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Mucormycosis the Black Fungus

Jinu Manoj[1] and M.K. Singh[2]
[1]Assistant Disease Investigation Officer
College Central Laboratory, College of Veterinary Sciences
Lala Lajpat Rai University of Veterinary & Animal Sciences, Hisar, Haryana, INDIA
[2]Assistant Professor, Department LPM
College of Veterinary and Animal Sciences, SVPUAT, Meerut.

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Introduction

Mucormycosis is a fatal but rare fungal infection caused by a group of molds called mucormycetes. They are filamentous molds within the order *Mucorales and* Class Zygomycetes. They were previously known as zygomycosis or Phycomycosis. Phycomycosis or zygomycosis was first described in 1885 by Paltauf and later coined as Mucormycosis in 1957 by Baker, an American pathologist for an aggressive infection caused by *Rhizopus*. It is an angioinvasive disease caused by molds of the genus *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella bertholletiae*, *Syncephalastrum*, *Apophysomyces* and *Lichtheimia (*formerly *Absidia)* species. They live throughout the environment particularly in soil and in decaying organic matter, such as leaves, compost piles, or rotten wood. Mucormycosis mainly affects people who have health problems or patients with altered immunity. Infections may result from ingestion of contaminated food, inhalation of spores into the nares or lungs, or inoculation into disrupted skin or wounds. It most commonly affects the sinuses or the lungs following inhalation of fungal spores from the air.

Types of mucormycosis

Based on anatomic localization, mucormycosis can be classified as one of six forms:

1. **Rhino orbital cerebral (sinus and brain) mucormycosis** is an infection in the sinuses that can spread to the brain. This form of mucormycosis is most common clinical presentation and found in people with uncontrolled diabetes and in people who have had a kidney transplant.
2. **Pulmonary (lung) mucormycosis** is the most common type of mucormycosis in people with cancer and in people who have had an organ transplant or a stem cell transplant

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3. **Gastrointestinal mucormycosis** is more common among young children than adults, especially premature and low birth weight infants less than 1 month of age, who have had antibiotics, surgery, or medications that lower the body's ability to fight germs and sickness.
4. **Cutaneous (skin) mucormycosis**: occurs after the fungi enter the body through a break in the skin (for example, after surgery, a burn, or other type of skin trauma). This is the most common form of mucormycosis among people who do not have weakened immune systems.
5. **Disseminated mucormycosis** occurs when the infection spreads through the bloodstream to affect another part of the body. The infection most commonly affects the brain, but also can affect other organs such as the spleen, heart, and skin.
6. **Mucormycosis of uncommon sites**.

   Mucormycosis exhibits a marked propensity to invade blood vessels, leading to thrombosis, necrosis, and infarction of tissue. Mortality associated with invasive mucormycosis is high (>30-50%), with 90% mortality associated with disseminated disease. Mortality rates are much lower, though still significant (10-30%), among patients with localized cutaneous disease. In developed countries, mucormycosis occurs primarily in severely immunocompromised hosts. In contrast, in developing countries, most cases of mucormycosis occur in persons with poorly controlled diabetes mellitus or in immunocompetent subjects following trauma.

Black fungus and COVID-19

India has highest cases of the mucormycosis in the world. Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million populations, while its prevalence is nearly 80 times higher in India compared to developed countries. Diabetes mellitus has been the most common risk factor linked with mucormycosis in India, although hematological malignancies and organ transplant takes the lead in Europe and the USA.

Many people recovering from COVID-19 had been afflicted by black fungus or mucormycosis disease. When a patient whose immune system has been compromised inhales Mucor spores, they may develop mucormycosis. The fungus invades the sinus and makes its way into the intraorbital and intracranial regions. When Mucor attacks the sinuses, it spreads to the lungs, the brain and the central nervous system. Common symptoms of the resulting

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mucormycosis include fever, headache, reddish and swollen skin near the nose or eyes, facial pain, cough producing bloody or dark fluids, and shortness of breath. This is a non-contagious disease having an overall mortality rate of 50%, but can be debilitating or fatal if not treated quickly. People suffering from COVID-19, HIV/AIDS and other viral diseases, congenital bone marrow disease, severe burns, cancers and untreated or irregularly treated diabetes, organ transplantation have reduced immunity and are prone to developing mucormycosis.

The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background co morbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators.

COVID-19 patients who have received steroids are particularly at risk of mucormycosis because steroids suppress the immune system. Steroids reduce inflammation in the lungs for COVID-19 and appear to help stop some of the damage that can happen when the body's immune system goes into overdrive to fight off coronavirus. But they also reduce immunity and push up blood sugar levels in both diabetics and non-diabetic COVID-19 patients.

Increase in mucormycosis in Indian context appears to be due to combination of three factors *viz*. diabetes (high prevalence genetically), rampant use of corticosteroid (increases blood glucose and opportunistic fungal infection) and COVID-19 (cytokine storm, lymphopenia, endothelial damage).

Diagnosis and Treatment

The rapidity of dissemination of mucormycosis is an extraordinary phenomenon and even a delay of 12 h in the diagnosis could be fatal. Mucormycosis can progress rapidly and delay in diagnosis and initiation of treatment by even a few days markedly worsens outcomes. The diagnosis of mucormycosis relies upon histopathology and culture. Blood tests are of limited diagnostic value. Even with disseminated disease, blood cultures are

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usually negative. Mucorales have a distinct histological appearance, with irregular, nonseptate hyphae that branch at right angles. Cultures and/or polymerase chain reaction (PCR) are important to identify the genera. Lipid formulations of amphotericin B are the mainstay of therapy, but the newer triazoles, posaconazole and isavuconazole may be effective in patient's refractory to or intolerant of amphotericin B. Early surgical debridement or excision plays an important adjunctive role.

Prevention

It is difficult to avoid breathing in of fungal spores because the fungi are common in the environment. There is no vaccine to prevent mucormycosis. For people who have weakened immune systems, there may be some ways to lower the chances of developing mucormycosis by protective measures like avoiding environmental exposures and by the use of antifungal medication.