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REVIEW ARTICLE

Association of Mucormycosis in Covid-19 and its Epidemiologic Study

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ABSTRACT

Mucormycosis, also known as Zygomycosis or Black Fungus, is an infection caused in humans via various causative agents from the Zygomycetes class. Several countries including India is afflicted by the covid-19 virus, which has infected approximately 3.7 million people across the country. Some of the corona-positive patients suffer from another fatal infection, Mucormycosis, commonly known as Black Fungus. The strategy should be to administer an effective antifungal drug as soon as possible at the optimum dose. However, India being an epicenter of Diabetes with enormous 80 million diabetics, is of particular importance in the present scenario of the COVID pandemic. COVID therapy with Steroids and immunesuppressants has increased the chances of infection in various individuals within the country with weaker immune system responses. The main purpose of this paper is to enlighten the community about the involvement of mucormycosis in covid-19 affected population and basic insights of its invasion.

Keywords: Mucormycosis; Black Fungus; Covid-19; Diabetes Mellitus; Amphotericin B; Immunosuppression; Apophysomyces; Renal Failure; Corticosteroids

INTRODUCTION

Filamentous fungi are a group of infectious organisms that give rise to Mucormycosis (Figure 1). Representational image of Mucormycosis, Image credit: Wikipedia). These filamentous fungi come under the Mucorales order of the subphylum Mucoromycotina, earlier called Zygomycetes. The infection generally initiates in the individual by inhalation of its spores and inoculation into the respiratory tract. The diseases can be present as localized or disseminated in the host body.[1]

Cases are reported in both Immunocompromised and regular immune status patients. However, the vulnerability of this infection is primarily reported in Immunocompromised individuals. The exposure of the host is directly associated with phagocytic dysfunction. The usual risk factors are as follows –

1. Poorly controlledDiabetes with or without ketoacidosis.
2. Immunosuppression.
3. Renal failure.
4. Neutropenia.
5. Long-term steroid use.
6. Haematological malignancies.

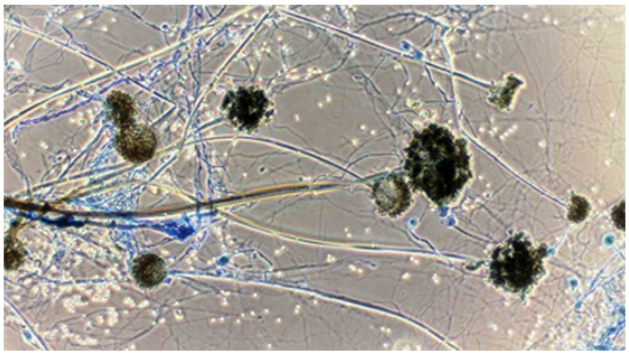


Fig. 1: Mucormycosis (also known as, Zygomycosis/Black Fungus)[2]

The risk of Mucormycosis gets increased by Desferrioxamine therapy. It chelates with iron forming a sideophore that stimulates fungal growth. Firstly, it has been reported in patients on voriconazole/itraconazole prophylaxis after allogeneic haematopoietic stem cell transplant. Mucormy-

cosis is a highly obtrude and progressive disease with high mortality, ranging from 70% to 100%.[3] In general, it gets under diagnosed and underreported.

The five dominant forms[4] of mucormycosis are as follows:

• **Rhino-cerebral (sinus and brain) mucormycosis :** In this kind of mucormycosis, the infection in the sinuses can spread to the brain.

• **Pulmonary (lung) mucormycosis :** Patients who have cancer or had an organ transplant or a stem cell transplant are most commonly affected by this type of mucormycosis.

• **Cutaneous (skin) mucormycosis :** This type of mucormycosis occurs when fungi enter the body. For example, after surgery, a burn, or any other type of skin trauma, this fungi can enter the skin. It mainly occurs in the patient who does not have weakened immune systems.

• **Gastrointestinal mucormycosis :** This type of mucormycosis is commonly seen among young children compared to adults. The chance of infection is more in premature and low birth weight infants who are less than a month and have gone through surgery or any medication that prevents the body's ability to fight against germs and sickness.

• **Disseminated mucormycosis :** when the infection spreads all over the body through the bloodstream, this can be designated as disseminated mucormycosis. This infection mainly affects the brain and affects other organs like the spleen, heart, and skin.

