Thoracic mycoses from opportunistic fungi: a review for the resident.

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Authors: F. M. Caballeros¹, J. M. Madrid¹, P. Bartolome¹, J. C. Pueyo¹, G. Bastarrika², ¹Pamplona/ES, ²Toronto, ON/CA
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Learning objectives

- To review the radiological features of four of the most frequent opportunistic fungi: aspergillous, candida, cryptococcus, pneumocystis.
- To get familiarized with X-ray and CT findings of each thoracic mycoses in order to help guide the diagnosis.
- To learn their differential diagnosis based on clinical, epidemiological and radiological findings.

Background

The frequency of invasive mycoses mainly due to an opportunistic fungi has significantly increased over the past decades. It is directly related to increasing populations at risk (elevated organ transplantation rates, neoplastic diseases, acquired immunodeficiency syndrome (AIDS), immunosuppressive therapy).

Although the radiologic manifestations of most opportunistic mycoses are usually nonspecific, it is imperative that radiologist recognize the full spectrum of clinical and radiologic manifestations associated with these diseases in order to correctly direct the diagnostic evaluation.

Findings and procedure details

Aspergillosis

Pulmonary aspergillosis represents a common, potentially lethal opportunistic infection that has four unique forms: allergic bronchopulmonary aspergillosis (ABPA), aspergilloma, invasive and semi-invasive aspergillosis. Each form is associated with specific predisposing host risk factors.

ABPA represents a complex hypersensitivity reaction to Aspergillus spores, occurring almost exclusively in asthma patients and occasionally as a complication of cystic fibrosis.

The most common species to produce ABPA is Aspergillus fumigatus.(5)
Clinically, patients with ABPA experience wheezing, cough and fever. Eosinophilia and elevated serum IgE levels are typically found in ABPA, being suggestive of the diagnosis.

It is radiographically characterized by fleeting pulmonary alveolar opacities caused by deposition of immune complexes and inflammatory cells within the lung parenchyma. Mucus plugging and bronchial wall thickening can be expected in time. The presence of central saccular bronchiectasis is highly suggestive of ABPA and is considered the hallmark of the disease. (Fig. 2). These airway abnormalities may in turn lead to areas of postobstructive atelectasis or air trapping and subsequent pneumothorax. If left untreated, chronic disease may progress to pulmonary fibrosis.

Aspergilloma formation represents a saprophytic infection in patients with preexisting structural lung disease. Patients at risk for aspergilloma development have cavitary, bullous, or cystic lung disease that is commonly a result of tuberculosis, sarcoidosis, or emphysema. The fungus replicates within an air-filled cavity creating a ball of intertwined hyphae, mucus, and inflammatory cells.

Although patients may remain asymptomatic, the most common clinical manifestation of saprophytic aspergillosis is hemoptysis. (4)

Radiographically aspergilloma, typically appears as a focal intracavitary mass and is characterized initially by an increase in the wall thickness of a preexisting cavity or cyst compared with that seen on baseline images.

The fungus ball often moves with changes in patient position. An aspergilloma may be surrounded by a crescent of air (Mounod sign). Occasionally, the fungus ball may completely fill the cavity, and no air crescent will be present. (Fig. 3)

Invasive aspergillosis, occurs primarily in profoundly immunocompromised patients, absolute neutrophil count < 500. (5)

Lesions caused by Aspergillus organisms are characterized by the invasion and occlusion of small to medium-sized pulmonary arteries by fungal hyphae. This leads to the formation of necrotic haemorrhagic nodules or infarcts. The clinical diagnosis is difficult, and the mortality rate is high.

On CT scans, Aspergillus nodules tend to have a characteristic halo of ground-glass attenuation ("halo sign") that represents areas of pulmonary haemorrhage. (Fig. 4)
Although this sign has been described in many diseases, in the appropriate clinical setting, the CT demonstration of the halo sign is highly suggestive. (8).

Another radiological finding are pleura-based, wedge-shaped areas of consolidation, which correspond to haemorrhagic infarcts.

During the convalescence phase, fragments of infarcted lung may separate from the adjacent parenchyma (pulmonary sequestra), resulting in a cavity with an air crescent (the air-crescent sign) similar to those seen in aspergylomas (2)

Semi-invasive aspergillosis is radiographically similar to the invasive form but differs in clinical course, being associated with mild immunosuppression or chronic illness and typically progressing over the course of months rather than weeks. (Fig. 5)

**Pneumocystis**

This form of pneumonia is caused by the fungal microorganism *Pneumocystis jiroveci*, formerly known as *Pneumocystis carinii*.

The radiographic findings typically consist of bilateral perihilar or diffuse symmetric interstitial or ground-glass opacities.

