WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 11, 1290-1301. Review Article ISSN 2277– 7105

A SHORT REVIEW ON MUCORMYCOSIS

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Article Received on
15 July 2021,

Revised on 04 August 2021,
Accepted on 25 August 2021

DOI: 10.20959/wjpr202111-21595

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ABSTRACT

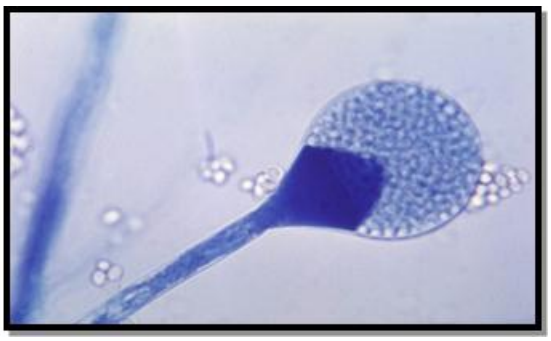
Due to the current COVID – 19[1] situation, the word Mucormycosis[2] is falling on everyone's ears. So, here we will look at exactly what is Mucormycosis ? And how it happens ? Symptoms of Mucormycosis. In Mythology, gods were cursed by sages, sometimes humans were cursed by gods, sometimes Gandharvas and Apsaras were cursed and then cursed. Let those cursed people be freed because of those curses. Mankind todays is cursed with the corona virus. Fungal infections, including mucormycosis, aspergillosis and invasive candidiasis, have been reported in patients with severe COVID-19 or those recovering from the disease and have been associated with severe illness and death. India has reported a recent surge in mucormycosis cases. Mucormycosis is a highly aggressive fungal infection affecting diabetic[4], immuno-compromised[5], and, occasionally, healthy patients. This infection is associated with significant mortality. 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[3][31], cutaneous[30], disseminated, gastrointestinal, and pulmonary types.[22] 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 and recent advances in diagnostic and treatment methods.[33]

KEYWORDS: COVID-19, Rhino-orbito-cerebral mucormycosis, Diabetes mellitus, Immunocompromise.

INTRODUCTION

American pathologist R.D. Baker coined the term Mucormycosis. It is also known as Zygomycosis[6][20] It can be defined as an insidious fungal infection caused by members of Mucorales and zygomycotic species. Mucormycotina[7] are the common saprobes originating from the rotten matter or soils. Infections with Mucorales are categorized by rapid progression. Mucormycosis is a fungal infection caused by certain types of mold. These molds are known as mucormycetes.[8] They are found throughout nature (ubiquitous) and can be found in the soil and decaying organic matter like decaying vegetation.

[Image source-[35]].



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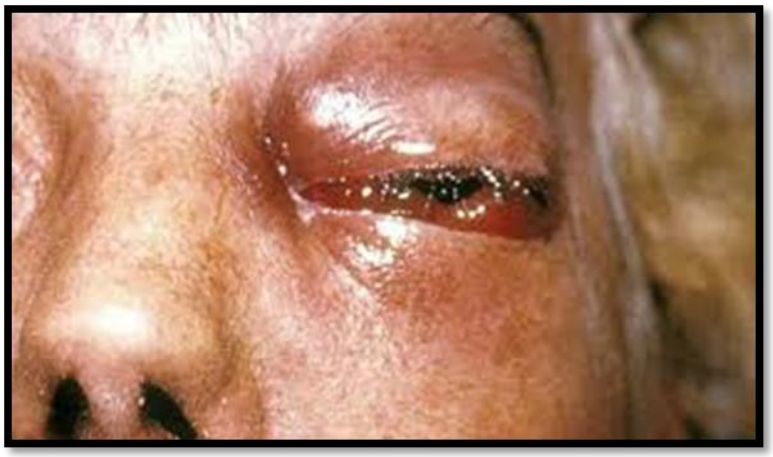
MUCORMYCOSIS

Mucormycosis is a systemic fungal infection caused by members of the class Zygomycetes, order Mucorales[9] It is seen in patients debilitated by immune or metabolic disorders.

