentgenograms. However, CT proffers more reliable information with characteristic features that include heterogeneous densities and serpiginous areas of increased attenuation on non-contrast scans. Early diagnosis, with the help of roentgenologic techniques, and appropriate therapy could alter the natural history of these diseases.

2. INTRODUCTION

The spectrum of *Aspergillus*-associated respiratory disorders ranges from saprophytic colonization of the respiratory tract to rapidly invasive disseminated disease. For clarity sake, it can broadly be classified into three clinical categories, viz. allergic aspergillosis, aspergilloma and invasive aspergillosis (Table 1) (1). Amongst the allergic aspergillosis disorders, allergic bronchopulmonary aspergillosis (ABPA), allergic *Aspergillus* sinusitis (AAS) and IgE - mediated asthma are seen in atopic subjects, while hypersensitivity pneumonitis is present in non-atopic individuals. This article will focus on the radiological features of ABPA and AAS.

3. ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

Allergic bronchopulmonary aspergillosis, the most frequently recognized manifestation of allergic aspergillosis, is an international disease with a worldwide distribution (2). The diagnostic criteria (3,4) for ABPA are summarized in Table 2 (see Chapter 1). A set of criteria has been evolved, as there is no single test that establishes the diagnosis apart from demonstration of central bronchiectasis (CB) with normal tapering bronchi. A minimal essential criteria has also been advocated that includes (i) asthma, (ii) immediate cutaneous reactivity to *Af*, and (iii) CB in the absence of distal bronchiectasis (5). When fungi other than *Aspergillus* cause a similar syndrome, the term allergic bronchopulmonary mycosis (ABPM) is used.

3.1. Roentgenologic Manifestations

Although the disease has received international attention, ABPA is still not diagnosed as frequently and as early as it should be. This results in patients receiving inappropriate therapy leading to lung damage which could

Table 1. *Aspergillus*-associated respiratory disorders [1]

I. Allergic aspergillosis
- Allergic bronchopulmonary aspergillosis (ABPA)
- IgE mediated asthma
- Hypersensitvity pneumonitis
- Allergic Aspergillus sinusitis (AAS)

II. Saprophytic colonization
- Aspergilloma

III. Invasive disease
- Invasive disseminated aspergillosis
- Chronic necrotizing pneumonia

[1] Shah A. *Indian J Chest Dis Allied Sci* 40, 41-54 (1998)

Table 2. Diagnostic criteria for ABPA [1,2]

Major criteria
- Asthma
- Presence of necrotizing pneumonia
- Immediate cutaneous reactivity to *a. Fumigatus*
- Elevated total serum ige
- Precipitating antibodies against *a. Fumigatus*
- Peripheral blood eosinophilia
- Elevated serum ige and igg to *a. Fumigatus*
- Central/proximal bronchiectasis with normal tapering of distal bronchi

Minor criteria
- Expectoration of golden brownish sputum plugs
- Positive sputum culture for *aspergillus* species
- Late (arthus-type) skin reactivity to *a. Fumigatus*

[1] Rosenberg M *et al. Ann Intern Med* 86, 405-414 (1977)
[2] Wang J *et al. Am Rev Respir Dis* 117, 917-927 (1978)

Table 3. Radiological changes in ABPA [1]

Transient changes
- Perihilar infiltrates simulating adenopathy (Figure 2)
- Air-fluid levels from dilated central bronchi filled with fluid and debris
- Massive consolidation--unilateral or bilateral (Figures 1,2 and 3)
- Radiologic infiltrates
- 'toothpaste' shadows due to mucoid impaction in damaged bronchi
- 'gloved finger' shadows from distally occluded bronchi filled with secretions
- 'tramline' shadows representing oedema of the bronchial walls
- Collapse--lobar or segmental

Permanent changes
- Central bronchiectasis with normal peripheral bronchi
- Parallel-line shadows representing bronchial widening
- Ring-shadows 1-2 cm in diameter representing dilated bronchi *en face*

Pulmonary fibrosis
- late changes--cavitation contracted upper lobes and localized emphysema

[1] Shah A. *Indian J Chest Dis Allied Sci* 40, 41-54 (1998)

have been prevented with early diagnosis. Radiological techniques have been crucial to the diagnosis of ABPA. Not only do imaging techniques help to establish the diagnosis, but also help to monitor the progress of the disease (6,7).