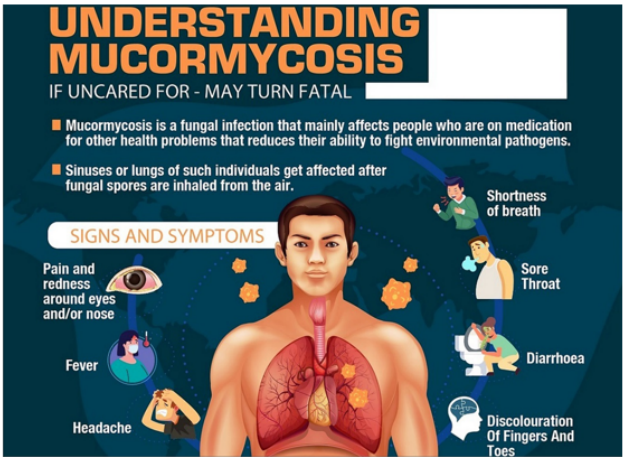


Fig. 2: Mucormycosis General Overview[5]

Patients who have Diabetes, haematological malignancies, organ transplants, and renal failure are most prone to be affected by pulmonary mucormycosis. Clinically this form of mucormycosis resembles bacterial pneumonia with productive or non-productive cough and dyspnoea.[6]

SIGNS AND SYMPTOMS

Infection follows different signs and symptoms[7–9] (Figure 2).

Introduction of Mucormycosis in human body with its signs and symptoms are as follows:

- Sinus infection (sinusitis) is the most common observation seen in patients. It is accompanied by nasal congestion, nasal discharge, and sinus pain. Fever and headache are the common symptoms that occur. If the infection spreads outside the sinuses, the following symptoms are also observed:

1. Tissue loss (necrosis) on the roof of the mouth (palate)
2. The disintegration of the thin wall of the cartilage and bone
3. Swelling of the area around the nose (perinasal area)
4. Redness (erythema) of the skin overlying the sinus and the eye socket (orbit).

Occasionally, there is bluish discoloration of the skin near the sinuses or the eye socket, which occurs due to a lack of oxygen (cyanosis). Sometimes, there can be the development of blurred vision or double vision. If unrecognised and untreated, notable tissue death can occur, and the infection can cause significant damage to facial structures.

- The spreading infection of mucormycosis to the brain leads to lethargy, seizures, slurred speech, partial paralysis, abnormalities of the nerves of the face and eyes (cranial neuropathies), brain abscess, altered consciousness, coma.
- When the infection spreads to the eyes, there can be swelling due to fluid build-up around the eyes, termed as periorbital edema, bulging or displacement of the eye or proptosis, vision loss, and potentially lead to blindness. Occasionally, few affected individuals experience paralysis or weakness of the muscles that move the eyes (opthalmolegia), making it difficult and painful to move the eyes.
- When the spores are inhaled and reach the respiratory system, it affects the lungs, which causes pulmonary mucormycosis. It is a progressive disease distinguished by fever and a cough that does produce any mucous (non-productive cough). Infrequently, spitting or coughing up blood (haemoptysis), chest pain, and breathing difficulty (dyspnoea) occur.
- When mucormycosis spreads to the skin, it leads to cutaneous mucormycosis; it causes the development of the single, painful, hardened area of the skin and inflammation of the underlying tissue in the affected individuals. The skin may become reddened, warm, swollen, painful, hardened and inflammation of the underlying tissue. In some cases, open sores and blisters are formed, and necrosis can also occur with the affected tissue turning black. The development of this form of mucormycosis is slow or acute, and fulminant.

- The gastrointestinal system is also affected by mucormycosis; this mainly occurs when spores are breathed into the mouth and swallowed or consumed with contaminated food.Symptoms include abdominal pain and blood vomiting (hematemesis). Lesions can develop that cause a hole in the stomach or intestines.
- In some patients, severe pain in the bowels occurs due to lack of blood flow (bowel infarction), and due to blood loss, the affected individuals can go into haemorrhagic shock.
- In few instances, mucormycosis spreads to affect the kidneys, the inner lining of the heart's chambers and the heart valves (endocarditis), and the bone (osteomyelitis).
- Signs and symptoms of disseminated mucormycosis differ greatly depending upon the organ system involved.

