



Mucormycosis (The black fungus): A quick look

Abdullah Al Noman*, Honufa Akter, Md Maruf Parves

Department of Pharmacy, Brac University, Dhaka, Bangladesh

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Abstract

Mucormycosis is a fungal infection which is caused by a growing number of mucorales in the body. It infects people through air, soil, food or open wound. Generally, infecting immunosuppressed persons and people with Diabetes Mellitus, Diabetic ketoacidosis, organ transplant patients, autoimmune disorders, burns, and trauma. It has high mortality rate as well which can be up to 51%. As it is seen in immunosuppressed people, the people having weak immunity or disease that weaken the immunity or having treatments that affect our body's immunity are at risk of mucormycosis. Recently, mucormycosis is also found in COVID-19 patients. COVID-19 associated immune dysfunction and medication are a suspect for situation. This paper contain an overview to easily understand the diseases with recent and updated information.

Keywords: mucormycosis, black fungus

Introduction

Mucormycosis also termed as black fungus is a fungal infection caused by the zygomycete, mucorales and Entomophthorales [1-3]. Mucorales come together and generate various genera (e.g. *Mucor*, *Lichtheimia* [formerly *Absidia*], *Rhizomucor*, *Cunninghamella*, *Apophysomyces* spp., and *Saksenaea*) which cause infections, where *Rhizopus* is most common [2, 4]. In addition to that, Entomophthorales is causing acute infection in the patients with weakened immunity [4]. Maximum time, these mycocytes which cause infection are around the environment like soil or decaying organic matter but also can be found in air [5]. People most often affected by inhalation, swallowing with other foods or via open wounds [4]. In the current situation when the whole world is stunted because of COVID-19, this black fungus has added to the suffering. As the black fungus can not cause any pathogenic reaction to the persons having good immunity, it is more often seen in the patients of COVID-19 nowadays, either the patient is suffering from COVID-19 or a patient who has suffered earlier [1, 6]. Though it is alarmingly seen in COVID-19 patients now, but most common in people with immunity issues or Diabetes mellitus. A recent study shows that 40% people with Diabetes mellitus are at risk of Mucormycosis [4]. It is not commonly transmitted from person to person [7]. Site of infection includes Rhino-orbital-cerebral site, Pulmonary site, Cutaneous/soft tissue, Gastrointestinal sites also some less common infection sites are bone/joints, heart, peritoneum [4].

Signs and symptoms

Mucormycosis has a variety of signs and symptoms depending on where the infection is located in the body, and it can be classified into six categories based on the site of infection: (1) rhinocerebral, (2) pulmonary, (3) cutaneous, (4) gastrointestinal, (5) disseminated, and (6) uncommon presentations [8].

Rhinocerebral Mucormycosis

The sinuses and the brain are mainly affected and are the most frequent among all other types [8-10]. Signs and symptoms include:

- Fever
- Headache
- One-sided facial swelling
- Congestion in the nose or sinuses
- Black lesions on the bridge of the nose or the upper part of the mouth that swiftly worsen
- Blurry vision or loss of vision.

Pulmonary mucormycosis

Affect the lungs and are common in people who have had an organ or stem cell transplant in the past [8-11]. Signs and symptoms are:

- Fever
- Cough
- Chest pain
- Shortness of breath

Cutaneous Mucormycosis

The skin is associated with this, and in this case blisters or ulcers may appear, and the infected region may turn black. Pain, extreme redness, warmth, and swelling around a wound are some of the other symptoms [8, 9].

