

Mucormycosis or Black fungus affecting COVID-19 patients

Aarti Patidar¹, Nandu Kayande², Pankaj Kushwah³, Rekha Birle⁴ and Nandini Kushwah⁵

1, Dr. A. P. J. Abdul Kalam University Indore, (M.P.) - India

2, Thakur Shiv Kumar Singh Memorial Pharmacy College, Burhanpure, (M.P.) - India

Article info

Received: 12/06/2021

Revised: 26/07/2021

Accepted: 20/08/2021

© IJPLS

www.ijplsjournal.com

Abstract

Mucormycosis or black fungus infection is a rare but deadly disease with a 46–96% mortality rate depending on the underlying health condition of patients. This life-threatening new enemy has challenged the Indian healthcare system during the massive second wave of covid-19 pandemic. Mucormycosis caused by the mucorales group of fungi affecting various parts of the body. This opportunistic fungal infection progress rapidly. Recently, the covid patients in India are getting infected by this uncommon fungus at higher rates than ever. At present, the prevalence of this black fungus infection is skyrocketing among covid-19 and post-covid-19 patients in India]. Generally, black fungus affects the body surface and internal organs such as the sinus, brain, lungs, eyes, bones, nerves, body tissues and becomes fatal if left untreated. Usual signs of this disease are sinus pain, nasal blockage on one side of the face, swelling or numbness, one-sided headache, loosening of tooth and toothache, pain in the eyes, and more. The infected patients primarily suffer from eyelid loss, blindness, and blurred vision.

The diagnosis and treatment of mucormycosis are challenging. The incidence of the disease seems to be increasing. Mucormycosis is an angio invasive fungal infection, due to fungi of the order Mucorales. Its incidence cannot be measured exactly, since there are few population-based studies, but multiple studies have shown that it is increasing. Patients who have high levels of diabetes are at a higher risk of contracting covid-19. When this occurs, they are treated with steroids which compromise their immunity. According to doctors, steroids can prove to be a trigger for mucormycosis. While steroids help in reducing inflammation in lungs they can decrease immunity and increase blood sugar levels in both diabetics and non-diabetic covid-19 patients alike. The black fungus disease is an additional burden on the country that is already grappling with more cases and fatalities due to the second wave of the covid-19 pandemic.

Keywords: Black fungus, Covid-19, Amphotericin B, Steroid, Diabetic

Introduction

Mucormycosis is a fungal infection that mainly affects people who are on medication for other health problems that reduces their ability to fight environmental pathogens. Mucormycosis, commonly called black fungus, is a rare but serious fungal infection caused by a kind of fungus called mucormycete, which is

abundant in the environment. It mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness. It is being detected relatively frequently among Covid-19 patients in some states of India.

***Corresponding Author**

E.mail: rti.patidar@gmail.com

The disease often manifests in the skin and also affects the lungs and the brain. People who have been unwell with COVID-19 and are still recovering have a compromised immune system, which means they're more at risk because their body can't fight off the infection. Those who were hospitalized with severe COVID-19 disease were likely to be prescribed steroids for the reduction of infection. The steroid act by reducing the inflammation in the lungs and dampen the body's immune response in order to stop it attacking the body's healthy cells it leads to the decreased immune surveillance. Those patients were easily affected by means of mucormycete. While there is no major outbreak, the national Covid task force has issued an advisory regarding this disease. Mucormycosis caused by the mucorales group of fungi affecting various parts of the body. This opportunistic fungal infection progress rapidly. Recently, the covid patients in India are getting infected by this uncommon fungus at higher rates than ever. At present, the prevalence of this black fungus infection is skyrocketing among covid-19 and post-covid-19 patients in India. As of June 28, 2021, India recorded 28,252 mucormycosis cases. the 29th meeting of the high-level Group of Ministers (GoM) on Covid-19, Vardhan apprised the members that of the total number of black fungus infections, 34,940 patients had Covid (85.5 per cent), 26,187 (about 64.11 per cent) were co-morbid for diabetes, while 21,523 (52.69 percent) of those infected were on steroids.

A total of 13,083 patients were in the age group of 18-45 years (32 per cent), 17,464 were in the age group of 45-60 years (42 per cent), while 10,082 (24 per cent) patients were 60-plus years of age, a health ministry statement said.

Among them, 85.5% had a history of covid-19 and 64.11% had a history of diabetes. Mucormycosis (also called zygomycosis) is a rare infection caused by organisms that belong to a group of fungi called Mucoromycotina. At one time these fungi were called Zygomycota, but this scientific name has recently been changed. These fungi are typically found in the soil and in association with decaying organic matter, such as leaves, compost piles or rotten wood.^[1]

Who gets mucormycosis?