HISTORY OF MUCORMYCOSIS

The first case of mucormycosis was reported in the year 1885 by Paltauf.[10] In 1943, a publication by Gregory et al. the first time reported observation of rhino-orbital cerebral mucormycosis.[11] In 1955, Harris reported the first case with cerebro-rhino orbital mucormycosis, who survived the disease.[12]There is little change in the diagnosis and outcome of this disease. Even though mucormycosis isof many forms – cerebral, cutaneous, rhino cerebral, intestinal, or pulmonary – it is still a rarity. It should be suspected in patients who are diabetic or immuno compromised.[13]

The standard treatments for mucormycosis –

- Amphotericin B.
- Surgical debridement of infected tissue.
- Use of adjunctive HBO therapy

ETIOLOGY

Zygomycetesare a class of fungus that causes Mucormycosis. The most repeated species isolated from patients are Apophysomyces (*A. variabilis*), Cunninghamella (*C. bertholletiae*), Lichtheimia [Absidia] (*L. corymbifera, L. ramosa*), Mucor(*M. circinelloides*), Rhizopus (*R.arrhizus* (oryzae) *R. microsporus*), Rhizomucor (*R. pusillus*), and Saksenaea (*S. vasiformis*). These are common environmental organisms that are not harmful to immuno competent humans. Immuno compromised patients (i.e., transplant patients, HIV, patients of chronic steroids or disease-modifying anti-rheumatic medications, leukemia, or other cancer patients) can present with rapidly progressive necrotizing infection (Figure 3). Describes the Growth of Sporangiospores in human body followed by spreading of infection through blood stream). Likewise, uncontrolled diabetics (particularly those with a history of diabetic ketoacidosis) are also at high risk. Mucormycetes are the moldsthat cause fungal infection and lead to mucormycosis. They are found ubiquitous. Therefore,they can be found in the soil and decaying organic matter like decaying vegetation.

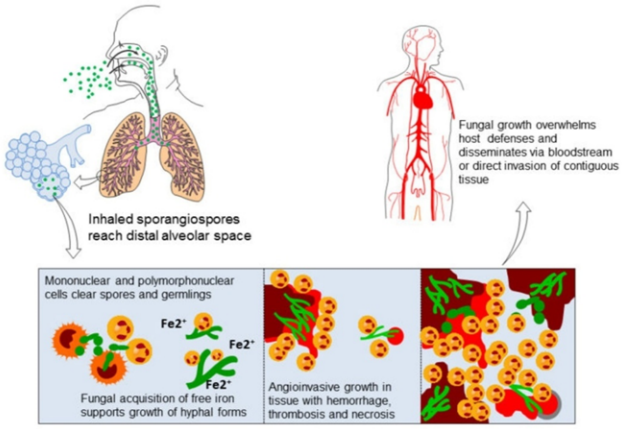


Fig. 3: Etiology of Mucormycosis[14]

Usually they do not cause problems, as these molds are found commonly all over nature. However, those individuals who have weak and compromised immune systems, these molds can cause severe, and even life-threatening infections. Breathing in mold spores increases the chance of developing infection. Cuts or open wounds can also contribute to the development of infection.

In the case of uncontrolled diabetes, the patient is at a high risk of developing mucormycosis, and in the end, they may develop diabetic ketoacidosis. Ketoacidosis is a complication in which any individual having poorly- controlled Diabetes in which the body produces high levels of blood acids termed as ketones. Ketoacidosis is a diabetes complication that leads to a variety of symptoms.

