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MYCOLOGY - CHAPTER FIVE

FILAMENTOUS FUNGI

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CHROMOBLASTOMYCOSIS

This is a chronic, localized infection of subcutaneous tissues caused by several species of dematiaceous fungi. The 3 most common agents are:

- *Fonsecaea pedrosoi* (figure 1)
- *Cladosporium carrionii* (figure 2 and 4)
- *Phialophora verrucosa* (figure 3)

These fungi, recognized by a variety of names, are **saprobies** located in soil and decaying vegetation. The route of entry is usually by trauma. The lesions are sub-cutaneous and the surface can be flat or verrucous (figure 4A). The lesions take several years to develop. These organisms are called dematiaceous fungi, because they have a black color in the mycelium cell wall (in culture and in tissue). In tissue these fungi form sclerotic bodies which are the reproductive forms dividing by fission (figure 4B). These organisms induce a granulomatous reaction. The etiologic agents of chromoblastomycosis are septate, mold-like, branching, darkly pigmented which produce asexual fruits called conidia. We identify these fungi in culture by the shape and formation of the conidia. The fungi have a worldwide distribution especially in warmer climates like the tropics or the southern U.S. The melanin in the pigment may be a virulence factor. These organisms are distributed worldwide. There is no really successful therapy. Excision and local heat have been used with some success. Flucytosine (5-FC) and itraconazole have also been used to treat (or control) this disease. Posaconazole is showing some promise as a therapeutic agent. There are no serological tests to aid in the diagnosis.



Figure 1.

This slide culture of the fungus *Fonsecaea pedrosoi*, revealed the presence of a phialide with accompanying phialospores. *Fonsecaea pedrosoi* is one of the etiologic pathogens responsible for the infection known as chromoblastomycosis, especially in the more humid regions of the world. Normally it is found amongst rotting woods and soil debris. CDC/Dr. Lucille K. Georg



Figure 2

Cladosporium (Cladophialophora) carrionii, magnified 475X. The *C. carrionii* fungus is a common cause of chromoblastomycosis infections, and is particularly prevalent in arid and semi-arid areas, most often in tropical and subtropical zones. CDC/Dr. Lucille K. Georg



Figure 3

Conidia-laden conidiophores of a *Phialophora verrucosa* fungal organism from a slide culture. Note the flask-shaped phialides, each lipped by a collarette. Each phialide terminates in a bundle of round, to ovoid conidia. *Phialophora spp.* are known to be a cause of both chromoblastomycosis, and phaeohyphomycosis. CDC/Dr. Libero Ajello



Figure 4

Plate culture of *Cladosporium carrionii*, at four weeks growth. *C. carrionii* infection is a common cause of chromoblastomycosis, and is particularly prevalent in arid and semi-arid areas, most often in tropical and subtropical zones. CDC/Dr. Lucille K. Georg



Figure 4A

Chromoblastomycosis lesions are sub-cutaneous and the surface can be flat or verrucous

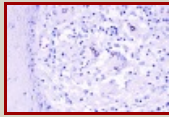


Figure 4B

Dematiaceous fungi: In tissue these fungi form sclerotic bodies which are the reproductive forms dividing by fission

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MYCETOMA (Maduromycosis)

Mycetomas (fungous tumors) are also chronic, subcutaneous infections (figure 5). These are called eumycotic mycetoma (tumors caused by the TRUE fungi as opposed to those caused by actinomycetes) (figure 6). These tumors frequently invade contiguous tissue, particularly the bone. A diagnosis of the etiologic agent is essential for patient management because the prognosis and therapy differs. Mycetoma characteristics:

1. tumefaction - swelling
2. granules - a variety of colors (white, brown, yellow, black)
3. draining sinus tracts

The three most common etiologic agents are:

1. *Madurella mycetomatis* (figure 7 and 8)
2. **Exophiala jeanselmei* (figure 9)
3. **Pseudallescheria boydii* (figure 10 and 11)

*The most common in the US. These organisms are associated with the soil, thus you see many infections in the feet and legs.

Clinical specimens for diagnosis:

1. pus - with granules
2. tissue - for histological examination

The color, size and texture of the granules are an aid in the diagnosis of mycetomas. The agents of mycetoma are all filamentous fungi which require 7-10 days for visible growth on the culture media and then another several days for specific identification. These fungi are identified by the colonial morphology, conidia formation and biochemical reactions. The species of fungi cannot be distinguished in histopathological tissue sections. Treatment is very difficult, but terbinafine and itraconazole have been used with some success. Posaconazole seems to be efficacious.

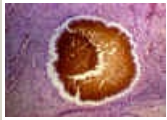


Figure 5.

Black grain mycetoma: subcutaneous nodule due to *Madurella Mycetomatis*, magnified x 100 © Bristol Biomedical Image Archive. Used with permission



Figure 6.

