



Mucormycosis

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ABSTRACT

Mucormycosis is an angio invasive infection that occurs due to the fungi mucorales. It is a rare disease but increasingly recognized in immunocompromised patients. It can be categorized into rhino-orbito-cerebral, cutaneous, disseminated, gastrointestinal, and pulmonary types. Overall increased mortality rate is reported, even though the aggressive treatment is given. The main aim and purpose of this review related to overview and Etiopathogenesis of Mucormycosis, fatality of rhinocerebral Mucormycosis, recent advances in diagnostic and treatment methods.

KEYWORDS: Mucormycosis, mucorales, rhino-orbito-cerebral

INTRODUCTION

A rare but serious fungal infection, known as mucormycosis and colloquially as “black fungus”, is being detected relatively frequently among Covid-19 patients in some states. The disease often manifests in the skin and also affects the lungs and the brain. With a number of mucormycosis cases detected in Delhi, Maharashtra and Gujarat, experts in the national Covid-19 task force on Sunday issued an evidence based advisory on the disease.

Definition

Mucormycosis is a rare but often fatal disease caused by certain fungi. It is sometimes called zygomycosis or phycomycosis Mucormycosis is an opportunistic infection that typically develops in patients with weakened immune systems, diabetes,kidney failure, organ transplants, or chemotherapy for cancer. It may also develop in patients receiving an iron chelating drug called desferrioxamine (Desferal) as treatment for acute iron poisoning.



INCIDENCE

- The incidence rate of mucormycosis globally varies from 0.005 to 1.7 per million population.
- In India, prevalence of mucormycosis is estimated as 140 per million population, which is about 80 times higher than the prevalence in developed countries.
- More than 4,300 people have died of the deadly "black fungus" in India in a growing epidemic that mainly affects Covid-19 patients.
- India has reported 45,374 cases of this rare and dangerous infection, called mucormycosis, Health Minister Mansukh Mandaviya has said.
- The two worst-affected states are Maharashtra and Gujarat, where 1,785 people have died from mucormycosis.

CAUSES

Although rare, it is a serious infection. It is caused by a group of moulds known as mucormycetes present naturally in the environment. It mainly affects people who are on medication for health problems that reduces their ability to fight environmental pathogens, say experts from the Covid-19 task force task force.

Sinuses or lungs of such individuals get affected after they inhale fungal spores from the air. Doctors in some states have noted a rise in cases of mucormycosis among people hospitalized or recovering from Covid 19, with some requiring urgent surgery. Usually, mucormycetes does not pose a major threat to those with a healthy immune system.

Mucormycosis is caused by exposure to mucormyete molds. These organisms occur in:

- Leaves
- Piles of compost
- Soil
- Rotting wood

You can contract mucormycosis by breathing in affected mold spores in the air. This is referred to as a sinus (pulmonary) exposure. In turn, you may develop the infection in your:

central nervous system (rarer)

- Eyes
- Face
- Lungs
- Sinuses

The fungus can also infect your skin via a cut or burn (cutaneous exposure). In such cases, the wound or burn ends up becoming the area of infection.

While these types of molds can naturally occur in the environment, not everyone exposed will get the fungal infection. You may be at an increased risk of contracting this type of infection if you have a weakened immune system. Conditions that may increase your risk include:

- Burns
- Cuts and scrapes
- Cancer
- Recent organ transplant
- HIV or AIDS
- Diabetes (especially if it's not being treated properly)
- Surgery

PATHOPHYSIOLOGY

Pathogenesis

Agents

- Fungi of the order Mucorales (class Zygomycetes) are causes of mucormycosis, a life-threatening fungal infection affecting immunocompromised hosts (transplant recipients, diabetics, leukopenic, acidotic patients and patients on dialysis who receive deferoxamine- an iron chelator) in either developing or industrialized countries.
- Species belonging to the family Mucoraceae are isolated more frequently from patients with mucormycosis.
- Among the Mucoraceae, *Rhizopus oryzae* (*Rhizopus arrhizus*) is by far the most common cause of infection. Increasing cases of mucormycosis have been also reported due to infection with *Cunninghamella* spp.

Transmission

- The skin represents a major barrier to fungi causing mucormycosis. The agents of mucormycosis are typically incapable of penetrating intact skin.
- However, burns, traumatic disruption of the skin or implantation of contaminated soil or water, and persistent maceration of skin enables the organism to penetrate into deeper tissues and cause infection.
- In addition, contaminated surgical dressings and nonsterile adhesive tape have been shown to be the source of primary cutaneous mucormycosis.
- Ingestion is the mechanism of transmission for gastrointestinal mucormycosis.
- Inhalation of Mucorales sporangiospores by immunocompromised patients leads to development of pulmonary mucormycosis and eventual hematogenous dissemination.

Mechanism

- Neutrophils play a major part in destroying fungal hyphae, once spores germinate.
- Macrophages and monocytes also play part in host defense mechanisms against fungi causing mucormycosis (specifically alveolar macrophages prevent germination of spores).
- Consequently, mucormycosis develops exclusively in immunocompromised patients who lack these defense mechanisms.
- Hyperglycemia, acidosis and corticosteroid treatment have also been known to hinder immunity (specifically the actions of phagocytic cells), which also puts patients with diabetes and DKA at an increased risk of acquiring mucormycosis.
- In order to cause disease, the agents of mucormycosis must acquire from the host sufficient iron for growth, must evade host phagocytic defense mechanisms, and must access vasculature to disseminate.
- In immunocompromised hosts (including diabetics), iron is released from sequestering proteins making it available to fungi for growth within the body.
- Acidotic conditions decrease the iron-binding capacity, suggesting that acidosis per se disrupts the capacity of transferrin to bind iron, probably by proton-mediated displacement of ferric iron from transferrin.
- Fungi can obtain iron from the host by using high-affinity iron permeases or low-molecular-weight iron chelators (siderophores).
- This process along with a reduced number of neutrophils and phagocytes leads to fungal proliferation.
- Damage to the endothelial cells by fungi causing mucormycosis leads to vascular invasion, subsequent dissemination and tissue necrosis.
- *R. oryzae* spores but not germlings (i.e., pregerminated spores) have the ability to attach themselves to subendothelial matrix proteins including laminin and type IV collagen.
- Glucose regulated protein 78 (GRP78) serves as a receptor that promotes the ability of Mucorales to penetrate endothelial cells.

