

Different Complication of Black Fungus and Its Treatment: A Review

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ABSTRACT

In recent years, substantial advances have been achieved in the treatment of Mucormycosis. It is now clear that early initiation of therapy results in substantially better outcomes, underscoring the need to maintain a high index of suspicion and aggressively biopsy potential lesions. Increasing data support the need for surgical excision of infected and/or necrosed tissue whenever feasible. Based on their superior safety and efficacy, lipid formulations of amphotericin B have become the standard treatment for Mucormycosis. Posaconazole may be useful as salvage therapy, but cannot be recommended as primary therapy for Mucormycosis based on available data. Pre-clinical and limited retrospective clinical data suggest that combination therapy with lipid formulations of amphotericin and an echinocandin improves survival during Mucormycosis.

Keywords: Mucormycosis, Amphotericin, Liposomal amphotericin, Amphotericin B lipid complex, Posaconazole, Echinocandins, Deferasirox

INTRODUCTION

What is Black fungus infection(Mucormycosis)

Black fungus, also known as Mucormycosis, is a rare but dangerous infection. Black fungus is caused by getting into contact with fungus spores in the environment. It can also form in the skin after the fungus enters through a cut, scrape, burn, or another type of skin trauma. ⁽¹⁾

Fungi live in the environment, particularly in soil and decaying organic matter such as leaves, compost piles, rotten wood, and so on. This fungal infection is caused by a type of mould known as 'mucromycetes'. It should be noted that this rare fungal infection affects persons who have health issues or who use drugs that weaken the body's ability to fight the infections ⁽²⁾.

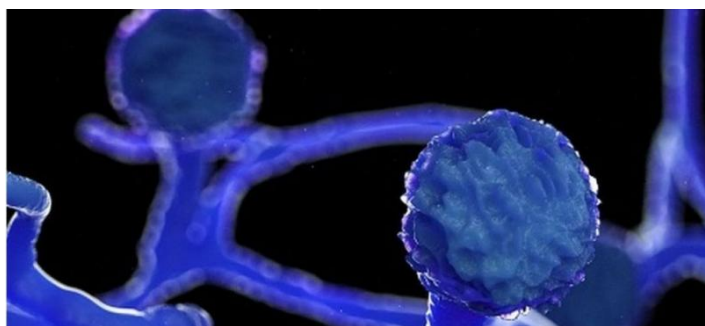


Figure 1: Black Fungus

Black Fungus Causes:

Mucormycetes are a type of mould that causes fungal infections. These moulds can be found everywhere in the environment, including soil, air, and food. They enter the body via the nose, mouth, or eyes and can have an impact on the brain if it is not treated on time^(3,4,5). According to medical experts, the main cause of black fungus (Mucormycosis) is steroid misuse during COVID treatment. Black fungus (Mucormycosis) primarily affects people who have health problems or who take medications that reduce the body's ability to fight germs and illness. The person's immunity is low after covid treatment, which makes them vulnerable to black fungus infection. People with diabetes and COVID-19 patients are at greater risk of developing an infection.

Black Fungus Symptoms:

The symptoms of black fungus will vary depending on where the fungus is growing in your body. They may include the following^(6,7)

- Fever
- Cough
- Chest pain
- Shortness of breath
- Swelling on one side of your face
- Headache
- Sinus congestion
- Black lesions on the top of the nose or the inside of the mouth
- Belly pain
- Nausea and vomiting
- Gastrointestinal bleeding
- Blood in your stool
- Diarrhea

If your skin is infected, the affected area may appear blistered, red, or swollen. It may turn black, feel warm, or be painful. Through your blood, the infection can also spread to other parts of your body^(8,9). This is referred to as disseminated black fungus (Mucormycosis). When this occurs, the fungus can attack organs such as your spleen and heart. In severe cases, you may experience mental changes or fall into a coma. It can even be fatal.



Figure 2: Black fungus infection

Black Fungus Risks:

- People who fall into the following categories are more likely to develop black fungus:
- Uncontrolled diabetes, diabetic ketoacidosis, and diabetics taking steroids or tocilizumab^(10,11,12).
- Patients taking immune-suppressants or receiving anticancer treatment, as well as those suffering from a chronic debilitating illness
- Patients taking high doses of steroids or tocilizumab for an extended period
- Cases of COVID-19 Severity^(13,14)
- Patients on oxygen who required nasal prongs, a mask, or a ventilatory support

Black Fungus Treatment:

- Mucormycosis treatment must be fast and aggressive. The concern is due to the fact that by the time even a presumptive diagnosis is made, the patient has often suffered significant tissue damage which cannot be reversed^(13,14).
- Most patients will need surgical and medical treatment.
- Most infectious disease experts say that without aggressive surgical debridement of the infected area, the patient is likely to die.
- Medicines play an important role. Two main aims are sought simultaneously: antifungal drugs to slow or stop the fungal spread and drugs to treat debilitating underlying diseases^(15,16)
- Amphotericin B (initially intravenous) is the usual drug of choice for antifungal therapy.
- Posaconazole or isavuconazole can treat Mucormycosis.
- Patients may even require an intravenous antifungal procedure lasting 4 -6 weeks.
- Patients with underlying diseases like diabetes need to be in optimal control of their diabetes.
- Patients normally on steroids or taking deferoxamine (Desferal; used to remove excess iron from the body) are likely to have these drugs stopped because they can increase the survival of fungi in the body^(17,18)
- Patients may need additional surgeries and usually need antifungal treatment for an extended period (weeks to months) depending on the severity of the disease.