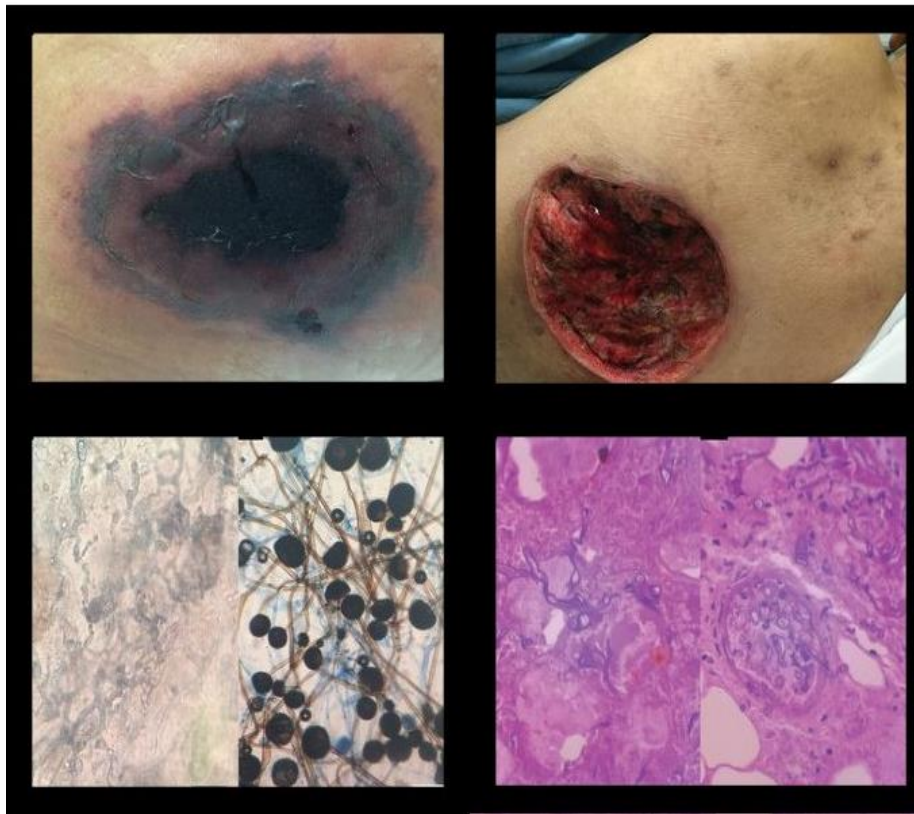


Fig 1: Cutaneous mucormycosis with histological examination ^[12].

Gastrointestinal mucormycosis: The symptoms are nonspecific this time, with stomach pain, distention, nausea, and vomiting. Hematochezia and fever are also noticed. Tenderness to palpation or a mass may be seen in certain patients. Peritonitis symptoms may develop as a result of the rupture ^[8, 9, 13].

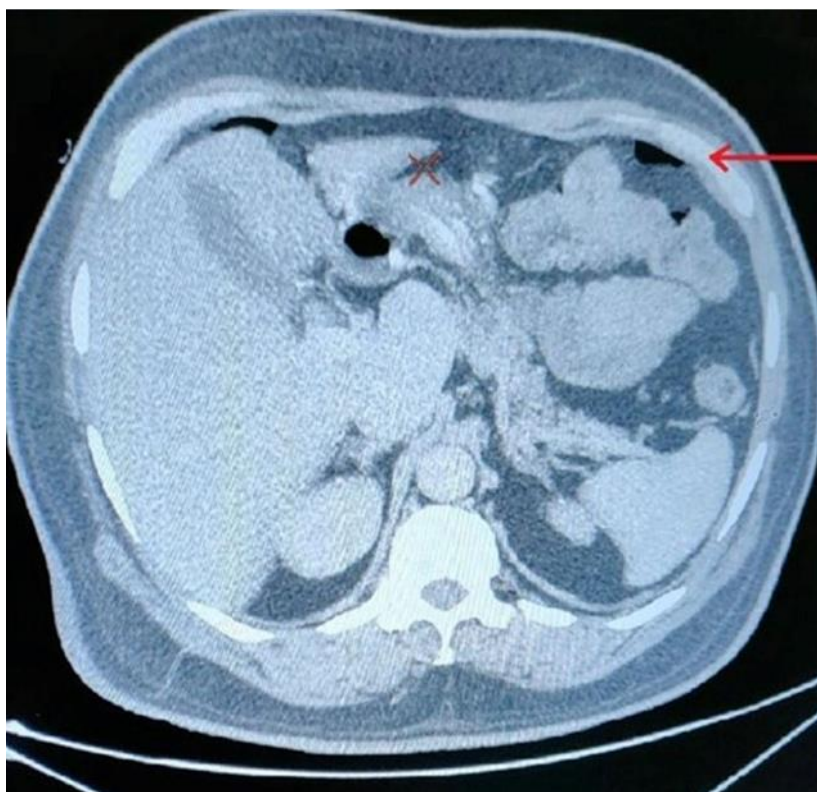


Fig 2: Gastrointestinal mucormycosis (CT scan view) (red arrow indicating the infected area ^[14]).

Disseminated mucormycosis

It's difficult to tell which symptoms are due to mucormycosis because it usually develops in patients who are already sick with other medical diseases. Usually, mental status changes or coma can occur in patients with disseminated infection in the brain [8, 9].