3.1.1. Plain Chest Roentgenography

A wide spectrum of plain chest radiographic appearances is seen in ABPA (7-10). The changes can be either transient or permanent (Table 3).

3.1.1.1. Transient changes

Transient opacities (9) usually occur at different sites in the lung over a period of time and affect a segment, lobe or the entire lung. These changes reflect disease activity and are usually seen in either the acute or the exacerbation stage of the disease. These may be the result of mucoid impaction caused by secretions in the damaged bronchi and parenchymal infiltrates, and may clear with or without therapy. No area of the lung remains unaffected, but the upper lobes are predominantly involved (6). The radiological appearances can closely resemble those seen in tuberculosis, but serial roentgenograms in ABPA may reveal the transient nature of these migratory infiltrates that have been termed as 'fleeting shadows' (Figure 1 -3). Sometimes these opacities may keep recurring at the same sites and have been described as recurrent fixed shadows. Though characteristic, fleeting shadows are not pathognomonic of ABPA.

Consolidation or non-homogeneous infiltrations are the most commonly observed patterns. These shadows produced as a result of parenchymal infiltration by inflammatory cells, especially eosinophils, have been described in up to 90% of patients with ABPA (8-10). The consolidation often clears after therapy and is not specific for ABPA. The 'tramline' sign (11), when present, signifies bronchial wall edema. The diameter of the bronchi is normal but there is thickening of the bronchial wall. McCarthy *et al* (8) have described tramline shadows as "two parallel hair-line shadows extending out from the hilum in the direction of the bronchi, the width of the transradiant zone between the lines being that of a normal bronchus at this level." These shadows have been observed in 45-92% of patients (8-10). This transient change is not specific for ABPA as it can also be seen in patients with asthma, cystic fibrosis and acute left heart failure.

Mucoid impaction and retention of respiratory secretions in the bronchi of the upper lobes may lead to 'V'-shaped shadows. These shadows, also known as 'wine glass' shadows, are highly suggestive of ABPA. When mucoid impaction occurs in distorted bronchi, the bandlike shadows are known as 'toothpaste' shadows (11). The incidence of band shadows ranges from 24-45% (8-10). The ends of the distal bronchi, if occluded, become expanded and rounded. These cast shadows that resemble 'gloved fingers' (11) and may disappear after coughing or with treatment. The presence of 'gloved fingers' shadows, reported in 11-20% of patients (8-10), should raise the possibility of ABPA.

Figure 1. Plain chest roentgenogram showing consolidation in the left mid and lower zones. A left pseudohilar opacity is also seen.

Figure 2. Plain chest roentgenogram of the same patient taken 14 months later showing clearance of the left sided consolidation with the appearance of a consolidation in the right upper and mid zones. An ovoid density is also visible in the left upper zone.

Figure 3. Plain chest roentgenogram of the same patient taken 9 months after the second roentgenogram showing patchy consolidation in all zones of the left lung. 'Gloved fingers' shadows are also visible in the right upper and mid zones. (Figures 1-3 reveal transient pulmonary infiltrates, or 'fleeting shadows', which are characteristic of ABPA.).

Perihilar infiltrates simulating adenopathy, also known as pseudohilar opacities, were first described by Mintzer and colleagues (9). These shadows, seen surrounding the dilated, central bronchi that are filled with secretions, were observed in 40% of their patients. True hilar adenopathy, which resolved on therapy, has also been reported in ABPA (12,13). Air-fluid levels in the central bronchi occur when these dilated bronchi are filled with fluid secretions and debris. This too was first described by Mintzer *et al* (9) in 20% of their patients with ABPA.