Black Fungus Preventions:

Preventive measures to be followed:

- Humidifier cleaning and replacement (for those using Oxygen Concentrators)
- The humidifier bottle should be sterilized with normal saline and refilled on a regular basis^(19,20,21)
- Masks should be disinfected regularly, and they should not be used for weeks.
- Those who use steroids should also monitor their blood sugar levels.
- During the COVID-19 therapy, mortified oxygen should be utilized
- Practicing good hygiene and maintaining the cleanliness of their surroundings
- Brushing and gargling daily is extremely beneficial.
- If you have recovered from COVID, it is critical to wear masks to prevent the infection from entering the body⁽²²⁾
- Diabetics patients must keep their diabetes under control and monitor their blood glucose levels
- These must be monitored, especially after infection with Covid-19. Steroid use is to be reduced, and immune modulating drugs are to be discontinued.

Diagnosis^(23,24):

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.

Drug Profile:

Amphotericin B is an antifungal medication used for serious fungal infections and leishmaniasis. The fungal infections it is used to treat include mucormycosis, aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, and cryptococcosis. For certain infections it is given with flucytosine⁽²⁵⁻²⁸⁾ It is typically given by injection into a vein.

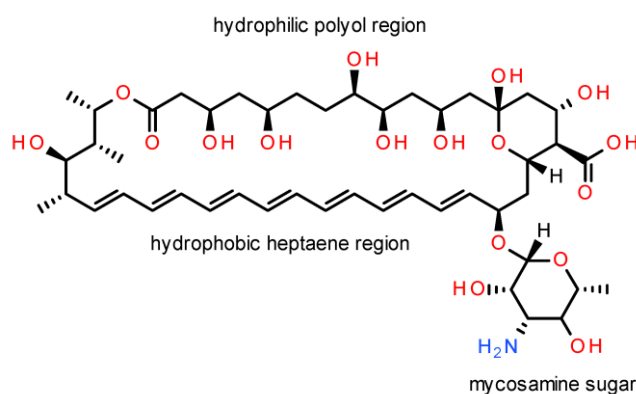


Figure 3: Structure of Amphotericin B

Background:

Amphotericin B shows a high order of in vitro activity against many species of fungi. *Histoplasma capsulatum*, *Coccidioides immitis*, *Candida* species, *Blastomyces dermatitidis*, *Rhodotorula*, *Cryptococcus neoformans*, *Sporothrix schenckii*, *Mucormyces*, and *Aspergillus fumigatus* are all inhibited by concentrations of amphotericin B ranging from 0.03 to 1.0 mcg/mL in vitro⁽²⁹⁻³⁰⁾. While *Candida albicans* is generally quite susceptible to amphotericin B, non-*albicans* species may be less susceptible. *Pseudallescheria boydii* and *Fusarium* sp. are often resistant to amphotericin B.

Mechanism of action:

Amphotericin B is fungistatic or fungicidal depending on the concentration obtained in body fluids and the susceptibility of the fungus. The drug acts by binding to sterols (ergosterol) in the cell membrane of susceptible fungi. This creates a Trans membrane channel, and the resultant change in membrane permeability allowing leakage of intracellular components. Ergosterol, the principal sterol in the fungal cytoplasmic membrane, is the target site of action of amphotericin B and the azoles. Amphotericin B, a polyene, binds irreversibly to ergosterol, resulting in disruption of membrane integrity and ultimately cell death⁽³¹⁻³³⁾

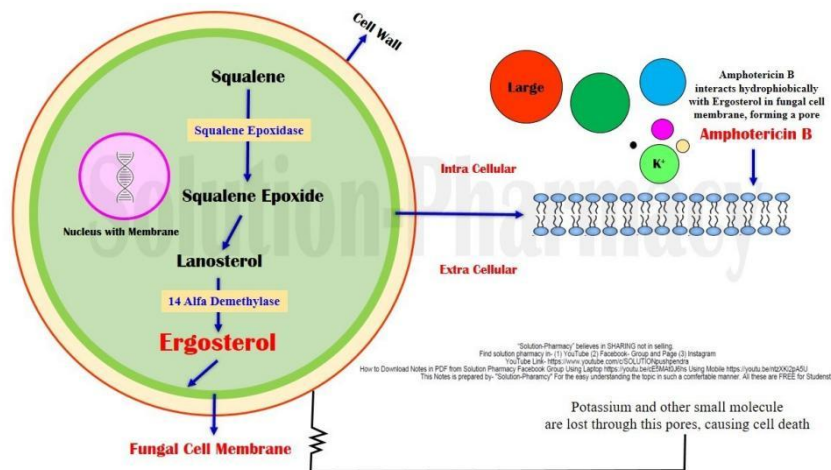


Figure 4: Mechanism of action of Amphotericin B

CONCLUSION

Amphotericin B is generally considered cidal against susceptible fungi at clinically relevant concentrations. Despite the introduction of newer antifungal agents for the treatment of systemic mycoses, amphotericin B remains the standard treatment for many severe, invasive fungal infections.



'BLACK FUNGUS' IN COVID-19 PATIENTS

Mucormycosis (previously zygomycosis), a rare but serious fungal infection, is affecting some COVID-19 patients. The disease manifests in the skin, affects lungs and brain, and can lead to loss of the upper jaw or eye. It's been declared a notified disease in Haryana, the national COVID-19 task force has issued an advisory, and the Union health ministry has asked states/UTs to declare Black Fungus as an epidemic



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