The class Zygomycetes[10] consists of aseptate hyaline molds that reproduce by both sexual and asexual means. These fungi are ubiquitous in soil and decaying vegetation. Five genera in the order Mucorales are responsible for disease in humans: Rhizopus, Mucor, Absidia, and rarely, Saksenaea and Cunninghamella.

Julie Djordjevic, head of the fungal pathogenesis group at the Westmead Institute for Medical Research, described the fungi as "nature's decayer". It mainly affects people who are on medication for health problems that reduces their ability to fight environmental pathogens. Sinuses or lungs of such individuals get affected after they inhale fungal spores from the air. It may also affect brain, skin and kidneys. People can get sick if they breathe in or eat some types of spores from the environment, but they can also enter the body through a cut or broken skin. They're very effective at replicating themselves. They make spores which are very airborne and they can produce billions of them. It affects the sinuses, the brain and the

lungs and can be life-threatening in diabetic or severely immunocompromised individuals, such as cancer patients or people with HIV/AIDS.[11]



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HISTORY

In 1885, the German pathologist Paltauf, reported the first case of Mucormycosis and described it as Mycosis Mucorina.[12] During 1980s and 1990s Mucormycosis was increasingly seen among immuno compromised individuals. Based on the prevalence rate, a study carried out in France reported amplification by 7.4% per year. Worldwide occurrence along with the possibility of seasonal variation of mucorales infection has been reported.

