Medical mycology (9)

Opportunistic Systemic Mycoses

2- Cryptococcosis

Cryptococcosis is a chronic, subacute to acute pulmonary, systemic or meningitic disease, initiated by the inhalation of basidiospores and/or desiccated yeast cells of *Cryptococcus neoformans*. Primary pulmonary infections have no diagnostic symptoms and are usually subclinical. On dissemination, the fungus usually shows a predilection for the central nervous system, however skin, bones and other visceral organs may also become involved. Although *C. neoformans* is regarded as the principle pathogenic species, *C. albidus* and *C. laurentii* have on occasion also been implicated in human infection. *Cryptococcus* is an encapsulated basidiomycete yeast-like fungus with a predilection for the respiratory and nervous system of humans and animals. Two species, *C. neoformans* and *C. gattii* are distinguishable biochemically and by molecular techniques.

Clinical manifestations:

1. Pulmonary Cryptococcosis:

Subclinical cryptococcosis may result of environmental exposure, normal individuals may experience a self-limiting pneumonia with accompanying sensitization. Most primary infections of this type have no diagnostic symptoms and are usually discovered only by routine chest x-ray. When present, symptoms include cough, low-grade fever and pleuritic pain.

Invasive pulmonary cryptococcosis may occur in some patients when primary infections may not readily resolve in some patients, leading to a more chronic pneumonia progressing slowly over several years.

2. Central Nervous System:

Dissemination to the brain and meninges is the most common clinical manifestation of cryptococcosis and includes **meningitis, meningoencephalitis and cryptococcoma**.

Meningitis Symptoms usually develop slowly over several months, and initially include headache, followed by drowsiness, dizziness, irritability, confusion, nausea, vomiting, neck stiffness

Meningoencephalitis due to invasion of the cerebral cortex, brain stem and cerebellum is an uncommon, rapid fulminate infection, often leading to coma and death within a short time

Cryptococcoma is a rare entity, characterized by localized, solid, tumor-like masses, usually found in the cerebral hemispheres or cerebellum, or more rarely in the spinal cord.

3. Cutaneous Cryptococcosis:

Primary cutaneous cryptococcosis

Disseminated cutaneous *Cryptococcus* infection

4. Cryptococcosis of Bone:

5. Ocular Cryptococcosis:

Laboratory diagnosis:

1. Clinical material: Cerebrospinal fluid (CSF), biopsy tissue, sputum, bronchial washings, pus, blood and urine.

2. Direct Microscopy: (a) For exudates and body fluids make a thin wet film under a coverslip using India ink to demonstrate encapsulated yeast cells. Sputum and pus may need to be digested with 10% KOH prior to India ink staining. (b) For tissue sections use PAS digest, GMS and H&E, mucicarmine stain is also useful to demonstrate the polysaccharide capsule. Examine for globose to ovoid, budding yeast cells surrounded by wide gelatinous capsules. Note, non-encapsulated variants, although rare, may also occur.

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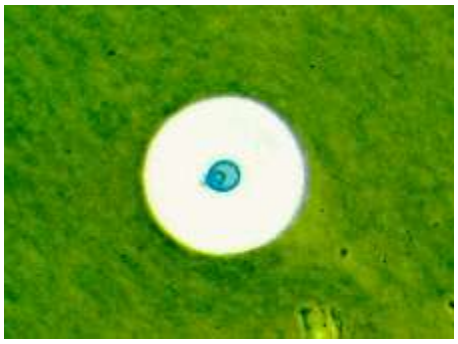

India ink preparation of CSF showing a typical yeast cell of *C. neoformans* surrounded by a characteristic wide gelatinous Spherules (10-80um) with endospores (2-5um).

3. Culture: Inoculate specimens onto primary isolation media, like Sabouraud's dextrose agar. Look for translucent, smooth gelatinous colonies, later becoming very mucoid and cream in color..

Bird seed agar plate showing the typical brown colour effect seen with *C. neoformans*.