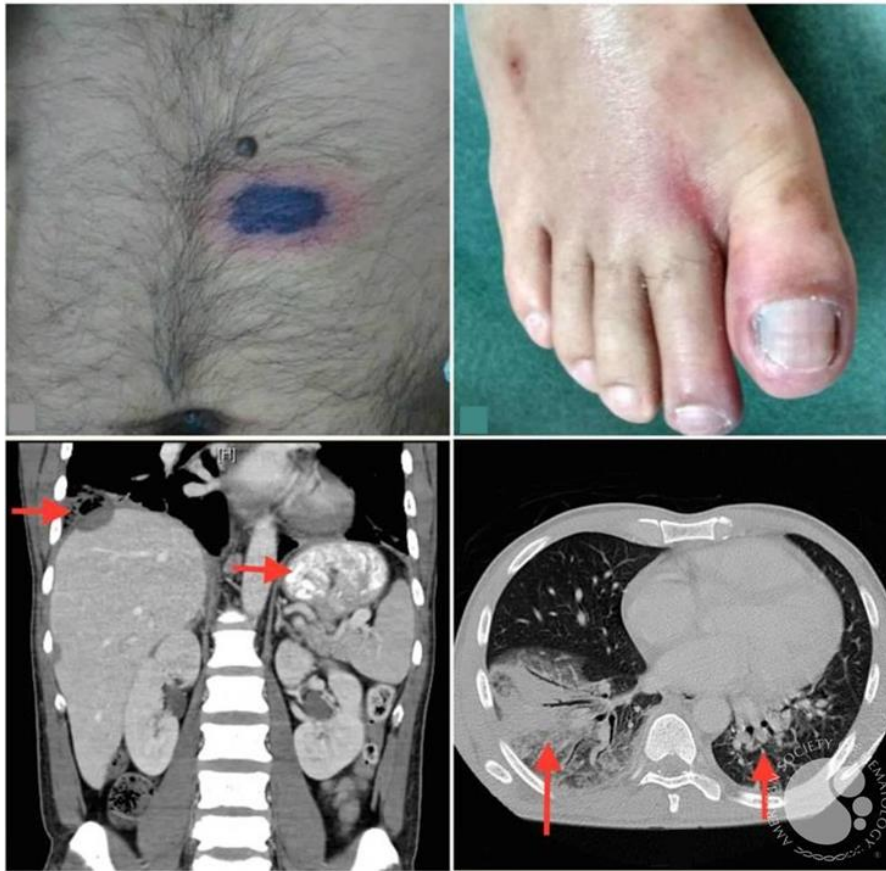


Fig 3: Disseminated mucormycosis (red arrow showing infected area) [15].

Uncommon presentations

Other types of mucormycosis can affect the kidneys, bones, heart, CNS, and other organ systems, causing symptoms to be attributed to these organ systems. Peritonitis has also been reported in the context of continuous ambulatory peritoneal dialysis. Central nervous system (CNS) disorder is characterized by headaches, a loss of consciousness, and localized neurologic symptoms/signs such as cranial nerve impairments. Patients suffering from CNS involvement may have a history of open head trauma, intravenous drug use, or cancer [8, 9].

Diagnosis

To diagnose mucormycosis Clinical tests of a patient such as medical history, symptoms, physical examination, imaging technique (CT scan) for internal infections, etc, and laboratory diagnosis are considered [16, 17]. A person who is suspected as infected after clinical tests goes through laboratory testing for diagnosis. This step involves tissue biopsy, where a small sample of infected tissue is analyzed in a laboratory under a microscope or in fungal culture for evidence of mucormycosis [17]. Fungi culture is also performed in the laboratory by collecting fluid samples from the respiratory tract to diagnose mucormycosis in the lungs or sinuses. Molecular techniques such as PCR are used for more precise diagnoses. [16, 17]

Causus of mucormycosis

Mucormycosis is caused by fungi, especially of the order mucorales, so it is a fungal infection [18]. Generally, it is caused by *Rhizomucor* and *Mucor* [19]. Less commonly by *Lichtheimia*, *Apophysomyces* [4]. These are commonly found in our environment like soil and air [7]. More often than or not we get infected by swallowing it with food or through open wounds [7, 18].