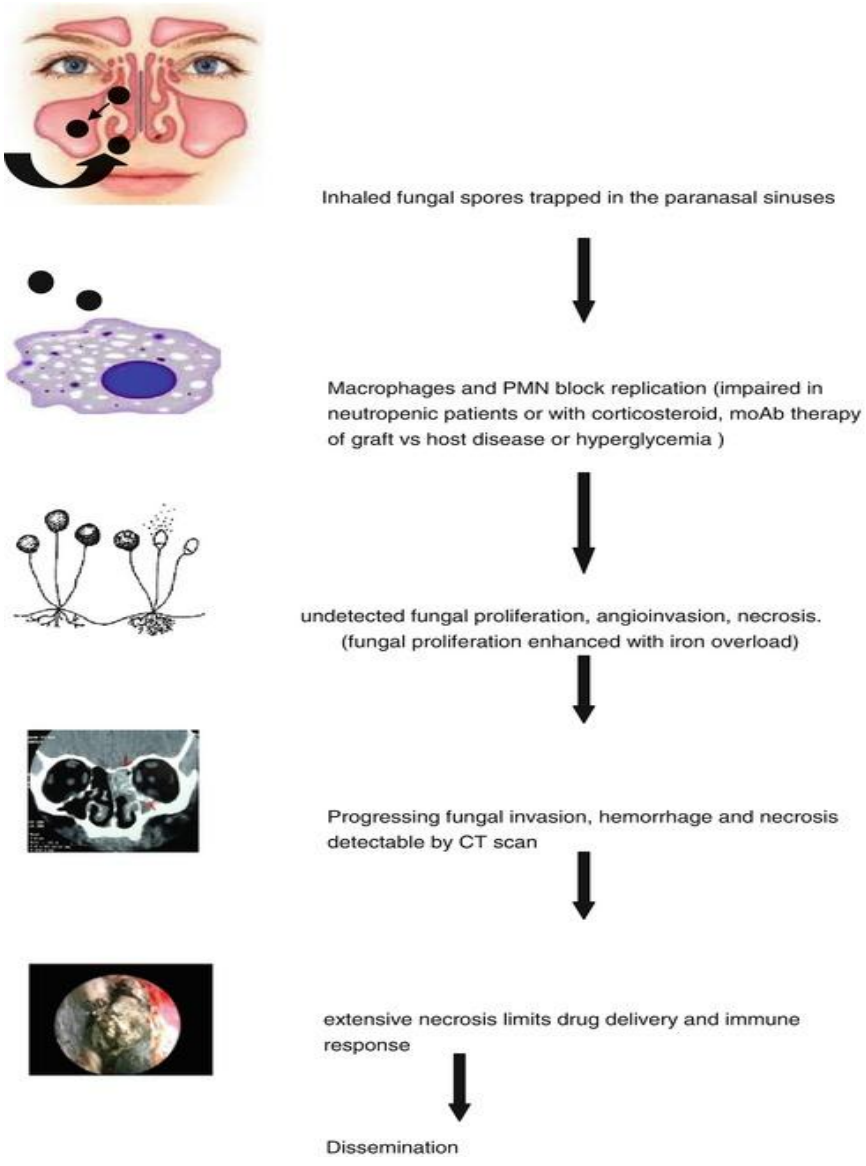
ETIOPATHOGENESIS

Mucorales[9] attack deep tissues by means of ingestion or inhalation of spores, and percutaneous injection of spores. As soon as the spores penetrate into lung or cutaneous tissues, the first line of defence in the healthy host is capable of destroying the spores via oxidative metabolites and cationic peptides. Risk factors include uncontrolled diabetes mellitus, especially ketoacidosis, steroid use, extremes of age, neutropenia; especially with hematologic malignancy[14][26], AIDS[11], renal insufficiency[15], organ or stem cell transplantation, iron overload, skin trauma, broad-spectrum antibiotics, intravenous drug abuse, prophylactic voriconazole for aspergillosis and malnutrition.

In diabetic patients, mucormycosis occurs as a destructive and potentially critical condition due to augmented availability of micronutrients and diminished defence mechanism of the body.Various hypotheses include (i) Low serum inhibitory activity against Rhizopus species.(iii)Improved availability of iron for the pathogen at decreased PH level and (iii)

Pulmonary macrophages of persons with diabetes mellitus show diminished facility to inhibit germination of Rhizopus species. Ketone reductase innRhizopus allows the organism to increase the glucose and acidic environment.

In DM particularly with ketoacidosisall types of mucormycosis will occur. Neutrophils play a major role in host defence against mucorales. Its function is impaired at different level in DM. Ketoacidosis in diabetes accelerate the fungal invasion. The acidic milieu produces more free iron by reducing its binding to transferrin and low level of dialyzable inhibitory factor in diabetics present suitable conditions for fungal duplication. Mortality rate was reported 90% or even more with Mucormycosis, before the administration of amphotericin B and radical surgery.[25]



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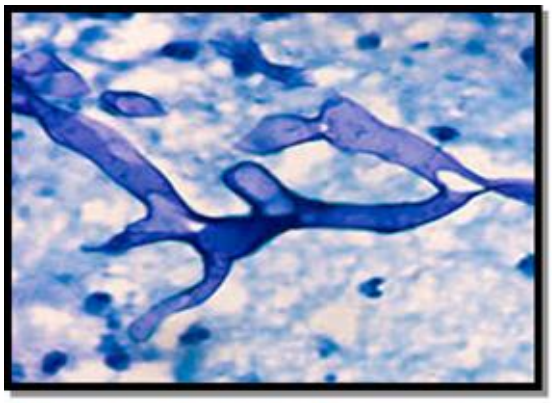
CAUSES

Black fungal infection is usually seen among Covid recovered patients with comorbidities such as diabetes or kidney, heart failure, or cancer. Use of steroids[17] in the treatment of Covid infection plus the fact that many Covid patients have diabetes as comorbidity could be one of the reasons for this rise in black fungus infection again. Covid patients with weak immunity are more prone to this deadly infection. According to medical experts, patients with weak immunity are usually more prone to mucormycosis.