The patient with ABPA may also present with lobar or segmental collapse. Lobar collapse is more frequently seen because of proximal occlusion of the bronchi. Atelectasis has been observed in 17-39% of patients (8,10). A patient with concomitant ABPA and AAS presenting as a middle lobe syndrome has been described by us (14). After one month of therapy, the chest roentgenogram showed a reinflated middle lobe. Ipsilateral pleural effusion due to the mechanical effect of lung collapse has also been reported in a patient with ABPA, AAS and an operated aspergilloma (15). Such an association of three different clinical categories of *Aspergillus*-related respiratory disorders has been documented only once. The effusion cleared after reexpansion of the lobe following therapy with steroids. An earlier report of pleural effusion in two patients with ABPA could also have been caused by the mechanical effect of collapse of the lung (16). Spontaneous pneumothorax too has been reported in a patient with ABPA with chronic fibrotic lung disease (17), while development of bronchopleural fistula along with spontaneous pneumothorax has also been described in another case (18).

3.1.1.2. Permanent changes

Permanent opacities (9) reflect the irreversible, fibrotic changes in the bronchial walls and parenchyma. Unlike the transient changes, these tend to persist throughout life even when the patient is in remission. The most characteristic permanent change is CB with normal peripheral bronchi. This, when seen, is considered to be pathognomonic of ABPA. It is believed that bronchiectasis occurs in areas with previous radiological lesions and may result in fibrosis (19). On plain chest roentgenograms, it is seen either as parallel-line opacities representing widening of the bronchi, or as ring opacities, 1-2 cm in diameter, representing dilated bronchi *en face*. Parallel line shadows were seen in 65-70% of patients (8,9), while ring shadows were observed in the roentgenograms of 45-68% of patients with ABPA (8-10). Central bronchiectasis can be demonstrated either by bronchography, linear tomography or by computed tomography.

Other permanent changes include parenchymal fibrosis, contracted upper lobes, cavitation and localized emphysema (7). Parenchymal fibrosis may present as linear scars, reticulonodular markings or sometimes with a honeycomb appearance. Honeycombing was present in 27 (24%) of 111 patients described by McCarthy and colleagues (8). Cavities were seen in 3-14% (8,10) and localized emphysema has been described in up to 27% patients (8,10). McCarthy *et al* (8) reported that the initial
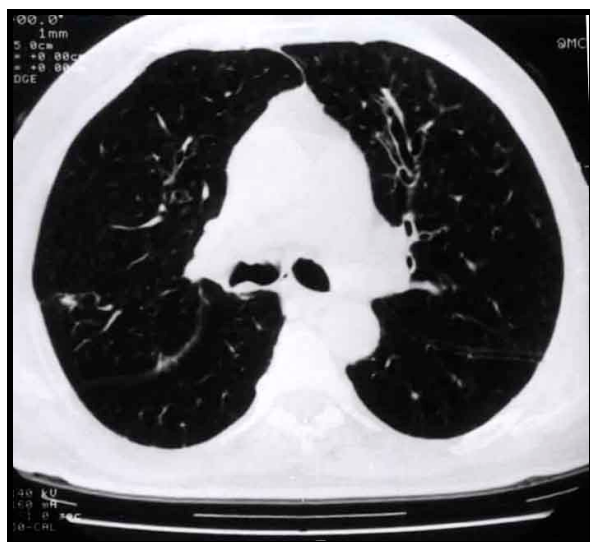
Figure 4. Computed tomography of the thorax showing 'string of pearls' appearances, indicative of central bronchiectasis.
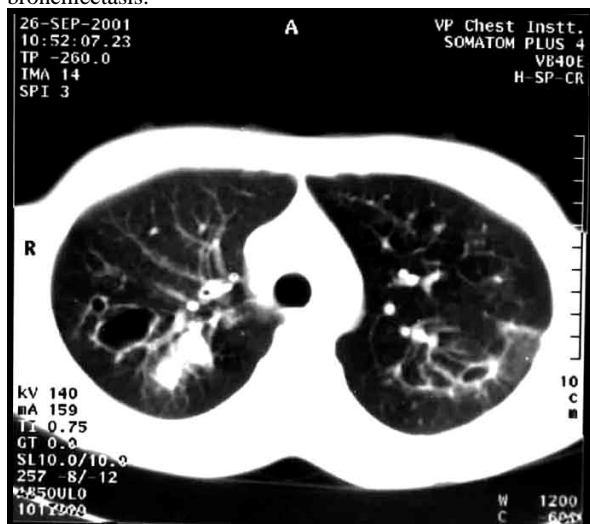

Figure 5. Computed tomography of the thorax showing 'signet ring' appearances, indicative of bronchiectasis.

radiograph in 10% of their patients had local emphysema. This figure increased to 25% when they reviewed the current or 'final' radiographs of these patients. Recently, a six stage radiograph score has also been proposed, the severity of which was found to correlate with peak *Aspergillus fumigatus* index and eosinophil counts (20).