People who are at greater risk of developing mucormycosis are:

- People having low levels of neutrophils (neutropenia). Neutrophils are white blood cells that help to fight off infection. Neutropenia is an abnormal condition where the count of white blood cells decreases.[15]
- People receiving broad-spectrum antibiotics.[16]
- Individuals receiving immuno suppressant drugs that suppress the activity of the immune system.[17]
- People having recently undergone hematopoietic stem cell transplantation (HSCT). Hematopoietic stem cells are found in the bone marrow and, in due course, grow into red blood cells, white blood cells, and platelets. Transplant involves eliminating the existing infected bone marrow and replacing it with bone marrow from a healthy donor. Affected individuals should be administered immuno suppressant drugs to help fight off rejection. This make them more susceptible to infections, including mucormycosis infection.[18]
- Individuals who have surfeit iron in the body (iron overload), which occurs due to frequent blood trans-

fusions or certain blood disorders, are also at risk of developing mucormycosis. Many of the researchers believe that these moldscan use excess iron to grow and spread.[19]

- Some other conditions which can increase the risk of developing mucormycosis include -kidney insufficiency, HIV/AIDS, the usage of contaminated medical equipment in open wounds; long-term use of corticosteroids (which are powerful anti-inflammatory medicines), skin trauma including burns or other injuries to the skin; extreme malnutrition; and illegal Drug use.[20]

Following fungi cause mucormycosis –

i. Rhizopus species
ii. Mucor species
iii. Rhizomucor species
iv. Syncephalastrum species
v. Cunninghamellaberthollетiae
vi. Apophysomyces species
vii. Lichtheimia (formerly Absidia) species.

RISK FACTORS FOR MUCORMYCOSIS[21]

Graphical overview for healthcare associated risk factors in Mucormycosis is presented in (Fig4 :

- Diabetes mellitus
- Myeloproliferative disorders
- Acquired immune deficiency syndrome (AIDS)
- Organ transplantation
- Renal failure
- Polytrauma
- Burns
- Intravenous drug abuse
- Long-term corticosteroid therapy
- Cytotoxic chemotherapy
- Broad-spectrum antibiotic therapy
- Desferrioxamine therapy and all causes of iron overload
- HIV patients
- Malnourished individuals, especially children
- Hematologic and solid malignancies

DIAGNOSIS OF MUCORMYCOSIS

The diagnosis is made based on the patient's medical history, including a physical examination and the patient's risk factors for a fungal infection. Although some tests, such as CT or MRI[23], may assist in characterizing the degree of infections or tissue loss, a precise diagnosis is challenging. Mucormycosis is diagnosed utilizing histology and/or the identification of the organism by culture from afflicted sites. In the absence of particular biomarkers, the isolate is recognized at the species level. No accurate serological

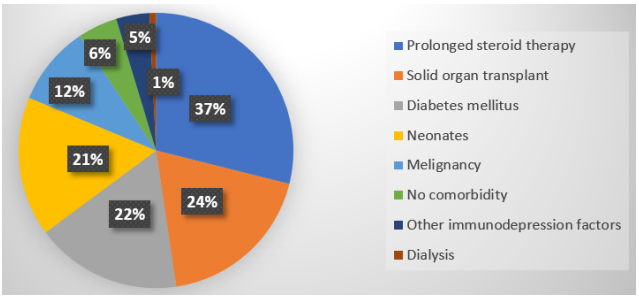


Fig. 4: Distribution of healthcare-associated mucormycosis risk factors[22]

or blood test exist. A biopsy (tissue collected by surgical removal or endoscopes with biopsy instrument) of infected tissue, together with specific tissue stains looking for distinct structural components, may help identify the fungus and aid in the ultimate diagnosis.[24]

Although there is no circulating antigen detection test for mucormycosis, it is commonly noticed that the 1,3-β-d-glucan detection test is negative in Mucorales infections. On the other hand, these two tests can help rule out invasive aspergillosis, which is the most common differential diagnosis, as well as mixed Aspergillus and Mucorales infections. There is currently no standardized blood polymerase chain reaction (PCR) test. As a result, biological specimens from clinically affected locations must be analyzed for diagnosis. Obtaining tissue biopsies for histopathology and culture should be a top priority.[25]

TREATMENT OF MUCORMYCOSIS

The treatment for mucormycosis needs to be fast and aggressive. The need for urgency derives from the fact that the patient has usually already sustained permanent tissue damage by the time a presumptive diagnosis is made.

Mucormycosis is treated with a multimodal approach that includes antifungal agents, surgical debridement, and correction of the underlying condition that predisposes the patient to the disease. In mucormycosis, it is crucial to keep the underlying problems under control. Uncontrolled Diabetes necessitates immediate treatment of metabolic imbalances.