Mucormycosis is a rare infection. The infection is more common among people with weakened

immune systems, but it can occur (rarely) in people who are otherwise healthy. Risk factors for developing mucormycosis include:

- Uncontrolled diabetes
- Cancer
- Organ transplant
- Neutropenia (low white blood cells)
- Skin trauma (cuts, scrapes, punctures, or burns)

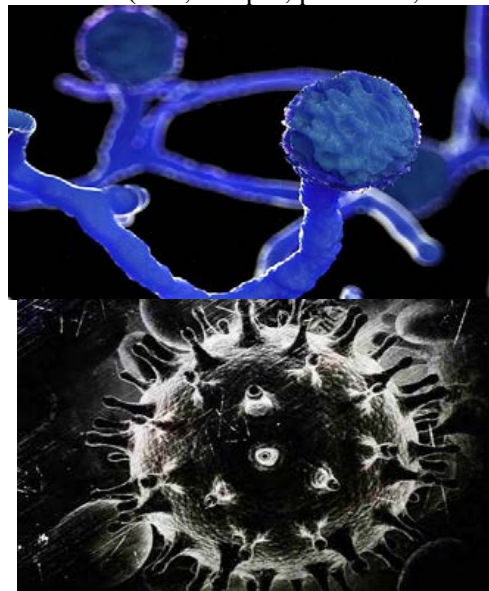


Fig. 1:1 Black fungus

How does someone get mucormycosis?

There are two main types of infection that people can get, and these depend on the route of exposure. In the pulmonary or sinus form, exposure occurs by inhaling fungal spores from the environment. These spores can cause an infection to develop in the lungs, sinuses, eyes, and face, and in rare cases can spread to the central nervous system. In the cutaneous form, the fungus can enter the skin through cuts, scrapes, puncture wounds, or other forms of trauma to the skin. Mucormycosis is not contagious and does not spread from person to person.

What are the symptoms of mucormycosis?

The symptoms of mucormycosis depend on where in the body the fungus is growing. Mucormycosis most commonly affects the sinuses or lungs. Symptoms of sinus infections include

- fever,
- headache,
- sinus pain.

- Lung infections with the fungus can cause fever and cough symptoms.
- Skin infections can develop after the fungus enters through a break in the skin due to surgery, burns, or trauma.
- A skin infection can look like blisters or ulcers, and the infected tissue may turn black. Other symptoms of a skin infection include fever, tenderness, heat, excessive redness, swelling around a wound. If the infection is not treated quickly, the fungus can spread throughout the body.

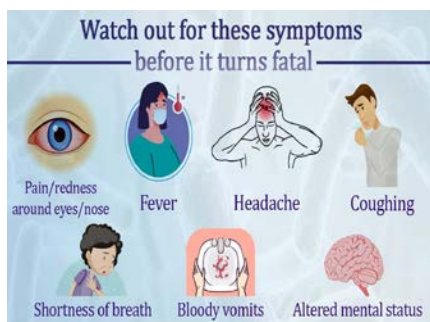


Fig. 2: Symptoms of black fungus

How to manage :

- Control diabetes and diabetic ketoacidosis
- Reduce steroids (if patient is still on) with aim to discontinue rapidly
- Discontinue immunomodulating drugs
- No antifungal prophylaxis needed
- Extensive Surgical Debridement - to remove all necrotic materials
- Medical treatment
 1. Install peripherally inserted central catheter (PICC line)
 2. Maintain adequate systemic hydration
 3. Infuse Normal saline IV before Amphotericin B infusion Antifungal Therapy, for at least 4-6 weeks (see the guidelines below)

4. Monitor patients clinically and with radio-imaging for response and to detect disease progression^[2]

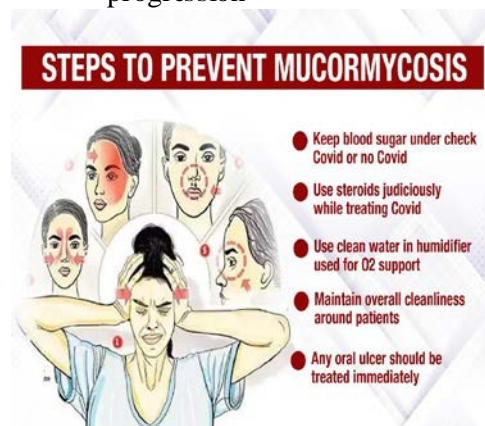


Fig .3: Prevent black fungus

Myths about transmission

Several theories about the source of mucormycosis infections are circulating on social media, many of them unfounded.

Person-to-person transmission

Crucially, mucormycosis cannot be transmitted from person to person, so there is no need for people to isolate — unless, of course, they have an ongoing SARS-CoV-2 infection. Rather, the source of infection is environmental, from airborne spores produced by the fungi.