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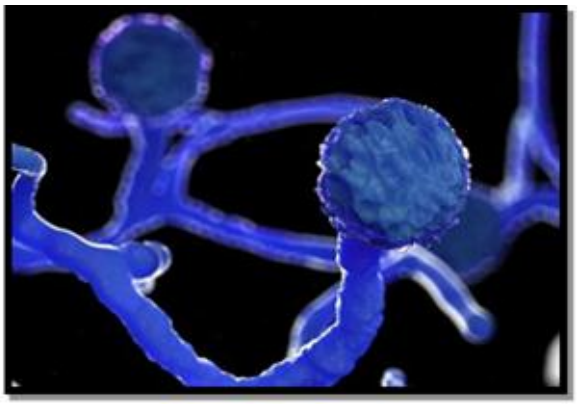

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- **MUCORMYCOSIS COMPLICATIONS AND OUTLOOK**

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.

❖ **Diagnosis**

Medical professionals diagnose mucormycosis with a medical history and physical exam. They may also take fluid or tissue samples send them to a lab. Other tests may include CT scan or MRI. There are no specific blood tests to detect mucormycosis.[32]

History, symptoms, physical examinations, and laboratory tests when diagnosing mucormycosis. Healthcare providers who suspect that you have mucormycosis in your lungs or sinuses might collect a sample of fluid from your respiratory system to send to a laboratory. Your healthcare provider may perform a tissue biopsy, in which a small sample of affected tissue is analyzed in a laboratory for evidence of mucormycosis under a microscope

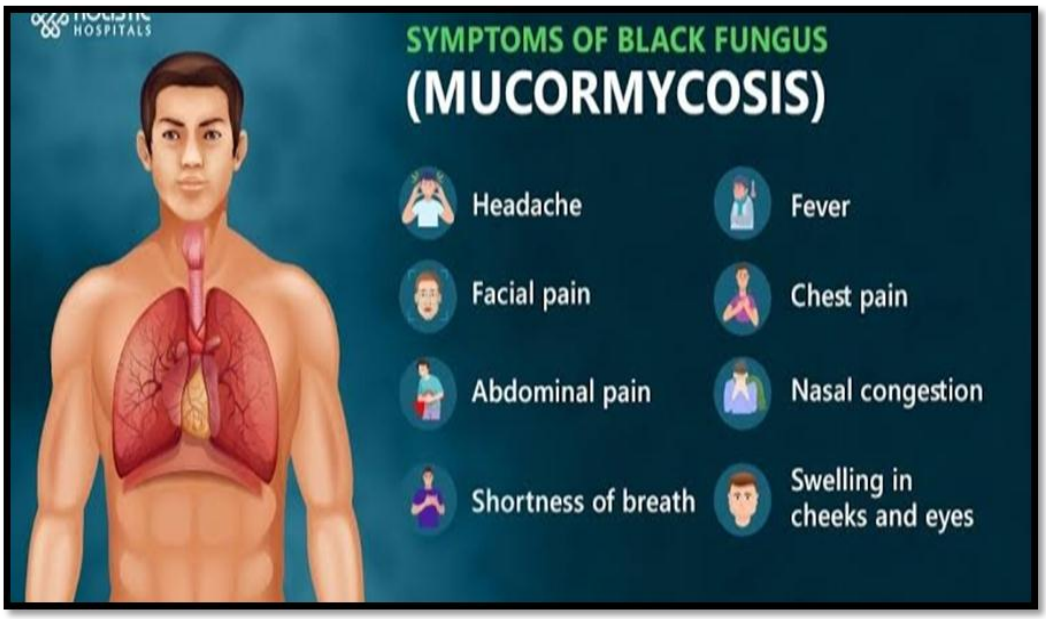
or in a fungal culture. You may also need imaging tests such as a CT scan of your lungs, sinuses, or other parts of your body, depending on the location of the suspected infection.[27]

Diagnosis and testing for Mucormycosis

Your healthcare provider may perform a tissue biopsy**,** in which a small sample of affected tissue is analyzed in a laboratory for evidence of mucormycosis under a microscope or in a fungal culture.