Recent therapeutic advances may improve mucormycosis outcomes. Amphotericin B lipid complex (ABLC) has emerged as the cornerstone of primary therapy for mucormycosis. Table 1 depicts possible First and Second line treatments of mucormycosis. Posaconazole may be effective as salvage therapy. However, based on the existing data, it cannot be recommended as first-line therapy for mucormycosis. Preclinical and limited retrospective clinical data suggest that combining ABLC and echinocandin therapy may improve mucormycosis survival. A definitive trial is required to confirm these findings. In animal models

Table 1: Preferred line of Treatment for Mucormycosis[26]

First-line treatment	Second-line treatment
AmB deoxycholate	Posaconazole, 400mg bid
Liposomal AmB, 5-10mg/kg	Combination lipid AmB & Caspofungin
ABLC, 5-7.5mg/kg	Combination lipid AmB & Posaconazole
Posaconazole, 400mg bid	Combination with Deferasirox
	Maintenance Therapy – Posaconazole

of mucormycosis, combining ABLC with the iron chelator deferasirox improved outcomes.[27,28]

PRESENT SCENARIO OF MUCORMYCOSIS IN RELATION WITH COVID-19

As of 7 June 2021, India is facing a dangerous increase in coronavirus disease 2019 (COVID19) cases during its second wave, with a total of 28, 996, 949 cases and 351, 344 deaths, which is growing by the day.[29] Mucormycosis is another fatal infection that highly affects the COVID sufferer. Black fungus is the common name given for Mucormycosis. The fight from COVID is not yet over. India has been facing another deadly challenge of mucormycosis.

Steroid preparations such as Dexamethasone, Methyl-prednisolone, or prednisolone are administered by patients with moderate to severe COVID infection. Even various antimicrobial agents are also prescribed to prevent and treat pulmonary infections that may cause pneumonia.

CO-MORBIDITIES OF CONCERN DURING TREATMENT OF COVID-19 PANDEMIC

Numerous COVID patients have been suffering from comorbid conditions. India being an epicenter of Diabetes with enormously more than 50 million diabetics,[30] is of particular importance in the present scenario of the COVID pandemic. COVID therapy with Steroids and immune-suppression predisposing conditions such as old age, cancer chemotherapy or radiotherapy, organ transplant recipients on immune-suppressors, or any disease requiring steroid treatment are well-recognized comorbid conditions.

The immuno suppressive state becomes very profitable for opportunistic fungal infections. Aspergillus being ubiquitous in the atmosphere and Candida being inhabitant of human body are most frequent fungal infections that wait for the host to be immune-suppressed. Mucor is the next fatal and challenging life-threatening infection. Mucormycosis is also called Black Fungus due to black bruises it forms in the infected area. Mucor infects deeper tissues starting from the sinus and then expanding its effect to the eyeball, including bone and the soft tissues, and ultimately reaches brain tissues. Mucormycosis is so terrible and gruesome that it may cause rapid deterioration of the eyes, leading to perpetual loss of vision. Once Mucor goes in for infecting the brain, the patient declines rapidly, leading to paralysis, organ failure, other related complications, and eventually death.

Every COVID patient recovered and discharged from the hospital should be warned to be watchful of the early symptoms of Mucormycosis. Symptoms involve blood-stained or black discharge from the nose, localized pain, redness over the cheek bone or palate, redness of the eye, headache, and fever.

CHALLENGES IN THE MANAGEMENT OF MUCORMYCOSIS

Mucor infection is generally rigidly established, which makes early diagnosis difficult. The choice of extensive apparent surgical intervention is not all the time possible, especially if the infection has reached the brain. The best approach is to start antifungal drugs immediately, and if possible, surgical-intervention should be carried out. If there is advancing infection to the brain, the only remaining option will be aggressive treatment with appropriate antifungal drugs. The plan of action should be to give effective antifungal Drugs as early as possible with the best dose for the optimum duration until the infection is eradicated.

According to Global Guidelines on Treatment of Mucormycosis by the European Confederation of Medical Mycology, the choice of anti-Mucor drugs is limited to three molecules –

(1) Amphotericin B
(2) Isavuconazole
(3) Posaconazole

In case of pre-existing renal compromise, Isavuconazole and Posaconazoleare exceedingly recommended.