3.1.2. Bronchography and Linear Tomography

Bronchography, which was once regarded as the gold standard for the demonstration of CB, gave a one time complete picture of the whole tracheo-bronchial tree (21). The classical lesion is a localized area of varicose bronchiectasis affecting the medium-sized bronchi proximally with normal tapering bronchi distally. However, CB may extend to the periphery in a small number of segments (6). Marked variations can occur in the extent, type and site of bronchiectasis, even in the same patient. Linear tomography was also used to document CB in view

of the fact that it was non-invasive in nature (22). However, both these methods have largely been replaced by computed tomography (CT), which is discussed below.

3.1.3. Computed Tomography

Currently, CT of the thorax has emerged as the investigation of choice for the demonstration of bronchiectasis. We have already shown that CT, in comparison to bronchography, a procedure thought to be unsafe in asthma, has a sensitivity of 83% and a specificity of 92% in detecting CB in patients with ABPA (21). CT scans also enabled us to rapidly and safely establish the diagnosis in children with ABPA who presented with acute severe asthma (23).

Bronchiectasis on CT is characterized by the 'string of pearls' (Figure 4) and the 'signet ring' (Figure 5) appearances (24). In ABPA, bronchiectasis is more commonly seen in the upper lobes (6,25) in contrast to the 'usual' bronchiectasis that predominantly affects the lower lobes. In our study (6), CB was identified in all patients, involving 114 (85%) of the 134 lobes and 210 (52%) of the 406 segments studied. Extension of CB to the periphery was observed in 30% of the lobes and 21% of the segments (6). However, demonstration of CB with normal peripheral bronchi which occurs in the majority of segments should continue to be regarded as a *sine qua non* for the diagnosis of ABPA in the absence of cystic fibrosis (6). Studies have also shown that mild CB can also be seen in asthma and do not necessarily indicate the presence of ABPA (26-28).

Besides bronchiectasis, the other bronchial abnormalities observed on CT in our study (6) included dilated and totally occluded bronchi (48%) as evidenced by beaded, tubular opacities and dense, circular opacities, air-fluid levels within dilated bronchi (22%), bronchial wall thickening (43%) and parallel-line opacities extending to the periphery (30%). On high resolution CT, high-attenuation mucus plugs have also been reported in 28% of patients with ABPA (29). Atelectasis, due to proximal mucoid impaction, can sometimes be a presenting feature. The atelectasis may be segmental, lobar or may involve the entire lung (30).

The common parenchymal abnormalities seen in our study (6) were consolidation (43%), non-homogeneous patchy consolidation (67%) and parenchymal scarring of varying extent (83%). Segmental or lobar collapse (17%), cavities (13%) and emphysematous bullae (4%) were also observed (6). When cavitation occurs along with the fibrotic stage of ABPA, it may be difficult to distinguish from fibrocavitary pulmonary tuberculosis (31-33). Parenchymal lesions extending up to the pleura were seen in 43% of our patients (6). In another study, pleural thickening was also observed in 82% of the patients with ABPA (27). Pleural involvement in ABPA is yet to receive recognition, but may not be of major clinical significance. Our study (6) has shown that CT of the thorax can provide a sensitive method for the assessment of bronchial, parenchymal and pleural abnormalities in patients with ABPA and should constitute a part of the diagnostic work-up of the disease along with plain chest roentgenograms.

Figure 6. Coronal section of computed tomography of the paranasal sinuses showing mucosal thickening and areas of high attenuation in the sphenoid sinuses. Bony erosion of the lateral wall of the sphenoid sinus is also seen.

