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Review

# The many faces of pulmonary aspergillosis: Imaging findings with pathologic correlation

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**Abstract**

*Introduction*: Pulmonary *Aspergillus* infection can manifest as a variety of forms depending on the patients underlying immune status, the load of the organisms and the underlying condition of the lungs.
*Discussion*: Hypersensitivity pneumonitis and allergic bronchopulmonary Aspergillosis (ABPA) are typically seen in patients with hyper-immune status (asthma, atopy and hyper-eosinophilia). Aspergilloma or mycetoma is seen in patients with preexisting lung damage and cavities commonly from prior TB or sarcoidosis. In patients with immunosuppression, *Aspergillus* infection can present as semi-invasive or invasive (angioinvasive and airway invasive) aspergillosis.
*Conclusion*: In this article we correlate the radiologic findings of the various pulmonary manifestations of *Aspergillus* infection with their pathologic features to better understand the disease process and better comprehend the associated imaging patterns.


*Keywords:* Pulmonary aspergillosis; Radiology; Pathology

## 1. Introduction

*Aspergillus* fungus is ubiquitous and found in soil, decaying vegetation and dust. Exposure to the fungus is through the respiratory tract but the disease does not typically manifest unless it encounters weakened lungs or an impaired immune system [1].

The incidence of fungal infection has increased significantly over the last few decades in part because of the increased number of hematopoietic stem cell and solid organ transplants [2]. Aspergillosis is the most common fungal infection in stem cell transplant patients [3] and second most common fungal infection in solid organ transplant recipients [4]. These infections can be life threatening and early diagnosis and initiation of therapy is critical in these immunosuppressed patients.

Awareness of the clinical presentation and recognition of the different radiological and pathological findings may help the radiologist suggest the correct diagnosis and initiate life-saving antifungal therapy.

## 2. Discussion

### 2.1. Immune status and spectrum of disease

The probability of pulmonary aspergillosis and the radiologic imaging spectrum varies depending on the patients' immune status as well as the condition of the lungs (Table 1).

### 2.2. Allergic bronchopulmonary aspergillosis

Allergic Bronchopulmonary aspergillosis (ABPA) is a hypersensitivity reaction to *Aspergillus*, most commonly *A.*

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Table 1
Immune status and spectrum of disease.

| Immunity status | Lung condition | Disease spectrum |
|---|---|---|
| Hyperimmune | Normal | Hypersensitivity Pneumonitis/Allergic Bronchopulmonary Aspergillosis (ABPA) |
| Normal | Preexisting damage | Mycetoma (Aspergilloma) |
| Immunosuppressed | Normal | Semi invasive<br>Invasive (Airway invasive/ Angioinvasive) |

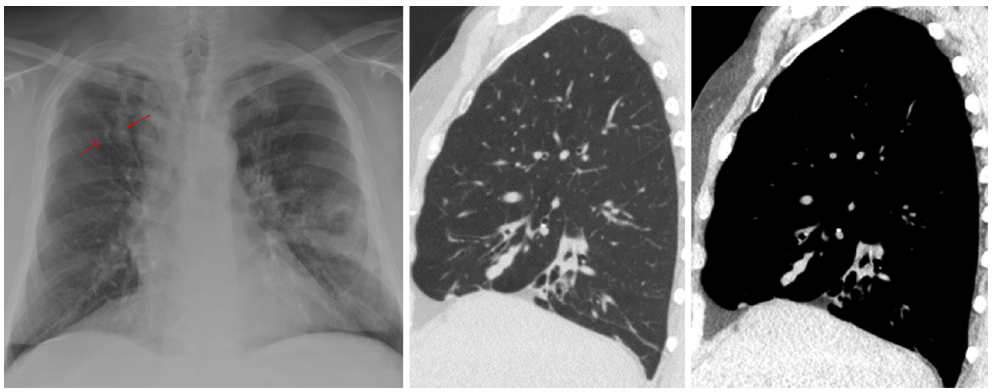
*fumigatus*. Clinically patients present with wheezing, cough, pain or low grade fever and nearly always have a prolonged history of asthma. Lab testing may reveal peripheral eosinophilia, elevated serum IgE levels, and skin reactivity to *Aspergillus* antigen [5]. The treatment usually consists of steroid therapy to blunt the hypersensitivity reaction, although some of the newer generation antifungal medications also show promise [6,7].

## Radiologic features

Plain radiographs are less sensitive early in the disease process and may only demonstrate thickening of the airways and hyperinflation suggestive of asthma. More advanced disease can demonstrate central tubular opacities in a branching pattern, more commonly in an upper lobe distribution (Fig. 1A). These findings represent central bronchiectasis with mucoid impaction classically described as the "finger in glove sign" (arrows Fig. 1A) [8–10]. On CT, "V" or "Y" central tubular opacities filled with high density are noted most compatible with dilated bronchi with mucoid impaction. These are often associated atelectasis or hyperinflation. The bronchiectasis is central and the mucoid impaction often demonstrates a characteristic increased attenuation on CT, high attenuation mucus or "HAM" (Figs. 1B–C, and 2A–F). High attenuation mucus in the setting of chronic fungal infection was first described in the setting of chronic fungal sinusitis and is thought to represent calcium and/or metallic ions from the fungus within the inspissated mucus [11]. Differential considerations may include bronchial atresia, tuberculosis or other endobronchial lesions. Rarely extensive ABPA may present with a miliary pattern on CT [12].

## Pathologic features

A spectrum of histologic changes may be seen in the setting of ABPA including mucoid impaction of bronchi, allergic mucin, eosinophilic pneumonia, bronchocentric granulomatosis, and acute and chronic bronchiolitis [13–16]. Mucoid impaction of bronchi or bronchioles is characterized by bronchiectasis or bronchioloectasis with mucin distention of the airway lumen (Fig. 3A). The mucin may show histologic features of allergic mucin including numerous eosinophils, layering of eosinophils, and Charcot-Leyden crystals (Fig. 3B and C). The fungal organisms may be quite rare and despite multiple GMS stains on separate levels, fungal elements are not identified on some cases (Fig. 3D). The respiratory epithelium in the background may show asthma-related changes, including goblet cell metaplasia, basement membrane thickening, and eosinophilic infiltration (Fig. 3C). Some cases of ABPA may have a component of eosinophilic pneumonia (EP) (Fig. 4). EP is characterized by airspace fibrin, numerous eosinophils embedded within the fibrin, and reactive type 2 pneumocytes (Fig. 5A). Bronchocentric granulomatosis (BG) is defined as the replacement of distal airways with necrotizing granulomas where the necrosis fills the airway lumen and the epithelium is replaced by palisaded histiocytes with or without giant cells (Fig. 5B). The key histologic feature is the recognition of the airway distribution of the granulomas. This can be assisted with the use of elastic tissue stains. BG can be seen in the setting of ABPA or may be an isolated finding of *Aspergillus* infection. The differential diagnosis of BG includes ABPA, other infection (bacterial, fungal, parasite), connective tissue disease (rheumatoid arthritis, granulomatosis



A B C

Fig. 1. Frontal radiograph in a patient with asthma shows central bronchiectasis and high density mucoid impactions (ABPA) in the bilateral upper lobes (finger-in-glove sign) (1A). Computerized tomography in two patients with ABPA shows central bronchiectasis and high density mucoid impactions (ABPA) in right middle lobe (1B, 1C).

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