Amphotericin B, which is a potent broad-spectrum fungicidal, is used for the treatment of mucormycosis. Fig 5 present comparative study of mortality rate with different modes of therapy. The treatment of mucormycosis should be initiated with a high dose of Amphotericin B. Considering the dose-related toxicity and nephrotoxicity, the first choice is liposomal Amphotericin B. In India, there are following two forms of liposomalformulations:

A. Liposomal Amphotericin B Suspended in Dextrose: This form of the formulation is recommended at the daily dose of 5-10 vials.

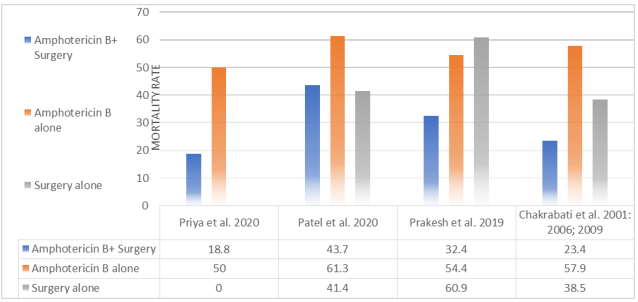
B. Liposomal Amphotericin B in Saline: A dose of 1-3 vials per day is recommended.

The replacement of Dextrose by Saline has been reported to contribute to reducing nephrotoxicity. The lower dose of drug prepared in Saline makes the treatment economical too.

As development of mucor takes place on high blood sugar levels, it more frequently occurs in Diabetics. Diabetic COVID patients, treated with steroids may have further raised levels of sugar which favorsmucor growth.Therefore,

Liposomal Amphotericin B in Saline will be a better option to resist mucor maturation and thus influential effective treatment.

The effective use of steroids and antimicrobials in COVID patients, early diagnosis, and early start of treatment with Liposomal Amphotericin B and its prolongation till the clearance of infection can save many lives.[31]



	Priya et al. 2020	Patel et al. 2020	Prakesh et al. 2019	Chakrabati et al. 2001: 2006; 2009
Amphotericin B+ Surgery	18.8	43.7	32.4	23.4
Amphotericin B alone	50	61.3	54.4	57.9
Surgery alone	0	41.4	60.9	38.5

Fig. 5: Modes of therapy and mortality rate in Indian population[32]

PRECAUTIONS

Folowing are some precautions[33] that can be taken to minimise the risk of infection :

Do's

- Control Hyperglycaemia
- Monitor blood glucose level post-COVID discharge and in Diabetes.
- Use steroid Judiciously.
- Encourage family members or friends to undergo treatment if they have ringworm.
- Use loose, absorbent clothing.
- Dry the skin after physical activities and bathing.
- Use clear, sterile water for humidifiers during oxygen therapy.
- Complete the recommended use of antifungals.

Don'ts

- Do not miss warning signs and symptoms.
- Do not consider all cases of the blocked nose as cases of bacterial sinusitis, especially in the case of immunosuppression and/or COVID patients on immunomodulators.
- Do not hesitate in seeking aggressive investigations as appropriate for detecting fungal etiology.
- Do not lose crucial time to initiate treatment for mucormycosis.
- Do not share personal articles like clothing, comb, towels, and footwear.
- Do not Discontinue treatment or take inadequate dosage.
- Do not self-medicate,especially steroids.
- Do not ignore medical advice.

REPORTED CASE STUDIES OF MUCORMYCOSIS

1st case study

A 55-year-old man who has been long-lived with diabetes mellitus, hypertension, and ischemic cardiomyopathy extended with fever, dry cough, and progressive breathlessness forthree days. Ten years before, he was detected with type 2 diabetes mellitus. He was on rough treatment with various oral hypoglycaemic drugs. The monitoring of blood sugar was infrequent. He was also a sufferer of last-stage renal disease and was continuously receiving maintenance haemodialysisfor one year. The older adult was neither a drug abuser nor a smoker. During the time of admission, the respiratory rate was 26 breaths/minute, blood pressure was 110/80 mmHg, and heart rate was 90 beats/minute. The oxygen saturation was 84% while breathing ambient air and improved to 95% with a venturi mask (fraction of inspired oxygen, 0.5). The patient was not obese (body mass index of 24kg/m2)

