

CONTINUING MEDICAL EDUCATION ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Medical Imaging Quiz – Case 41

A 35-year-old woman presented to the Emergency Department due to fatigue, fever and cough for at least three days. She referred being immunocompetent with a medical history of treated pulmonary tuberculosis five years ago. She mentioned living in a house under renovation construction. Medical examination revealed mild respiratory distress (SpO₂ 96%) and wheezing. Laboratory investigation showed mild leukocytosis and increased C reactive protein of 50 mg/L. Chest x-ray revealed well-defined cystic lesion involving the right lower lung lobe. She immediately started antimicrobial therapy and underwent a computed tomography (CT) scan that revealed a cystic lesion surrounded by consolidation in the right lower lobe (fig. 1). Laboratory testing

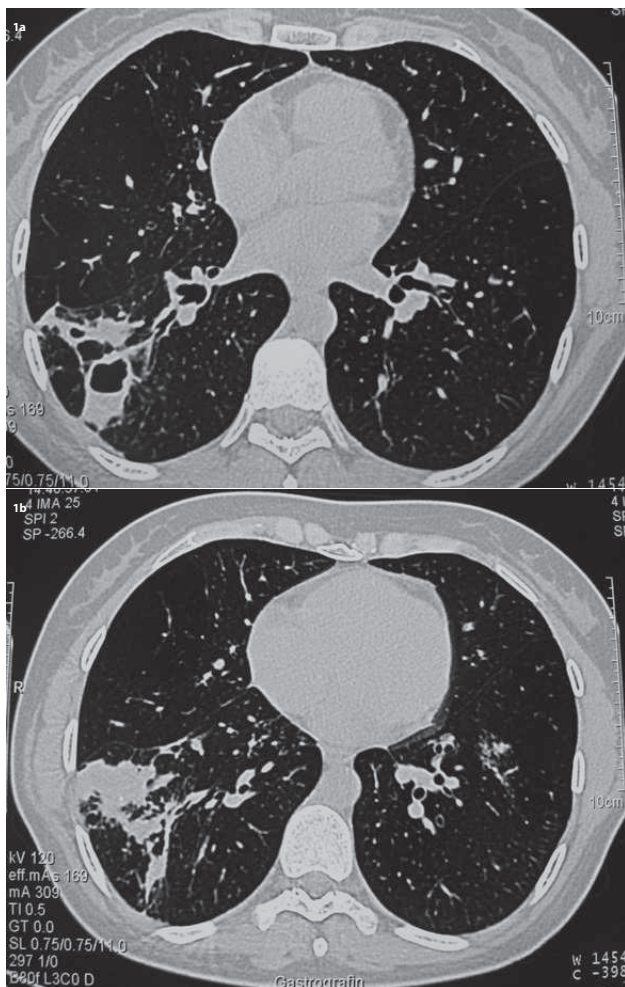


Figure 1. Computed tomography (CT) image revealing (a) cystic lesion of the lower right lobe with (b) pneumonic consolidation in the same area.

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to exclude tuberculosis and mycosis was taken. Due to lack of correspondence to the empirical antimicrobial medication she underwent a percutaneous fine needle biopsy under CT guidance (fig. 2). Samples obtained were sent for cultures and PCR and revealed certain pathogen.

Comment

*Aspergillus species are ubiquitous molds found in organic matter. Although more than 100 species have been identified, the majority of human illness is caused by *Aspergillus fumigatus* and *Aspergillus niger* and, less frequently, by *Aspergillus flavus* and *Aspergillus clavatus*. This difference in frequency is probably related to the ability of *A. fumigatus*, but not most other *Aspergillus* species, to grow at normal human body temperature. The transmission of fungal spores to the human host is via inhalation. *Aspergillus* may cause a broad spectrum of disease in the human host affecting primarily the lungs, causing the following four main syndromes: Allergic bronchopulmonary aspergillosis, chronic necrotizing aspergillus pneumonia, aspergilloma or invasive aspergillosis. In patients who are severely immunocompromised, aspergillus may hematogenously*

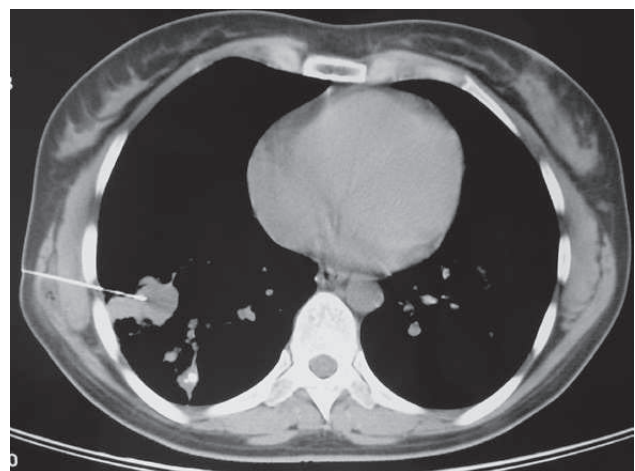


Figure 2. Computed tomography (CT) guided fine needle biopsy of the solid part of the lesion. Biopsy needle inside the lesion.