- Increased concentrations of glucose and iron, consistent with those seen during diabetic ketoacidosis, increase GRP78 expression and resulting invasion and damage of endothelial cells in a receptor-mediated manner. These findings likely explain the unique susceptibility of diabetic ketoacidosis to mucormycosis.

Gross Pathology

- The lesions in cutaneous or rhinocerebral mucormycosis appear varied in size, and ranging from raised red nodules or plaques, which sometimes produce purulent material, to ulcerated lesions with central cavitation, red exuding centres and raised epidermal margins.
- Older lesions may be covered either partly or fully by thickened and irregular epidermis. There may be a black eschar indicating necrosis and ischemia.

Microscopic Pathology

- Histological examination of skin biopsies reveal discrete, poorly encapsulated granulomas, or more commonly a diffuse granulomatous or pyogranulomatous inflammation. Inflammatory infiltrate consists of neutrophils or eosinophils, few plasma cells and lymphocytes, numerous macrophages and occasional multinucleated giant cells. Fibrovascular tissue is diffusely and irregularly scattered in the granulomatous areas.
- Nonpigmented, wide (5- to 20- μ m), thin-walled, ribbon-like hyphae with few septations (pauciseptate) and right-angle branching
- In lesions exposed to air, thick-walled spherical structures can form at the ends of the hyphae.

SIGNS AND SYMPTOMS

Mucormycosis presents itself as either a respiratory or a skin infection. Signs of a related sinus or respiratory infection may include:

- Cough
- Fever
- Headache
- Nasal congestion
- Sinus pain

With a skin infection, mucormycosis can develop within any part of your body. It may initially occur at the site of skin trauma, but it can quickly spread to another area. Be on the lookout for symptoms such as:

- Blackened skin tissue
- Blisters
- Fever
- Redness
- Swelling
- Tenderness
- Ulcers

DIAGNOSTIC EVALUATION

- Medical history
- Physical examination

Mucormycosis is diagnosed by looking at a tissue sample in the lab. Your doctor may collect a sample of phlegm or nasal discharge if you have a suspected sinus infection. In the case of a skin infection, your doctor may also clean the wounded area in question.

It depends on the location of the suspected infection. A sample of fluid from your respiratory system may be collected for testing in the lab; otherwise a tissue biopsy or a CT scan of your lungs, sinuses etc may be conducted.

MANAGEMENT OF MUCORMYCOSIS

The first steps in treating mucormycosis are receiving intravenous (IV) antifungal medications and having surgical debridement. Surgical debridement involves cutting away all infected tissue. Removing infected tissue has been shown to prevent the infection from spreading further.

Common antifungal medications that your doctor may prescribe for mucormycosis include:

- Amphotericin B (given through an IV)
- Posaconazole (given through an IV or orally)
- Isavuconazole (given through an IV or orally)

What is the outlook for mucormycosis?

Chances for mucormycosis recovery depend greatly on early diagnosis and treatment. The infection has the potential to spread throughout the body. Death is a possibility with this type of severe infection.

However, mucormycosis is relatively rare. To be on the safe side, you should always have your doctor evaluate any suspected form of infection to rule out such serious underlying causes.

DISEASE PREVENTION

Prevention of COVID-associated mucormycosis needs to focus on addressing the underlying risk factors:

- aiming for better glycemic control in those with diabetes,
- appropriate use of systemic corticosteroids and
- prevention of unnecessary use of antibiotic, antifungal and other immunomodulators.

IPC measures at the facility level are essential to prevent the environmental spread of this pathogen. These include:

- sterilization and disinfection of the equipment used by multiple patients (tracheal tubes, ventilators), ventilation systems (if there is poor ventilation in the hospital that can contribute to dampness and dust);
- proper wound management (bandage, tape, adhesives, including tapes to secure medical devices such as endotracheal tubes, ostomy devices must be sterilized and changed regularly);
- proper line management in health facilities

What happens when one contracts it?

Warning signs include pain and redness around the eyes or nose, with fever, headache, coughing, shortness of breath, bloody vomits, and altered mental status. According to the advisory, infection with mucormycetes should be suspected when there is:

- * Sinusitis — nasal blockade or congestion, nasal discharge (blackish/bloody);
- * Local pain on the cheek bone, one-sided facial pain, numbness or swelling;
- * Blackish discoloration over bridge of nose/palate;
- * Loosening of teeth, jaw involvement;
- * Blurred or double vision with pain;
- * Thrombosis, necrosis, skin lesion;
- * Chest pain, pleural effusion, worsening of respiratory symptoms.

COMPLICATIONS

- Blindness
- Blood clots or blocked vessels
- Nerve damage

Mucormycosis can be deadly without treatment. Because the infection is so rare, the exact mortality rate isn't clear. But researchers estimate that overall, 54% of people with mucormycosis die.

The likelihood of death depends on which part of the body is affected. The outlook is better for people who have sinus infections than it is for lung or brain infections.

CONCLUSION

Mucormycosis is a highly invasive and rapidly progressing form of fungal infection that can be fatal. Although rare, indolent disease course of this infection has been reported.

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