Chest radiograph revealed bilateral diffuse interstitial opacities and cardiomegaly. His nasopharyngeal swab was detected positive for SARS-CoV-2 by RT–PCR. The haemoglobin count at the time of admission was 7.8 g/dl, and glycated haemoglobin was 5.3%. His treatment was started on intravenous dexamethasone (6 mg once a day for 14 days) and remdesivir (200 mg on day 1 and 100 mg on days 2–5). Supportive care, including oxygen supplementation, thromboprophylaxis for venous thrombosis, and maintenance haemodialysis, were carried out. At admission, his random plasma glucose was 140 mg/dL, and during dexamethasone therapy, it got increased to a maximum of 300 mg/dL. After 14 days of therapy, he was noticed with clinical improvement, hypoxemia improved, and radiological resolution.

The patient complained of cough, expectoration, and burning micturition after three days. He was not diagnosed during hospitalization, and there was no fever during that time. After examination of urine culture, the growth of *Escherichia coli* was found. He was treated with intravenous meropenem 1 g every day (dose modified for renal impairment) for about ten days. After 21 days of admission, a chest radiograph was performed, which showed a cavity with intracavitary contents in the correct upper zone. Computed tomography (CT) of the thorax made confirmed a thick-walled cavity in the right upper lobe. Minimal pleural effusion was also sopped on the right side. Sputum examination with various stainings such as Gram stain, stain for acid-fast bacilli, and fungal smear was found negative. The sputum culture on Sabouraud dextrose agar (SDA) at 25 °C and 37 °C grew a pure culture of the cottony greyish white colony after six days of incubation. Lacto phenol cotton blue (LCB) that has been mount from the growth dilvulgedaseptate hyphae along with nodal rhizoids and short sporangiophores with terminal spherical sporangia pervaded with brownish

sporangiospores, evocative of *Rhizopus microsporus*.There cognition was confirmed spotted by matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF; Bruker Daltonics, Billerica, MA, USA), which gave an excellent discriminatory score of 2.1. The isolate was deposited in the National Culture Collection of Pathogenic Fungi (NCCPF), PGIMER, Chandigarh, India, with NCCPF 710,496. As per the Clinical Laboratory StandardsInstitute, I(CLSI)-M38A2 guidelines, the in vitro antifungal susceptibility testing (AFST) of the isolate was performed by the microbroth dilution method. The minimum inhibitory concentrations (MICs) of the isolate are as follows: -

1. Amphotericin B, 0 5 μg/Ml
2. Itraconazole, 0 03 μg/Ml
3. Posaconazole, 2 0 μg/Ml

The index value of Serum beta-d-glucan (Fungitell, Associates of Cape Cod, Inc, MA, USA) was reported 189 pg/mL and serum galactomannan index value was 0.18 (Platelia Aspergillus galactomannan antigen, Bio-Rad, France). The man was treated with liposomal amphotericin B (3 mg/kg) for expected pulmonary mucormycosis. His symptoms improved, and he was discharged after 54 days of hospitalization (cumulative dose of amphotericin B, 5 gm). The patient has undergone liposomal amphotericin (3 mg/kg/day) on an outpatient basis for 25 days after discharge and is arranged for right upper lobectomy. After completion of amphotericin therapy, the chest radiograph showed significant resolution of the right upper zone cavity during discharge.[34]

2nd case study

A boy of 17-years-old was diagnosed with cyanotic congenital heart disease when he was eight months old. He was admitted for intracardiac repair. When he was of 8 months, he had undergone palliative surgeries, and till ten years of age, he went through two of the palliative surgeries. When he was of 10 years, he had also undergone treatment for a cerebral abscess, intracardiac repair of the congenital anomaly was monotonous. However, the on-the-spot immediate postoperative period was marked by intra pericardial bleed for which re-exploration was performed. On a postoperative day (POD) 4 abnormal breathing pattern was noted. Over evaluation, ischemic myelopathy was diagnosed, and therapy for steroids was started. He developed peritonitis due to a sizeable ileocecal perforation warranting a right hemicolectomy on POD 25. Heavy growth of *Enterobacter aerogenes* and *Klebsiella pneumoniae* was spotted on Peritoneal fluid culture. Before the surgery, the absolute neutrophil count was 2400/μl.

