

Aspergillus in the Lung: The Spectrum of Diseases

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The infection caused by fungi associated with high mortality and morbidity rates. The frequency of pulmonary fungal infection is increasing over the past decades with the development of immuno-suppressed therapy, solid organ transplantation, steroid application and HIV-infection. Fungi causes the pulmonary infection include *Candida*, *Cryptococcus*, *Aspergillus* and others relatively uncommon fungus.¹ Although the treatment is difficult, but the results are encouraging. Hence, this is a need of today to know these diseases well so that we are able to manage them scientifically.

Aspergillosis is a mycotic disease caused by *Aspergillus* species, a genus of ubiquitous soil fungi. Although exposure to *Aspergillus* conidia through inhalation is common, only a minority of those exposed develop lung disease. The clinical features, course and prognosis of *Aspergillus* infections are largely depend on the host immune response and the number and virulence of the organisms.^{2,3}

Pulmonary aspergillosis can be subdivided into five categories: (a) saprophytic aspergillosis (aspergilloma), (b) hypersensitivity reaction (allergic bronchopulmonary aspergillosis), (c) tracheobronchial aspergillosis (d) chronic pulmonary aspergillosis, and (e) angioinvasive aspergillosis.

Saprophytic aspergillosis (aspergilloma) is an *Aspergillus* infection without tissue invasion. It consists of conglomeration of intertwined fungal hyphae admixed with mucus and cellular debris within a preexistent pulmonary cavity.⁴ The common underlying causes are tuberculosis, cystic fibrosis and sarcoidosis. The most common clinical presentation of aspergilloma is hemoptysis, although patients may remain asymptomatic. On imaging, aspergilloma are characterized by the presence of a solid, round or oval mass with soft-tissue opacity within a lung cavity. Usually the mass is separated from the wall of the cavity by airspace of variable size and shape, and present as “air crescent” sign.

Surgical resection is indicated for patients with severe life-threatening hemoptysis, and selective bronchial artery embolization can be performed in those with poor lung function.

In this issue of Journal Baseer and colleagues present their 12 years’ experience of surgical management of aspergilloma with excellent results with different surgical techniques. They also nicely review literature on this disease modality.

Allergic bronchopulmonary aspergillosis (ABPA) is caused by a complex hypersensitivity reaction to *Aspergillus*. ABPA is seen most commonly in patients with long-standing bronchial asthma. ABPA is characterized by the presence of plugs of inspissated mucus containing *Aspergillus* organisms and eosinophils. This results in bronchial dilatation and bronchiectasis in segmental and sub segmental bronchi. Patients usually cough up thick mucus plugs in which hyphal fragments can be demonstrated at culture or histologic analysis. Common clinical presentations include recurrent wheezing, malaise with low-grade fever, cough, sputum production, and a history of recurrent pneumonia. Radiologic manifestations include homogeneous, tubular, finger-in-glove areas of increased opacity in a bronchial distribution, usually predominantly involving the upper lobe and can migrate from one region to another. Treatment of ABPA aims to prevent progressive bronchiectasis. Corticosteroids are the main stay of treatment for several weeks or months. Itraconazole is used in patients with frequent exacerbations and to reduce the fungal burden and steroid dependence.⁵

Chronic Pulmonary Aspergillosis (CPA) has various patterns of presentation. Semi-invasive aspergillosis (SIA), also known as chronic necrotizing aspergillosis, is one of the commonest forms and characterized by the presence of tissue necrosis and granulomatous inflammation similar to that seen in reactivation of tuberculosis. Factors associated with the development

of this form of aspergillosis include diabetes mellitus, malnutrition, alcoholism, prolonged corticosteroid therapy, and chronic obstructive pulmonary disease.^{3,6} Another, more common pattern is chronic cavitary pulmonary aspergillosis (CCPA), characterized by slowly evolving, single or multiple lung cavities, usually with thick walls and with pleural fibrosis. In some cases of CCPA extensive pulmonary fibrosis may develop. These patients are classified as chronic fibrosing pulmonary aspergillosis.³

Clinical presentations of CPA are often insidious and include chronic cough, sputum production, fever, and constitutional symptoms. Management of patients with CPA is complicated and Azoles are the initial choice of treatment. Itraconazole, voriconazole and posaconazole can be used. The duration of treatment is usually prolonged and associated with side effects of drugs. The relapse rate is also high in this form of aspergillosis.^{3,7}

Angioinvasive aspergillosis usually occurs in immunocompromised patients with severe neutropenia. The clinical diagnosis is difficult, and the mortality rate is high. Angioinvasive aspergillosis is characterized by the invasion and occlusion of small to medium-sized pulmonary arteries by fungal hyphae. This leads to the formation of necrotic hemorrhagic nodules or pleura-based, wedge-shaped hemorrhagic infarcts. Characteristic CT findings consist of nodules surrounded by a halo of ground-glass attenuation known as “halo sign” or pleura-based, wedge-shaped areas of consolidation.⁸ Definite diagnosis is usually based on fungal culture, galactomannan, or PCR in blood and respiratory samples and on histopathology. Respiratory samples are better than blood for all tests except β -D-glucan. Voriconazole is the treatment of choice and has a significant mortality benefit. Duration of treatment in non-neutropenic patient is minimum of 12 weeks.⁹

Tracheobronchial aspergillosis or *Aspergillus* bronchitis is a less common form of aspergillosis and usually present in immunocompetent patients. These patients usually present with recurrent chest infections unsuccessfully managed with antibiotics and repeated isolation of *Aspergillus* from sputum or BAL and positive PCR but without pulmonary parenchymal disease.^{3,10} They respond well to antifungals, but relapses are common.

In summary, the spectrum of disease caused by *Aspergillus* in the lung is wide, ranging from aspergilloma to invasive aspergillosis and can be viewed as a continuous spectrum of disease. The manifestations are depending on interaction between fungus and host. A broad knowledge of clinical presentation and high suspicion are required for timely diagnosis and treatment of aspergillus related lung diseases.

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