Risk factors

Several medical conditions are found to be associated with mucormycosis [18]. The main condition is be found to be Diabetes Mellitus, Diabetic ketoacidosis, Hematological Malignancies with Neutropenia, Hematopoietic Stem Cell Transplant Recipients, Organ Transplant, Human immunodeficiency virus (HIV) [7, 20-22]. There are also other risk factors which include Autoimmune disorders [23], Immunosuppressive therapy [7], Iron overload, Burns, Trauma [24], including surgery Peritoneal dialysis, Malnutrition, tuberculosis [25]. Now it's also seen in the

COVID-19 patients. It may be due to coronavirus damaging the immune system as the disease can not harm the active immune person so it is causing problems in COVID-19 patients [6, 26-28].



Fig 4: Risk factors of Mucormycosis.

Covid-19 associated mucormycosis (CAM)

Corona virus disease (Covid-19) is an infectious disease caused by Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) [29]. This is recognised as a pandemic which till a significant problem worldwide. As the global coronavirus outbreak increase some life threatening opportunistic fungal infection are observed to be increased and one of them is mucormycosis [27, 30-32]. Highly immunocompromised people, uncontrolled diabetes mellitus, drug-induced immunosuppression during transplantation, autoimmune disorders, hematological malignancies, and so on are all risk factors for this rare disease [27, 32]. Overusing of high-dose glucocorticoids and immunosuppressor drug facilitate the fungal infection and there is evidence that shows that COVID-19 is associated with immune dysfunction in addition with iatrogenic immunosuppression induced by these medications i.e. lymphopenia [33, 34]. The risk of hyperglycemia-induced immunosuppression mediated mucormycosis is increased due to the combination of steroid therapy and diabetes mellitus [35]. COVID-19-associated mucormycosis (CAM) may manifest as rhino-orbital involvement in this group of individuals, but it frequently includes other organs (e.g., pulmonary, gastrointestinal, and intracranial), leading to catastrophic results [36-39].

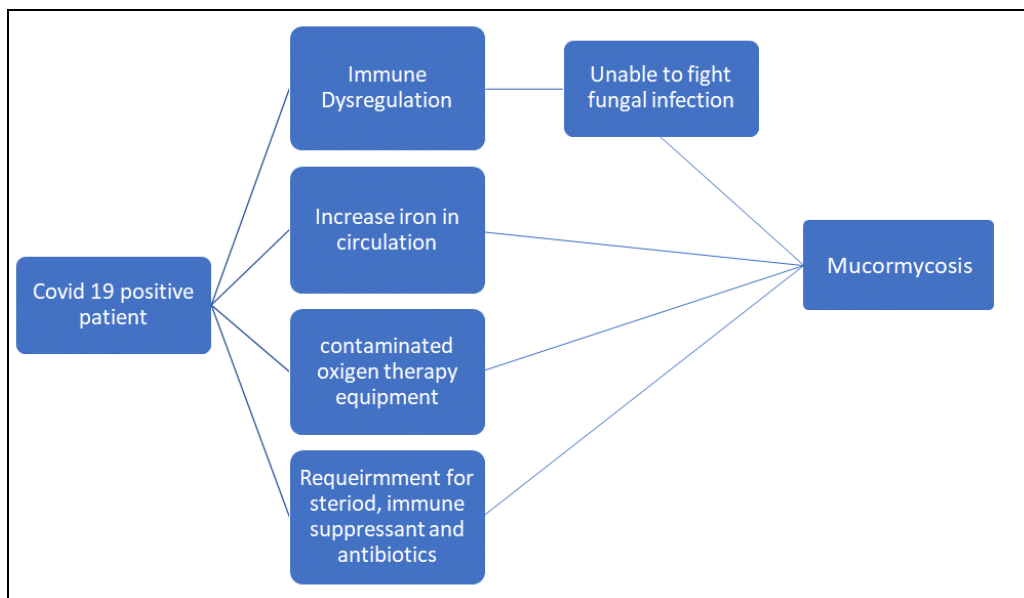


Fig 5: Pathogenesis of mucormycosis.

Figure.04: Covid-19 associated mucormycosis (CAM): with a dysregulated immune system, a COVID-19 patient is more susceptible to mucor mycosis and may be given immune suppressant medicines that hinder the body's phagocytic cells from fighting the fungus optimally [3]. COVID-19 also raises blood iron levels, which the fungus requires to grow and multiply, making the person more susceptible to infection. Infected with COVID-19, oxygen treatment is common. Contamination in these devices can cause mucormycosis. The steroid medication given to COVID-19 patients increases their risk [3].