SYMPTOMS

Indications of mucormycosis include Sinusitis, along with clogging of the nasal tract and bloody or blackish mucus emission from the nose. Pain on only one side of the face, cheekbones, with lack of sensation and bulging. Distinct blackish discoloration on the bridge of the nose. Prominent aching in teeth, jawbone, degrading of tooth.structures. Hazy vision, with objects appearing blurred or in double, with eye pain. Abnormal blood clotting or thrombosis of tissues, along with skin injury and damage or necrosis of dermal cells. Further deterioration of respiratory functions, with chest pain, excess fluid build-up in lungs i.e.pleural effusion and coughing up blood or haemoptysis.



The symptoms of mucormycosis depend on where in the body the fungus is growing. The most common presentation is a sinus infection (sinusitis) that is accompanied by nasal congestion, nasal discharge, and sinus pain. A fever and headache may also occur.

Type of Mucormycosis	Some common symptoms
Rhinocerebral (sinus and brain) mucormycosis	• One-sided facial swelling • Headache • Nasal or sinus congestion • Black lesions on nasal bridge or upper inside of mouth that quickly become more severe • Fever • Lethargy, seizures, slurred speech, partial paralysis
Pulmonary (lung) mucormycosis	• Fever • Cough • Chest pain • Shortness of breath • Hemoptysis
Cutaneous (skin) mucormycosis	• Skin lesion that resembles blisters or ulcers. The infected area may turn black. Other symptoms include pain, warmth, excessive redness, or swelling around a wound.
Gastrointestinal mucormycosis	• Abdominal pain • Nausea and vomiting • Gastrointestinal bleeding
Disseminated mucormycosis	• Tends to occur in people who are already sick from other medical conditions, which makes it difficult to identify which symptoms are related to mucormycosis. Patients with disseminated infection in the brain may develop mental status changes or coma.

Treatment

According to our research this can be treated through two methods, first one through specific detox under an expert's guidance to completely remove the disease from its root cause and second is to boost the immune system through natural remedies.". Mucormycosis is a serious infection and needs to be treated with prescription antifungal medicine, usually amphotericin B, posaconazole, or isavuconazole. These medicines are given through a vein (amphotericin B, posaconazole, isavuconazole) or by mouth (posaconazole, isavuconazole)[28]. Other medicines, including fluconazole, voriconazole, and echinocandins, do not work against fungi that cause mucormycosis. Often, mucormycosis requires surgery to cut away the infected tissue.[24]

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 toprevent 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.[39]

- **Prognosis**

Mucormycosis has poor prognosis with a mortality rate of 17–51%.[10] Mortality is higher in case of diagnostic delay of more than five days and monocytopenia in patients with active malignant blood diseases. Surgical treatment associated with antifungals improves prognosis.[40]

Median treatment duration was 102 days for patients with primary mucormycosis, 33 days for those with refractory mucormycosis, and 85 days for those with intolerance to other antifungal therapy.[38]

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. Here, we described a very rare case of rhinocerebral mucormycosis with an indolent disease course. Absence of tissue necrosis is also an unusual feature of our case. Principles of management for mucormycosis include early disease diagnosis, reversal of predisposing conditions, and prompt surgical and antifungal management. In our case, diagnosis was delayed due to its unusual presentation as well as initial cultures showing bacterial infection in the presence of

abscesses. When diagnosis was made, appropriate medical management was initiated; however, the patient refused any surgical intervention. Improvement in the patient's symptoms was observed; however, resolution of the infection was not achieved at the time of writing this paper. Due to the rarity of mucormycosis, particularly the indolent presentation, knowledge and awareness of the disease is emphasized amongst physicians. The importance of early detection and appropriate management with surgical and antifungal combination therapy is also emphasized in our case.

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