In his cross-examination of the right hemicolectomy specimen, a large near circumferential perforation was spotted at the ileocecal junction with exudate-covered serosal and adventitial surfaces. The perforated edges have crowed, and the rest of the ileal and colonic mucosa was unnoted. Microscopy from the ileal and the cecal ends of the perforation revealed transmural necrosis with acute inflammatory exudate and vegetable matter along the serosa in the presence of numerous fungal hyphae transmurally. The hyphae were broad, irregular, and aseptate with right-angled branching evocative of Mucorales. There was confirmation of angio invasion with many small and large caliber blood vessels that were completely obstructed by fungal balls with thrombosis and vascular wall invasion. The mycosis was also entailing the appendix.[35]

3rd case study

A woman of 54-year-old age with poorly controlled Diabetes (Glycated haemoglobin[HbA1C] of 10.5%) and grade 4 chronic kidney disease (creatinine of 3.2 mg/ dL) was admitted to a clinic with a history of productive cough and dyspnoea of grade 4 Modified Medical Research Council scale for one week. She had a history of high-grade squamous intraepithelial lesion on her pap smear a year ago, for which she has not consulted further. In her physical examination, tachypnoea was spotted and manifestly reduced breath sounds on the left side. At the time of admission, her blood gas analysis showed respiratory alkalosis with the partial pressure of Oxygen (PaO2) of 64.7 mm Hg and saturation of 94% in room air. The revelation of her chest X-ray stated a complete homogenous opacity on the left side. High-resolution evaluated tomography of the thorax manifested a complete collapse agglomeration of the left lungs with hasty left main bronchial cut off and a mild left pleural effusion. Her report for cardiac status was normal, and the ultra-sonogram of her abdomen was also normal except for a simple renal cortical cyst in the right kidney. The pleural fluid analysis divulged a sterile abnormal collection of fluid (effusion), negative for malignancy. She was treated with linezolid as her sputum culture grew methicillin-resistant *Staphylococcus aureus*. The revelation of bronchoscopy showed a fleshy vascular growth completely blocking the left main bronchus. Bronchial carcinoid or a bronchogenic carcinoma was inferred. The biopsy report was sent for histopathological examination that revealed bronchial mucosa and fragments of necrotic tissue with numerous broad aseptate hyphae capturing the stroma and the vessel wall blocking the vascular lumen redolent for invasive mucormycosis. Bronchial lavage also let out aseptate hyphae and was negative for any malignant cells. Histopathology affirms mucormycosis, so the fungal culture was not conducted. The family of the patient has gone for medical management considering the high risks cognate with the surgery. She was treated with oral posaconazole based on her renal functions. Unfortunately, she died due to worsening of renal failure.[36]

DISCUSSION

Mucormycosis, often known as Black Fungus, belongs to the order Mucorales and the subphylum Mucormycotinea. Mucormycosis has been found to be contagious in persons with impaired immune systems. This is often reported to be seen in people with a history of Diabetes, haematological malignancies, organ transplantation, and so on. Desferrioxamine medication increases the risk of Mucormycosis, and several steroid formulations, such as Dexamethasone and Mehtylprednisolone, used in patients with severe to moderate COVID-19 infection, are also susceptible to Mucormycosis infections. Along with the drug therapy used for COVID treatment, many patients with a history of diabetes and other disorders, as well as old age, increase their risk of mucosmycosis infection. This complicates the recovery of infected individual and reduces the likelihood of total recovery.

CONCLUSION

While fighting the battle with covid-19, a new deadly infection also spread, which is more dreadful for the COVID sufferers. The treatments used for COVID patients include a risk of infection therefore patients should be monitored by professionals, if possible or kept under watch for the various early symptoms of mucormycosis like blood-stained or black discharge from nose, localized pain, redness over the cheekbone or palate, redness of eye, headache and fever. CT or MRI are the two tests that are convenient for the scanning of mucormycosis. Amphotericin B, Isavuconazole, Posaconazole are the Drug of choice for Mucor infection. Regions like India which is an epicentre for diabetic patients have higher risks and so the first line of treatment preferably is liposomal Amphotericin B which is a potent broad spectrum fungicidal.

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