Fungi growing in water, oxygen cylinders, humidifiers

Some media pundits have concluded that the fungi must be growing in dirty water in hospital oxygen cylinders or humidifiers. However, there is no evidence that this can occur, and mycologists have pointed out that fungi cannot produce spores in fluid. What is more, the pure oxygen stored in cylinders is likely to be detrimental to the growth of microorganisms of all kinds.

Face masks harbor black fungus

This is a myth. There is no evidence that face masks can harbor the fungi.

Onions are to blame

Another popular theory is that the black mold sometimes seen on onions in refrigerators is *Mucorales* fungus and, therefore, a potential source of infection.

As we have seen, the species in question are not black. In fact, the black mold found on onions and garlic is usually the fungus **Aspergillus niger**. In a 2019 paper, Prof. Richardson and his co-author explain that Mucorales fungi grow on moldy bread, decaying fruit and vegetables, crop debris, soil, compost, and animal excreta. He points out that they have a high moisture requirement and are unlikely to survive on common building materials, such as wood, painted surfaces, and ceramic tiles. He concludes: "All of these observations suggest that house residents are not generally exposed to zygomycetes in their home environment, apart from mould-contaminated food items, such as bread and fruit."

Possible routes of transmission

Published evidence points to several potential sources of the infection in hospitals, but it does not mention oxygen tanks, humidifiers, or face masks. Two studies — published in 2014^{Trusted Source} and 2016, respectively — implicate hospital linens from poorly managed laundries as a source.

A 2009 review of research into hospital outbreaks identifies ventilation systems, wooden tongue depressors, adhesive bandages, and ostomy bags as other possible sources of infection. Pathologists at the University of Kentucky in Lexington report^{Trusted Source} that another possible transmission route is the inhalation of spores in dust from nearby building works, or contaminated air-conditioning filters. They also highlight the importance of infection through the skin, for example via burns, catheter insertion sites, needlestick injuries, insect bites, and stings

Proven treatments

A video doing the rounds on social media proposes that a concoction of mustard oil, potash alum, rock salt, and turmeric can cure mucormycosis. In reality, the only proven treatments are surgery to remove necrotic tissue, and the antifungal amphotericin B. However, India now faces severe shortages of the drug. Just as importantly, doctors are advised to address the underlying causes of impaired immunity,

especially poorly managed diabetes and overzealous use of corticosteroids.

In their recent review, Dr. Singh and his colleagues conclude:

"An unholy trinity of diabetes, rampant use of corticosteroid in a background of COVID-19 appears to increase mucormycosis. All efforts should be made to maintain optimal glucose and only judicious use of corticosteroids in patients with COVID-19^[2]

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

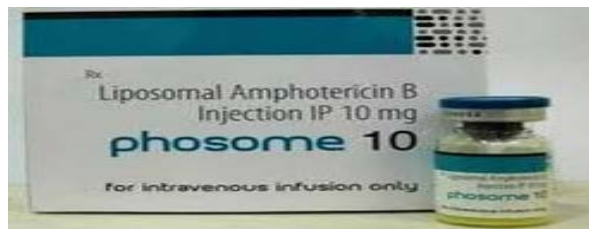
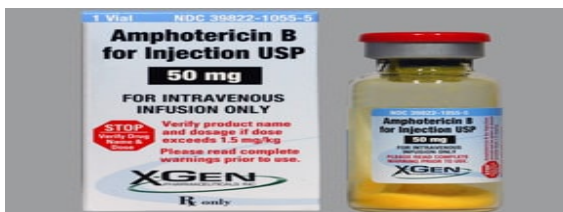
Physical examination, swab test, tissue biopsy, imaging tests like CT or MRI scans to understand about the severity.

What's the treatment?

While it is treated with antifungals, mucormycosis may eventually require surgery. Doctors have said that it is of utmost importance to control diabetes, reduce steroid use, and discontinue immunomodulating drugs. To maintain adequate systemic hydration, the treatment includes infusion of normal saline (IV) before infusion of amphotericin B and antifungal therapy, for at least 4-6 weeks.

Experts in the task force have stressed the need to control hyperglycemia, and monitor blood glucose level after discharge following Covid-19 treatment, and also in diabetics. One should use steroids judiciously — correct timing, correct dose and duration are important.