Mycetoma with presence of *geotrichum* © Bristol Biomedical Image Archive. Used with permission

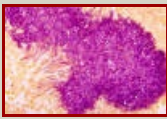


Figure 7.

Histopathologic appearance of "black grain mycetoma" due to *Madurella mycetomatis* using a Gridley stain.

"Black grain mycetoma", though usually a localized infection, can involve not only the superficial layers of skin, but underlying fascia and bones as well, with the fungal pathogen entering the body through a traumatic wound. CDC/Dr. Libero Ajello

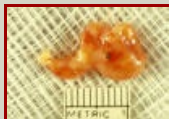


Figure 8.

Specimen of fibroadipose tissue containing "black grain" mycetoma due to the fungus *Madurella grisea*. Some *Madurella spp.* are a cause of mycetoma, a fungal infection characterized by sclerotia, or large black masses of hyphae. The fungus enters the human body via trauma, which usually affects the foot. This disease process may take several years. CDC

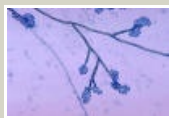


Figure 9.

Conidiophores of the fungus *Exophiala jeanselmei*. *Exophiala jeanselmei*, is a well documented human pathogen. Clinical manifestations include mycetoma, localized cutaneous infections, subcutaneous cysts, endocarditis, cerebral involvement, and systemically disseminated infections. CDC/Dr. Libero Ajello.



Figure 10.

Conidiophores with conidia of the fungus *Pseudallescheria boydii* from a slide culture. *Pseudallescheria boydii* is pathogenic in humans, especially those who are immunocompromised, causing infections in almost all body regions, and which are classified under the broad heading of "Pseudallescheriasis". CDC/Dr. Libero Ajello

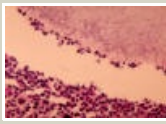


Figure 11.

Eumycetoma due to the fungus *Pseudallescheria boydii*. *Pseudallescheria boydii* is the most common etiologic agent associated with eumycetoma in the United States. The disease is a chronic cutaneous and subcutaneous infection with the foot being the most common site for lesions. CDC/Dr. Hardin

MUCORMYCOSIS

Also known as zygomycosis and phycomycosis. Mucormycosis is an acute inflammation of soft tissue, usually with fungal invasion of the blood vessels. This rapidly fatal disease is caused by several different species in this class. The zygomycetes, like the *Candida* species, are ubiquitous and rarely cause disease in an immunocompetent host. Some characteristic underlying conditions which cause susceptibility are: diabetes, severe burns, immunosuppression or intravenous drug use.

The three most common genera causing this clinical entity are:

- *Rhizopus* species (figure 12)
- *Mucor* species (figure 13)
- *Absidia* species

Characteristics

These fungi are found world-wide, commonly in soil, food, organic debris etc. They are seen on decaying vegetables in the refrigerator and on moldy bread. Rhinocerebral infections are common. This disease is frequently seen in the uncontrolled diabetic patients.

Typical case

An uncontrolled diabetic patient comes to ER (may be comatose depending on the state of diabetes) and a cotton-like growth is observed on the roof of the mouth or in the nose. These are the hyphae of the organism. If untreated, the patient will die within a few hours or days. What do you do to help this patient first? Controlling the diabetic state is most important before administering amphotericin.

These fungi have a tendency to invade blood vessels (particularly arteries) and enter the brain via the blood vessels and by direct extension through the cribriform plate (figure 14). This is why they cause death so quickly.

Culture

A rapid growing, loose, white mold is visible within 24 to 48 hours. With age, and the formation of sporangia, the colony becomes dark gray. The sporangia contain the dark spores (figure 16). The mycelium is wide (10-15 microns), ribbon-like and non-septate (coenocytic). This same appearance is clear in tissue sections. The species are identified by the morphology in culture.

Treatment

Treatment consists of debridement and amphotericin

Identification

There is an immunodiffusion test available, but the physician cannot wait for these results before instituting rapid, vigorous intervention. The diagnosis and treatment must be immediate and based primarily on clinical observations.

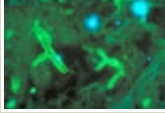


Figure 12.

Histopathologic changes seen in zygomycosis due to *Rhizopus arrhizus* using FA stain technique. *Rhizopus arrhizus*, the most common *Rhizopus spp.*, is known to be the cause of zygomycosis, an angiotropic disease, which means that it tends to invade the blood vessels, thereby, facilitating its systemic dissemination. CDC/Dr. William Kaplan

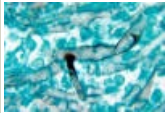


Figure 13.