Treatment for mucormycosis: Mucormycosis can be treated via several approaches like medication (e.g. antifungal drugs), surgical removal of the tissues which are infected, also by treating the underlying causes or a combination approach of the mentioned treatments [28]. It is now the standard treatment for mucormycosis to use lipid forms of amphotericin B [40-42]. Posaconazole may be useful as a last resort, but it can't be used as the main treatment for mucormycosis because of the available data [41, 42].

Pathogenesis of mucormycosis: Generally mucormycosis spreads through spore that's enter the body via inhalation or ingestion of adulterated food or being implanted in injured skin [1, 2]. To cause disease host pathogen interaction is necessary and after invading in host start to grow that leads to angioinvasion and dissemination [3]. Normally having a normal immune response host with intact skin and innate immunity is resistant to develop the disease but some factors such as neutropenia, hyperglycemia, immunosuppression, ketoacidosis and several other factor reduce host defense mechanisms [4-6]. As a result, this make increasing of serum iron which in turns helps to growth for pathogen. Since patients who has excess of iron are susceptible to mucormycosis [1]. Then interaction of fungal spore with epithelial cells promote host invasion as secretion of lipolytic or protease enzyme by mucorals has the ability to destroy stroma [7, 8]. After that, interaction with endothelial cells also facilitate angioinvasion. Since spore can attach to the endothelium cells that's promote endocytosis as result cell damage occur [1]. Apart from that mucorals can regulate the gene that's involved in pathogen identification and tissue repair mechanisms in that way promote fungal growth [1, 3].

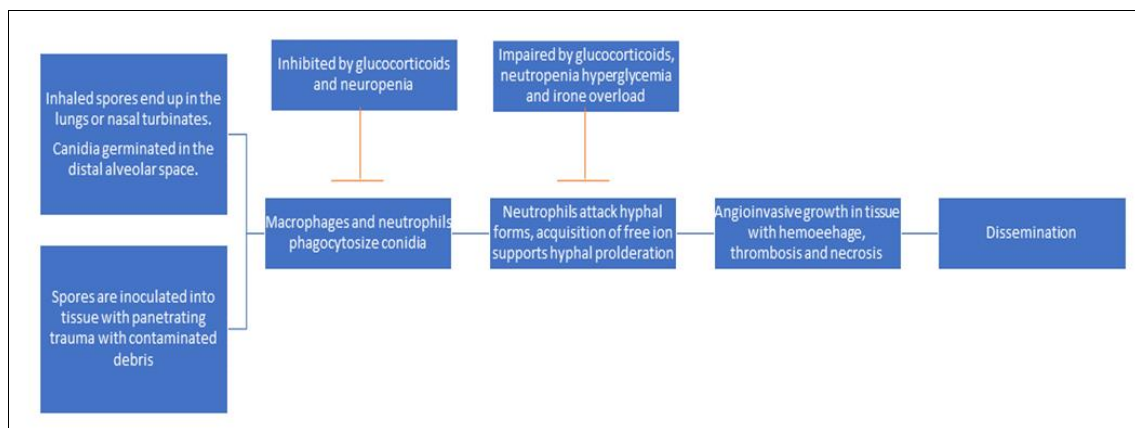


Fig 6: Pathogenesis of mucormycosis.

Prognosis

Mucormycosis tends to have rapid progress and it could be fatal for different cases that has notable mortality rate and this is up to 51% [43]. and the mortality rate mainly depends on the patients underlying condition, site of affected area and types of fungus. Such as mortality rate was 76% for the people who has pulmonary infection, 46% among the people of sinus infection, 96% for disseminated mucormycosis and 85% patients were died who has gastrointestinal infection [20]. In case of diagnostic delay mortality rate could be increased for the patients who has active malignant blood disease [44]. On the contrary, the mortality rate of skin involvement patient is lower compared to other conditions. There are several complications due to fungal infections such as blindness, loss of partial neurological function etc [45].

Conclusion

Mucormycosis is deadly fungal infection that is basically caused by host pathogen interaction and occurs mainly immunosuppressive patients. And in spite of having treatment there is high mortality rate depending on affected area. In addition, determination of fungal spreading is quite challenging though for that now various diagnostic tool has been developed for earlier detection. In consequence physician can take immediate measures for the treatment. However, if the fungal infection is not diagnosed earlier then there is a chance of increased mortality rate. So early diagnosis and intervention and therapeutic drug are the main anticipate to upgrade the condition of this deadly fungal infection

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Conflict of interest

The authors declare no conflict of interest.

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