3.2. ABPA and aspergilloma

Coexistent ABPA with aspergilloma has been described (32-34). Although cavitation is known to occur in ABPA and chronic lung damage appears to provide a favourable milieu for aspergilloma formation, aspergillomas are rather infrequent in patients with ABPA (32). In a background of cavitary lung disease, formation of an aspergilloma might be accelerated by corticosteroid therapy (34). The occurrence of ABPA consequent to aspergilloma formation has also been recorded. It has been postulated that an aspergilloma may function as a nidus for antigenic stimulation in a genetically predisposed individual, thus leading to ABPA (35).

On chest roentgenograms, an aspergilloma typically appears as a solid, rounded mass within a cavity and is separated from the wall of the cavity by air (meniscus sign or air-crescent sign). If the fungus ball is not attached to the cavity wall, positional movement may be demonstrable within the cavity (36).

4. ALLERGIC *ASPERGILLUS* SINUSITIS

Allergic *Aspergillus* sinusitis is a comparatively more recently recognized clinicopathologic entity in which mucoid impaction akin to that of ABPA occurs in the paranasal sinuses (37-39). This too occurs in atopic individuals and it is possible that, as in ABPA, the release of antigenic material by the fungi sets into motion a host of immunologic reactions culminating in the development of AAS. It has been reported that a fourth of the patients with perennial rhinitis had a positive skin reactivity to *Aspergillus* antigens (40). Since rhinitis is an important predisposing factor for sinusitis, these patients could possibly be at a greater risk of developing AAS.

A diagnostic criteria has been evolved which is principally based on pathologic findings in the specimens obtained from the paranasal sinuses. These findings are characteristically similar to those seen in the mucoid impaction of ABPA. The term `allergic mucin' has been coined to describe the nasal pathologic material comprising eosinophils, Charcot-Leyden crystals, cellular debris and scattered fungal hyphae (38). This led to enunciation of a set of criteria (41,42) for the diagnosis of AAS, viz. (1) sinusitis of one or more paranasal sinus on x-ray film, (2) necrosed amorphous tissue along with oedematous polyps infilterated with eosinophils on histopathological evaluation of material from the sinus, (3) demonstration of fungal elements in nasal discharge or in material obtained at the time of surgery by stain or culture, (4) absence of diabetes, previous or subsequent immunodeficiency disease, and treatment with immuno-suppressive drugs, and (5) absence of invasive fungal disease at the time of diagnosis or subsequently. In addition, this is supported by other features which are also seen in ABPA and include (1) peripheral blood eosinophilia, (2) type I and type III cutaneous hypersensitivity to *Aspergillus*, (3) precipitating antibodies to *Aspergillus* antigens, and (4) elevated total as well as *Aspergillus* specific IgE levels (43).

Fungi other than *Aspergillus* may also cause allergic sinusitis and hence a comprehensive term allergic fungal sinusitis (AFS) has been introduced. In a recent study (44) of 67 patients with AFS from the United States, *Bipolaris spicifera* was cultured in more than two-thirds of the patients. This was followed by *Aspergillus*, which was seen in 9%.

4.1. Roentgenologic manifestations
4.1.1. Plain roentgenograms of the paranasal sinuses

The demonstration of sinusitis on one or more paranasal sinuses on plain sinus roentgenograms is one of the diagnostic criteria for AAS. The most common manifestation is haziness of one or more sinuses. More often than not multiple sinuses are opacified. Bilateral involvement has been observed in up to 83% of cases reported (42, 45). When sequential time related studies were performed, progressive involvement of multiple sinuses was the rule (45).

Other manifestations include mucosal thickening and varying degrees of bony sclerosis and/or destruction. These findings are, however, non specific as they may also be seen in chronic sinusitis or malignancy of the paranasal sinuses. Air fluid levels in the opacified sinuses have not been reported.

4.1.2. Computed tomography

A more reliable radiological diagnosis can be made with the help of CT of the paranasal sinuses. The characteristic feature in AFS is the presence of heterogeneous densities, signifying opacification of the sinuses, with serpiginous areas of increased attenuation on noncontrast scans (46, 47). These hyperdense areas (Figure 6) are due to the presence of allergic mucin. The serpiginous pattern of the central area of high attenuation

has also been described as 'star-filled sky' or 'ground glass' patterns (48). The heterogeneous image is said to be due to the presence of ferromagnetic elements that are produced by the fungi (46).