disseminate beyond the lung, potentially causing endophthalmitis, endocarditis, and abscesses in the myocardium, kidney, liver, spleen, soft tissue, central nervous system and bone.

Human host defense against the inhaled spores begins with the mucous layer and the ciliary action in the respiratory tract. Macrophages and neutrophils encompass, engulf, and eradicate the fungus. However, many species of *Aspergillus* produce toxic metabolites that inhibit macrophage and neutrophil phagocytosis. Corticosteroids also impair macrophage and neutrophil function. Underlying immunosuppression (e.g., HIV disease, chronic granulomatous disease, pharmacologic immunosuppression) also contributes directly to neutrophil dysfunction or decreased numbers of neutrophils. In individuals who are immunosuppressed, vascular invasion is much more common and may lead to infarction, hemorrhage, and necrosis of lung tissue.

Chronic necrotizing pulmonary aspergillosis (CNPA) manifests as a subacute pneumonia unresponsive to antibiotic therapy, which progresses and cavitates over weeks or months. Patients with CNPA have underlying disease, such as steroid-dependent chronic obstructive pulmonary disease or alcoholism, with symptoms that may include fever, cough, night sweats, and weight loss. Usually, patients have received prolonged courses of antibiotic therapy and sometimes empiric antituberculous therapy without response prior to diagnosis via biopsy or culture.

Physical findings in patients with aspergillosis are nonspecific. In CNPA and invasive aspergillosis, the patient is febrile and may have evidence of lung consolidation. Patients may have hemoptysis. Patients with invasive aspergillosis may be tachypneic and have rapidly progressive worsening hypoxemia.

Risk factors involved in the development of CNPA include underlying pulmonary disease (including chronic obstructive pulmonary disease [COPD], interstitial lung disease, and previous thoracic surgery) and altered immune status due to chronic corticosteroid therapy, alcoholism, collagen-vascular disease, or chronic granulomatous disease.

In aspergillosis, chest radiographic features are variable, with solitary or multiple nodules, cavitary lesions, or alveolar infiltrates that are localized or bilateral and more diffuse as disease progresses. CT images may be very helpful in the early diagnosis of aspergillosis because they may demonstrate a characteristic halo sign (i.e., an area of ground-glass infiltrate surrounding nodular densities). Later disease may show a crescent of air surrounding nodules, indicative of cavitation. Because *aspergillus* is angioinvasive, infiltrates may be wedge-shaped, pleural-based, and cavitary, which is consistent with pulmonary infarction.

Definitive diagnosis of invasive aspergillosis or chronic necrotizing aspergillus pneumonia depends on the demonstration of the organism in tissue. Procedures that may be helpful for the diagnosis of invasive aspergillosis include bronchoscopy, needle biopsy or open lung biopsy. At bronchoscopy, BAL in areas of pneumonia may provide evidence for the diagnosis. Transbronchial biopsy may be helpful, but it may not be possible, because patients are often

thrombocytopenic because of bone marrow suppression. Peripheral lesions may be amenable to transthoracic needle aspiration and biopsy. Open lung biopsy through a small thoracotomy or by video-assisted thoracoscopy may be the only way to obtain tissue samples large enough to confirm the presence of *Aspergillus* organisms in tissue. In the appropriate clinical setting of pulmonary infiltrates in a patient who is neutropenic or immunosuppressed, visualization of the characteristic fungi or a positive culture result from sputum, needle biopsy, or bronchoalveolar lavage fluid should result in the prompt institution of therapy.

Treatment of CNPA consists of administration of voriconazole, or, in some cases, itraconazole, caspofungin, or amphotericin B or amphotericin lipid formulation. A prolonged course of therapy with the goal of radiographic resolution is required. In addition, reduction or elimination of immunosuppression should be attempted, if possible.

Surgical resection may be considered when localized disease fails to respond to antifungal therapy. Patients with invasive aspergillosis or CNPA who respond to initial inpatient treatment may require several weeks of antifungal therapy. Oral voriconazole or itraconazole is administered until clinical and radiographic resolution.

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Diagnosis: Chronic necrotizing pulmonary aspergillosis