Histopathologic changes seen in a heart valve due to zygomycosis caused by *Mucor pusillus*. Using methenamine silver stain, one can detect the presence of fungal elements associated with zygomycosis, including sparsely septate hyphae, amongst a mostly acute inflammatory process with some island of chronic granulomatous inflammation. CDC/Dr. Libero Ajello

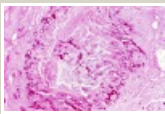


Figure 14

Mucor sp. enter the brain via the blood vessels
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Figure 15

This patient presented with a case of a periocular fungal infection known as mucormycosis, or phycomycosis. Mucormycosis is a dangerous fungal infection usually occurring in the immunocompromised patient, affecting the regions of the eye, nose, and through its growth and destruction of the

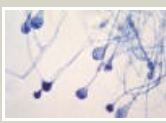


Figure 16

Young sporangia of a *Mucor spp.* fungus. *Mucor* is a common indoor mold, and is among the fungi that cause the group of infections known as zygomycosis. The infection typically involves the rhino-facial-cranial area, lungs, GI tract, skin, or less commonly other organ systems. CDC/Dr. Lucille K. Georg



Figure 16

Conidia: phialoconidia of *Aspergillus fumigatus* CDC

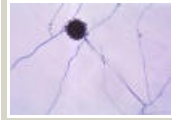


Figure 17

This photomicrograph shows the conidial head of an *Aspergillus niger* fungus. Conidial heads of *Aspergillus niger* are large, globose, and dark brown, and contain the fungal spores, facilitating propagation of the organism. This is one of the most common species associated with invasive "pulmonary aspergillosis".
 CDC/Dr. Lucille K. Georg

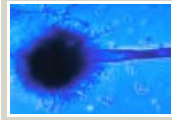


Figure 18

This photomicrograph depicts the appearance of a conidiophore of the fungus *Aspergillus flavus*. *Aspergillus spp.* are filamentous, cosmopolitan and ubiquitous fungi found in nature, are commonly isolated from soil, plant debris, and indoor air environments, and are the most commonly isolated filamentous fungi in invasive infections. CDC/Dr. Libero Ajello

ASPERGILLOSIS

Aspergilli produce a wide variety of diseases. Like the zygomycetes, they are ubiquitous in nature and play a significant role in the degradation of plant material as in composting. Similar to *Candida* and the Zygomycetes, they rarely infect a normal host. The organism is distributed world-wide and is commonly found in soil, food, paint, air vents. They can even grow in disinfectant. There are more than one hundred species of aspergilli. The most common etiologic agents of aspergillosis in the United States:

- *Aspergillus fumigatus* (figure 16)
- *Aspergillus niger* (figure 17)
- *Aspergillus flavus* (figure 18)

There are three clinical types of pulmonary aspergillosis:

- Allergic hypersensitivity to the organism. Symptoms may vary from mild respiratory distress to alveolar fibrosis.
- Aggressive tissue invasion. Aspergillosis is primarily a pulmonary disease, but the aspergilli may disseminate to any organ. They may cause endocarditis, osteomyelitis, otomycosis and cutaneous lesions.
- Fungus ball which is characteristically seen in the old cavities of TB patients. This is easily recognized by x-ray (figure 19), because the lesion (actually a colony of mold growing in the cavity) is shaped like a half-moon (semi-lunar growth). The patients may cough up the fungus elements because the organism frequently invades the bronchus. Chains of conidia can sometimes be seen in the sputum.

Culture

Aspergilli require 1-3 weeks for growth. the colony begins as a dense white mycelium which later assumes a variety of colors, according to species, based on the color of the conidia. The hyphae are branching and septate. Species differentiation is based on the formation of spores as well as their color, shape and texture.

Histopathology

The septate hyphae are wide and form dichotomous branching, i.e., a single hypha branches into two even hyphae, and then the mycelium continues branching in this fashion (figure 20).

Serology

There is an excellent serological test for aspergillosis which is an Immunodiffusion test. There may be 1 to 5 precipitin bands. Three or more bands usually indicate increasingly severity of the disease. i.e., tissue invasion.

Treatment

Voriconazole and Amphotericin B.

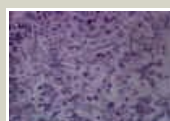


Figure 19

This chest radiograph shows probable aspergillosis with an aspergilloma, or fungus ball in the upper lobe of the right lung. Lung diseases that damage a lung can cause cavities that can leave a person more susceptible to developing an aspergilloma, or fungus ball. The fungus can then begin secreting toxic and



Aspergillosis. Human mouth. Gomori's silver methenamine stain © Bristol Biomedical Image Archive. Used with permission



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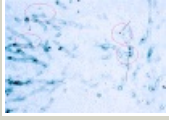
Lung: *Aspergillus* hyphae in fungal pneumonia © Bristol Biomedical Image Archive. Used with



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Fungal granulomas in lung caused by *Aspergillus fumigatus* © Bristol Biomedical

allergic products, which
may make the person feel
ill. CDC/M. Renz



Figure

20

Branching of aspergillus
hyphae
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Aspergillus pneumonia in lung of deer © Bristol Biomedical Image Archive. Used with permission



Nasal aspergillosis © Bristol Biomedical Image Archive. Used with permission



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