The most common CT findings are bilateral ground-glass opacities sparing the lung periphery and displaying a mosaic or nearly homogeneous pattern. Less common manifestations include airspace consolidations, patchy linear- reticular opacities, solitary or multiple nodules, parenchymal cystic lesions, and pneumothorax from the rupture of lung cysts to the pleural space. The combination of ground-glass opacities and superimposed intralobular linear opacities results in the crazy paving pattern. (Fig. 6)

**Candidiasis**

Pulmonary candidiasis is a rare opportunistic infection typically caused by candida albicans.

Most patients with pulmonary candidiasis are immunocompromised.
In these patients, candidiasis may be acquired through aspiration, manifesting as an acute bronchopneumonia, or through hematogenous dissemination with multiorgan involvement (candidemia). The clinical presentation of pulmonary candidiasis is nonspecific: prolonged fever despite broad-spectrum antibacterial therapy, cough, and hemoptisis. (4)

The radiologic manifestations are nonspecific.

Radiographs show segmental, or lobar consolidation most commonly bilateral. There may be superimposed interstitial and nodular opacities.

The most common CT finding is nodules, followed by consolidation and ground glass opacities. (Fig. 7)

Hematogenous dissemination may manifest as diffuse micro- or macronodular disease. Air-space consolidation is most commonly seen and is often patchy with a lower lobe distribution (1). An interstitial pattern may also be evident. Pleural effusions are seen in 25% of cases (3). Cavitation and adenopathy are rare. (4)

Cryptococcosis

Cryptococcus neoformans is an encapsulated fungus that is best known for affecting severely the central nervous system in immunocompromised patients.

Though it is important to take into consideration that once inhaled, the organism causes a localized granulomatous reaction and then spreads via the lymphatics to hilar and mediastinal lymph nodes, and then progresses to disseminated disease.

Radiographically, pulmonary cryptococcosis may manifest as a solitary lung mass, as multiple nodules, as a segmental or lobar consolidation or rarely as an interstitial pneumonia (more commonly seen in patients with AIDS).

On CT single or multiple pulmonary nodules with varied margins. Cavitation, effusions, and adenopathy are frequent manifestations of pulmonary cryptococcosis in immunocompromised patients. (Fig. 8)

Definitive diagnosis requires culture or demonstration of the fungus in pathologic material.
Fig. 2: ABPA in a 36-year-old asthma patient with allergic bronchopulmonary aspergillosis presenting with cough and fever. (A) Chest CT scan demonstrates central bronchiectasis and a right upper lobe consolidation. The presence of central saccular bronchiectasis is highly suggestive of ABPA. (B) In an upper slide, tubular shadowing are seen, which represents an area of mucoid impaction (red arrow). Diagnosis of a pneumonia was made.

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Fig. 3: Aspergilloma in a 71-year-old man with previous tuberculosis. (A) Posteroanterior radiograph shows a 2.5 cm intracavitary fungus ball (arrow) in the right upper lobe, which is better demonstrated on the prone CT scan (b).

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Fig. 4: Two different patients with invasive aspergillosis. (A) A 65-year-old man diagnosed with right upper lobe non-microcitic lung carcinoma. On the left upper lobe, a cavitaded new-appearing nodule is identified, associated with the "halo sign" (red arrows). (B) A 30-year-old woman with acute leukemia who had undergone bone marrow transplantation. CT scan demonstrates an, ill-defined nodule in the left upper lobe, which has a characteristic "halo sign", representing hemorrhage (red arrow). On both patient bronchoscopy was made.

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Fig. 5: Semi-invasive aspergillosis in a 68-year-old diabetic man with chronic bronchitis and 3 years of recurrent episodes of mild hemoptysis. Thin-section CT scan shows a fungal nodule in the right upper lobe (arrow) that proved to be Aspergillus at bronchoscopy. The prolonged clinical course of this case is typical of semi-invasive aspergillosis.

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**Fig. 6:** 58-year-old woman with Pneumocystis jiroveci pneumonia with renal transplant. (A) Posteroanterior chest radiograph shows a bilateral diffuse consolidations. Axial (B) and coronal (C) CT images show diffuse ground-glass opacity with relative peripheral sparing (red arrows).

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Fig. 7: 55 year-old-man who underwent liver transplantation. Presents with acute candidal pneumonia, proven by bronchoscopy: (A) Anteroposterior chest radiograph shows bilateral, diffuse parenchimal consolidation. (B) Axial CT images: nodular interstitial pattern (green arrow). (C) Bilateral air-space nodular disease (yellow arrows) and pleural effusion (red arrow).

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Fig. 8: Multifocal cryptococcosis in a 48-year-old man, renal transplant, with a 1-week history of cough and chest pain. Bronchoscopy provided the diagnosis. (A) and (B) CT images show bilateral multifocal air-space consolidation and left prevascular (C) and right paratracheal (D) adenopathy.

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Conclusion

The diagnosis of an opportunistic mycosis requires familiarity with the epidemiology of the disease, its clinical presentation, and the full spectrum of radiologic manifestations.

Personal information

References