Management of Covid patients with mucormycosis is a team effort involving microbiologists, internal medicine specialists, intensivists, neurologist, ENT specialists, ophthalmologists, dentists, surgeons (maxillofacial/plastic) and others.^[3]



Life after surgery for mucormycosis

Mucormycosis can lead to loss of the upper jaw and sometimes even the eye. “Patients would need to come to terms with loss of function due to a missing jaw — difficulty with chewing, swallowing, facial aesthetics and loss of self-esteem, doctors say. Be it the eye or upper jaw, these can be replaced with appropriate artificial substitutes or prostheses. While prosthetic replacement of the missing facial structures can commence once the patient stabilises after surgery, doctors it is important to reassure him about the availability of such interventions instead of leaving him to panic with the sudden unforeseen loss, augmenting a post-Covid stress disorder which is already a reality,” said Dr B Srinivasan, a maxillofacial prosthodontist. “Prosthetic reconstruction can be effected after surgery, but interim solutions should be planned even before surgery of the jaws for better long-term outcomes. Prosthetic reconstruction can ensure that the cure is not more dreadful than the disease itself,” he said^[4]

COVID-19 and mucormycosis

Higher rates of mucormycosis cases in India are due to a combination of factors. For instance, more than 30 million people in India have a diabetes diagnosis. Despite this, the number of cases of mucormycosis before the COVID-19 pandemic was relatively low, although prevalence was rising Trusted Source.

Since the start of the COVID-19 pandemic, however, there has been a dramatic increase. Dr. Arvinder Singh Soin, a pioneering surgeon in Delhi, notes that he has “seen more cases of black fungus in the past week than we normally treat in 2 years.” **COVID-19 leads to a weakened immune system, preventing the body from effectively protecting against infection. As a result, individuals**

Christopher Coleman, assistant professor of infection immunology at the University of Nottingham in the United Kingdom, told *Medical News Today*:

“The virus, as part of its replication cycle, suppresses the immune system, so the immune system cannot clear other bacteria or fungi. The most famous example of this is HIV, of course, which causes long-term immune suppression. But, other viruses do this on a much shorter timescale — i.e., the immune system is only slightly suppressed for a few days or weeks while the virus is there.”

Steroid treatments for COVID-19 may also act to suppress the body’s immune response, contributing to these increased mucormycosis infection rates.

In this case,” explained Coleman, “there seems to be a suggestion that steroids may be playing a role — in that they are suppressing normal immune responses and allowing a fungus to invade.”

In addition, oxygen support for people with severe COVID-19 can cause drying of the nasal cavity and further increase the risk of infection.

On May 19, the state of Rajasthan declared a mucormycosis epidemic. In the city of Surat, 8 out of 40 COVID-19 survivors who developed mucormycosis in the eye lost their eyesight.

The state of Maharashtra reported over 2,000 recent cases of mucormycosis, with 8 resulting in death. The state’s health minister, Rajesh Tope, announced that they will be creating special wards

and launching an awareness campaign to spread awareness about the disease^[5]

Next steps for treatment

It is difficult to determine the best course of action to simultaneously address both of these epidemics. Coleman raises some questions that experts need to address moving forward: “**Can the people be treated with an antifungal at the same time?**” and “**Is there a way to lower the COVID-19 treatment dose and still be effective while not suppressing the immune system enough to allow the fungus in?**” The combined risks of COVID-19 and mucormycosis raise challenging issues and require careful coordination of patient care and treatment.

Prevention

Ensuring personal hygiene by bathing and scrubbing the body thoroughly, particularly after returning home from work, working out or visiting neighbors, relatives, friends. Wearing face masks and face shields when going to dirty polluted environments such as construction sites. Making sure to don fully covered clothing of concealed shoes, long pants, long-sleeved shirts and gloves while coming in contact with soil, moss, manure, like in gardening activities^[6]

Conclusion

Patients most vulnerable to mucormycosis are those who have been treated with steroids and other drugs for Covid 19 to reduce inflammation. While there is no major outbreak, the national Covid task force has issued an advisory. Efforts are underway to collect data for large studies being done by the Fungal Infections Study Forum and Clinical infectious Diseases Society. It is very much essential to take this issue very serious since the people around the world pathetically affected mentally and economically, it should not produce further damage to the quality of life of the humans. Further research on this only would help in the eradication of the mucormycosis worldwide.

References

1. <https://www.medicalnewstoday.com/articles/black-fungus-and-covid-19-myths-and-facts>
2. <https://economictimes.indiatimes.com/news/et-explains/black-fungus-how-infection3-starts-death-rate-treatment-medicine-other-key-things-4.know/articleshow/82796816.cms>
3. <https://www.insightsonindia.com/2021/05/10/black-fungus/>
4. <https://www.outlookindia.com/website/story/india-news-40845-black-fungus-infections-reported-in-india-toll-due-to-disease-3129-harsh-wardhan/386445>
5. <https://www.insightsonindia.com/2021/05/10/black-fungus/>
6. <https://www.indiatoday.in/coronavirus-outbreak/story/black-fungus-tracing-existence-of-rare-disease-to-pre-covid-times-1804143-2021-05-18>

Cite this article as:

Patidar A., Kayande N., Kushwah P., Birle R. and Kushwah N. (2021). Mucormycosis or Black fungus affecting COVID-19 patients, *Int. J. of Pharm. & Life Sci.*, 12(8):9-14.

Source of Support: Nil

Conflict of Interest: Not declared

For reprints contact: ijplsjournal@gmail.com