4. Serology: It should be noted that the detection of cryptococcal capsular polysaccharide antigen in spinal fluid is now the method of choice for diagnosing patients with cryptococcal meningitis. Note, serum specimens should be pretreated with pronase to enhance detection of antigen and avoid false negative results.

Causative agents:

Cryptococcus albidus, Cryptococcus laurentii, Cryptococcus neoformans, Cryptococcus gattii.

Treatment

Amphotericin B in combination with oral flucytosine, is indicated as initial therapy for patients with meningeal and other serious cryptococcal infections. Patients with less severe disease can be treated with fluconazole or itraconazole,

3-Aspergillosis

Aspergillosis is a spectrum of diseases of humans and animals caused by members of the genus *Aspergillus.* These include

(1) mycotoxicosis due to ingestion of contaminated foods;

(2) allergy to the presence of conidia or transient growth of the organism in body orifices;

(3) colonisation without extension in preformed cavities and debilitated tissues;

(4) invasive, inflammatory, granulomatous, narcotising disease of lungs, and other organs; and rarely

(5) systemic and fatal disseminated disease. The type of disease and severity depends upon the physiologic state of the host and the species of Aspergillus involved. The etiological agents are cosmopolitan and

include *Aspergillus fumigatus, A. flavus, A. niger, A. nidulans*and *A. terreus.*

Clinical manifestations:

1. **Pulmonary Aspergillosis**: including **allergic, aspergilloma** and **invasive aspergillosis.**

Allergic aspergillosis ranging from extrinsic asthma to extrinsic allergic alveolitis to allergic broncho pulmonary aspergillosis (hypersensitivity pneumonitis) caused by the inhalation of *Aspergillus* conidia. Features include asthma, peripheral eosinophilia, positive skin test to *Aspergillus* antigenic extracts, positive immunodiffusion precipitin tests for antibody to *Aspergillus*, elevated total IgE, and elevated specific IgE against *Aspergillus*.

Non-invasive aspergillosis or aspergilloma (fungus ball), is caused by the saprophytic colonisation of pre-formed cavities.Features often include hemoptysis with blood stained sputum, positive immunodiffusion precipitin tests for antibody to*Aspergillus*, and elevated specific IgE against *Aspergillus*..

Acute invasive pulmonary aspergillosis. Common symptoms include fever, cough and sputum production; positive serum antibody precipitins may also be detected.

2. Disseminated Aspergillosis:

Hematogenous dissemination to other visceral organs may occur, especially in patients with severe immunosuppression or intravenous drug addiction brain (cerebral aspergillosis), kidney (renal aspergillosis), heart, (endocarditis, myocarditis), bone (osteomyelitis), and gastrointestinal tract.

4. Cutaneous Aspergillosis:

Cutaneous aspergillosis is a rare manifestation that is usually a result of dissemination from primary pulmonary infection in the immunosuppressed patient. Lesions manifest as erythematous papules or macules with progressive central necrosis.

Laboratory diagnosis:

1. Clinical material: Sputum, bronchial washings and tracheal aspirates from patients with pulmonary disease and tissue biopsies from patients with disseminated disease.

2. Direct Microscopy: (a) Sputum, washings and aspirates make wet mounts in either 10% KOH & Parker ink or Calcofluor and/or Gram stained smears; (b) Tissue sections should be stained with H&E, GMS and PAS digest. Note Aspergillus hyphae may be missed in H&E stained sections. Examine specimens for dichotomously branched, septate hyphae.

3. Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar. Colonies are fast growing and may be white, yellow, yellow-brown, brown to black or green in colour.

Serology:Immunodiffusion tests for the detection of antibodies to*Aspergillus*species have proven to be of value in the diagnosis of allergic, aspergilloma, and invasive aspergillosis.

Treatment

The goal of therapy is to treat any immune problems and to control the infection with antifungal medications, antifungal therapy involved amphotericin B. Several less toxic drugs have been introduced that work against aspergillus.