Respiratory Diseases Caused by Fungi

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The majority of fungi are harmless to human, but in certain circumstances some species may infect human tissue, promoting damaging allergic reactions or producing toxins. Most cases of bronchopulmonary aspergillosis are caused by Aspergillus fumigatus, but other members of the genus occasionally cause disease.

ABPA is a hypersensitivity reaction to germinating fungal spores, which may complicate asthma and cystic fibrosis. It is a recognised cause of pulmonary eosinophilia . The prevalence of ABPA is approximately 1-2% in asthma and 5-10% in CF. A variety of HLA antigens convey either an increased or a decreased risk of developing the condition, suggesting that genetic susceptibility is important.

Factors predisposing to fungal disease:

- Metabolic disorders: diabetes mellitus
- Chronic alcoholism
- HIV and AIDS
- Corticosteroids and other immunosuppressant medication
- Radiotherapy
- Tissue damage by suppuration or necrosis
- Alteration of normal bacterial flora by antibiotic therapy

Classification of bronchopulmonary Aspergillosis:

- Allergic bronchopulmonary aspergillosis (asthmatic pulmonary eosinophilia)
- Extrinsic allergic alveolitis (Aspergillus clavatus)
- Intracavitary aspergilloma
- Invasive pulmonary aspergillosis
- Chronic and subacute pulmonary aspergillosis

Management:

ABPA is generally an indication for regular low-dose oral corticosteroids (prednisolone 7.5-10 mg daily) to suppress the immunopathological responses and prevent progress to tissue damage.In some patients, itraconazole (400 mg/day) allows a reduction in oral steroids.Exacerbations, particularly when associated with new chest X-ray changes, should be treated promptly with prednisolone 40-60 mg daily and physiotherapy.If persistent lobar collapse occurs, bronchoscopy (usually under general anaesthetic) should be performed to remove impacted mucus and ensure prompt reinflation.

Aspergilloma:

Inhaled Aspergillus may lodge and germinate in areas of damaged lung tissue forming a fungal ball or aspergilloma. The upper lobes are most frequently involved, and fungal balls readily form in tuberculous cavities. Less common causes include damage from a lung abscess cavity, a bronchiectatic space, pulmonary infarct, sarcoid, ankylosing spondylitis or a cavitated tumour.

Simple aspergillomas are often asymptomatic, and are identified incidentally on chest X-ray. However, they may cause recurrent haemoptysis which can be severe and life-threatening .
The fungal ball produces a tumour-like opacity on X-ray, but can be distinguished from a carcinoma by the presence of a crescent of air between the fungal ball and the upper wall of the cavity .
HRCT is more sensitive , Elevated serum precipitins to A. fumigatus are found in all patients.
Sputum microscopy typically demonstrates scanty hyphal fragments, and is usually positive on culture.
Less than half exhibit skin hypersensitivity to extracts of A. fumigatus .
Rarely, other filamentous fungi can cause intracavitary mycetoma and are identified by culture.
Aspergilloma Treatment:
Aspergillomas complicated by hemoptysis should be excised surgically. In those unfit for surgery,palliative procedures range from local instillation of amphotericin B to bronchial artery embolization .Specific antifungal therapy is of no value and steroids may predispose to invasion.
Asymptomatic cases do not require treatment.

Invasive pulmonary aspergillosis (IPA):

IPA is most commonly a complication of profound neutropenia caused by drugs (especially immunosuppressants) and/or disease:

- Neutropenia: risk related to duration and degree
- Solid organ or allogenic stem cell transplantation
- Prolonged high dose corticosteroid therapy
- Leukemia and other hematological malignancies
- Cytotoxic chemotherapy
- Advanced HIV disease
- Severe COPD
- Critically ill patients on intensive care units
- Chronic granulomatous disease

Clinical features IPA:
Acute IPA causes a severe necrotising pneumonia, and must be considered in any immunocompromised patient who develops fever, new respiratory symptoms (particularly pleural pain or haemoptysis) or a pleural rub. Invasion of pulmonary vessels causes thrombosis and infarction, and systemic spread may occur to the brain, heart, kidneys and other organs.
Tracheobronchial aspergillosis complicates lung transplant and presents with large airway invasion, fungal plaques and ulceration.

Diagnosis of IPA:

- HRCT characteristically shows macronodules (usually ≥ 1 cm), which may be surrounded by a 'halo' of low attenuation if captured early (< 5 days). Culture or histopathological evidence of *Aspergillus* in diseased tissue gives a definitive diagnosis.
- Detection of *Aspergillus* DNA by PCR.

Management and prevention:

IPA carries a high mortality rate, especially if treatment is delayed .The treatment of choice is voriconazole. Second-line agents include lipid-associated amphotericin, caspofungin or posaconazole. Response is assessed both clinically and radiologically. Recovery is dependent on immune reconstitution, which may be accompanied by enlargement and/or cavitation of pulmonary nodules.

Chronic pulmonary aspergillosis:

It is indolent, non-invasive complication of chronic lung disease such as COPD, tuberculosis/non-tuberculous mycobacterial disease or fibrotic conditions; it may be associated with malnutrition, diabetes or liver disease, and co-infection with non-tuberculous mycobacteria.
CPA may mimic TB, resulting in its delayed diagnosis. Features include cough (with or without haemoptysis), weight loss, anorexia and fatigue over months or years, with associated fever, night sweats, and an elevated CRP and ESR. Radiological features include thick-walled cavities (predominantly apical), pulmonary infiltrates, pleural thickening and, later, fibrosis.

Diagnosis is achieved by a combination of radiological examination, histopathology, isolation of the fungus in sputum and detection of Aspergillus IgG in serum. Disease is usually treated with prolonged courses of itraconazole or voriconazole, but cure is unusual .
The most frequent pattern is chronic relapse/remission with gradual, deterioration. Surgical intervention is undesirable with complications and should be avoided.

Pulmonary Mucormycosis

Mucormycosis: may present with a pulmonary syndrome indistinguishable clinically from acute IPA. Diagnosis relies on histopathology (where available) and/or culture of the organism from diseased tissue. The principles of treatment are as for other forms of mucormycosis: correction of predisposing factors, antifungal therapy with high-dose lipid-amphotericin B or posaconazole, and surgical débridement .

Other fungal infections

Histoplasmosis, coccidioidomycosis, blastomycosis and cryptococcosis