The extent of disease is better visualized on CT, the features evaluated included bony erosion (Figure 6) and intracranial involvement. It is important to determine these prior to definitive surgery. Limited bony destruction has been noted in up to 80% of patients with AFS, the exact mechanism of which is not clear (46,49,50). This is either due to pressure necrosis causing reabsorption of the bone or bone destroying enzymes produced by the fungus. Inflammatory mediators such as major basic protein produced by the allergic response could also be responsible (51). This is in contrast to invasive fungal aspergillosis wherein bone destruction is evident (52).

In a retrospective review of 25 patients with AFS (53), extensive erosion of the skull base with intracranial extension of the disease was seen in 4 patients. However, histologic evidence of tissue invasion was absent in all 25 patients. CT helps in distinguishing AFS from desiccated secretions within mucocoeles and polyps. Chronic disease of the sinuses with desiccated secretions often result in thickening and sclerosis of the adjacent sinus walls, while the presence of expansion and thinning of the sinus walls is suggestive of AFS (47). Leakage of sinus contents into the orbit or brain may also occur. A case of pansinusitis with orbital involvement associated with an allergic response to the fungus *Curvularia lunata* has been described (54).

Mukherji *et al* (47) retrospectively reviewed CT scans along with surgical and histologic reports in 45 patients with AFS. All patients had increased intrasinus attenuation with mucosal thickening on non-contrast scans. The ethmoid sinus complex was most commonly involved (96%). This was followed by the maxillary sinus (93%), the frontal sinus (71%) and the sphenoid sinus (67%). Multiple sinus involvement was noted in 96% patients. There was an almost equal incidence of unilateral (49%) and bilateral involvement (51%). Complete opacification of at least one sinus was seen in 44 (98%) patients. Most of these 44 patients had expansion of the opacified sinus (98%), remodeling of the bony sinus walls (95%), and erosion of a sinus wall (93%). A fifth of the patients also had evidence of involvement of adjacent soft tissue structures.

CT also helps in distinguishing AFS from other forms of fungal sinusitis, which include acute (fulminant) invasive fungal sinusitis, chronic/indolent fungal sinusitis and sinus mycetoma (52, 55,56). Sinus mycetoma appears as a focal round area of increased attenuation that is usually centered within a diseased maxillary sinus. Aggressive bone erosion with extension of disease into the adjacent soft tissues is a feature of acute invasive fungal sinusitis. Unlike AFS, sinus expansion and sinus wall modeling is uncommon in acute invasive fungal sinusitis.

4.1.3. Magnetic resonance imaging

Magnetic resonance imaging (MRI) is more sensitive than CT in differentiating mycotic infections of the sinuses, but it is not considered the primary diagnostic modality. On MRI, AFS is characterized by decreased T1 and T2 weighted signal intensities. These hypodense regions are due to the presence of ferromagnetic elements within the fungal concretions (57-59). MRI also provides information about areas of critical importance including cavernous sinuses and the brain. Neoplasms appear, as moderately hyperintense areas while bacterial infections are even more hyperintense.

5. THE CO-OCCURRENCE OF ABPA AND AAS

The clinical categories of *Aspergillus*-related respiratory disorders seem to remain mutually exclusive. In spite of similar immunopathologic responses, concomitant occurrence of ABPA and AAS has rarely been reported (14,15,60). However, our recent review suggests that AAS may not be all that uncommon in patients with ABPA (42). Recently Venarske and deShazo coined the term 'sinobronchial allergic mycosis' (the SAM syndrome) to highlight the co-occurrence of ABPM and AFS (61). Since asthma and sinusitis are two diseases often treated by two different specialties, the occurrence of AAS in ABPA and of ABPA in AAS may thus be overlooked (42).

6. CONCLUSIONS

A high index of suspicion is required to establish the diagnosis of ABPA and AAS. The remarkable radiological similarity of ABPA to pulmonary tuberculosis has important clinical implications in high tuberculosis prevalent areas. Patients with ABPA in these countries often receive anti-tuberculous therapy for a long time while lung damage continues to progress relentlessly (7,62). The roentgenologic picture may provide critical inputs and play a pivotal role in the diagnosis of these two conditions. Early diagnosis and appropriate therapy could alter the natural history of these diseases (11).

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