Review Article

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Mucormycosis: Complication or Negligence!

Abstract:

As the COVID-19 pandemic continues to rush, several doctors have reported an increase in cases of mucormycosis infection, popularly known as 'black fungus', among patients recovering from COVID-19. As the mucormycosis crisis is increasing in India it is essential for every individual who has recovered from COVID-19 to identify the early alarming sign of this black fungal infection. Mucormycosis is a deep fungal infection that occurs as acute and aggressive forms infecting the air sinuses, brain, and lungs. The infection may cause severe pain behind eye and leads to blindness in the infected individuals. The loss of eyesight is begun when the fungus grows behind the eye due to compression of optic nerve. It can be life-threatening in severely immunocompromised patients. Several reports suggest that the oral and craniofacial region is highly susceptible to mucormycosisinfection. Probabilities for mucormycosis recovery depend on early diagnosis and treatment. The exact etiology of this infection is not evident. This fungal outbreak can be multifactorial may be due to steroid therapy, high glucose level in blood, free iron, or it may be hospital acquired.Careful vigilance is the key to catch the early signs of mucormycosis infection and initiate the appropriate management for successful clinical outcomes.

Key-words: mucormycosis, black fungus, comorbidities, diabetes, steroid therapy, hospital-acquired, outbreak.

Introduction:

Mucormycosis/Black fungus is a rare, life-threatening infection caused by fungi belonging to the order Mucorale.[1] It is caused by saprophytic like Rhizopus, Mucor, Cunninghamella, Rhizomucor, Saksenaea, Apophysomyces, or Lichtheimia.[2] Amongst all the pathogens "Rhizopusoryzae" is responsible for 70% of all cases of mucormycosis.[3] Rhizopus is also the chief pathogenic mycotic organism isolated from the patients of rhinocerebralmucormycosis.[4] According to the Centre for Diseases Control and Prevention (CDC), mucormycosis cases have an overall all-cause mortality rate of 54%. [5]

Mucormycosis naturally present in the environment and are identified on bread mold, soil, decaying vegetation/decaying organic matter like leaves, compost piles, animal manure, and rotting wood. 3-6 Fungal spores germinate to make hyphae within the host system upon entering the tissues. Hyphae are liable for the initiation of clinical symptoms, and persons with defective phagocytic function are in danger of developing an infection. [1]

Impaired phagocytic functions increase the hyphae levels within the blood vessels, which ends up in ischemia,

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thrombosis, and eventually infarction and tissue necrosis. In diabetic patients with ketoacidosis,elevated iron level is one of the promoting factors for the growth of mucormycosis. [6]

The optimal temperature for growth of this fungus is 28 to 30°C under aerobic conditions, with an incubation period of 2 to 5 days. Incubation begins with inhalation of the spores or their direct inoculation into abraded skin. [4]

Spread of Mucormycosis:

Black fungus (mucormycosis) is not contagious at all, and therefore, it cannot transfer from people to people or between people and animals. As the fungal spores naturally present in the environment, any individual who is coming in contact with these fungal spores can be infected by mucormycosis. But, not everyone exposed to these spores will get a fungal infection. People with a weakened immune system due to some underlying risk factors or comorbidities may be at an increased risk of contracting this type of infection.[6-7] Does it spread by hospital equipment's also? There are certain evidences in literature which reported the role of healthcare system or healthcare environment in the spread of mucormycosis.[12]

Risk Factors:

There are many predisposing factors for mucormycosis, but the major risk factor is uncontrolled diabetes mellitus. Other risk factors are categories as corticosteroid therapy, acidosis, neutropenia, organ or bone marrow transplantation, trauma, burns, malignant hematologic disorders, and therapy received by patients getting hemodialysis.[3,8-9] Apart from compromised immune system several studies have investigated whether mucormycosis infections may have seasonal patterns and also mucormycosis outbreaks that are likely to be healthcare-associated.[11,14] The black fungus is increasingly being seen in vulnerable patients in India, who are at high risk of mucormycosis like diabetes, cancer patient, and patient on long term steroids, organ transplantation or low neutrophil count.[8- 9]

Threat for Diabetic Patients:

Mucormycosis may become potentially fatal in some individuals including diabetics. Mycosis is understood to attack people that have compromised immune systems especially those with diabetes. The incidence of mucormycosis has also increased significantly in patients with diabetes which is that the commonest underlying risk factor globally. As fungal infections are opportunistic in nature and diabetes makes the immune system weaker. so, it is easier for the fungi to cause infection in a diabetic patient. Apart from this, diabetics are at a higher risk of mucormycosis since the fungi have a higher affinity for iron-rich, acidic environments, and diabetic ketoacidosis, a condition in diabetics that causes the blood to become acidic. [5, 10]

Healthcare-associated Mucormycosis:

The literature showed multiple reports of healthcare-associated mucormycosis, either as isolated cases or as outbreaks.[11] In 2009 Chakrabarti et al reported hospital-acquired mucormycosis cases in India, 75 cases of mucormycosis were reported during eighteen months, of which 9% were nosocomial.[12]

Mucormycosis associated with the healthcare system has been accredited to various exposures in the hospital environment.13 The use of non-sterile products like bandages, adhesives, contaminated linen, wooden tongue depressors, ostomy bags, nitroglycerin patches, and probiotics have all been implicated as a suspected cause of infection.[14] There has even been a report of an outbreak due to allopurinol tablets and prepackaged food also.[15- 18] It was also reported that various procedures and medical devices, such as catheters, insulin pumps, and finger sticks and insertion of tubes, tooth extractions, and surgery may promote fungal infection due to contamination. Outbreaks have also been linked to defective ventilation systems and water leakage.[19-20]

Environmental factors can also be a source of infection. These fungal molds can be found in the air, dust, water, or any surfaces in the hospital. Infections associated with bandages, adhesives, or contaminated wound dressings are mostly cutaneous while percutaneous exposure leads to disseminated infection specifically in immunocompromised patients. Inhalation exposure causes pulmonary and rhino-cerebral infection, whereas ingestion of tablets or food, and the use of tongue depressors, is responsible for gastrointestinal mucormycosis.[21]

Sign and Symptoms of Mucormycosis:

Any individual can contract mucormycosis by inhalation of fungal spores from the affected air. This is referred to as sinus (pulmonary) exposure. In turn, anyone can develop the infection in their central nervous system (rarer), lungs, eyes, and face. This fungal disease can also infect the skin (cutaneous exposure) by a cut, scrapes, or burn. The symptoms of mucormycosis vary according to the locationwhereit is developing in the body. The most common reported sites of invasive mucormycosis have been the

sinuses (39%), lungs (24%), and skin (19%) 22Dissemination developed in 23% of these cases. The overall mortality rate for the disease is 66% in patients with malignancies, 44% in diabetics, and 35% in patients with no underlying conditions.[22-23] There are six distinct types of mucormycosis with distinct clinical presentation.[23-26]

Six Distinct Clinical Presentations of Mucormycosis:[25, 26]

- Rhinocerebral
- Cutaneous
- Pulmonary
- Gastrointestinal
- Central nervous system
- Disseminated

Rhinocerebral Mucormycosis (Rocm):

Rhinocerebralmucormycosis (ROCM) also called zygomycosis. ROCM is a rare disease caused by filamentous fungi involving the nose, paranasal sinuses, and brain. This (ROCM) is the most common form of mucormycosis in patients with diabetes mellitus.[27-28] It can also infect patients with underlying malignancies, recipients of solid organ transplants or hematopoietic stem cells, and individuals with other predisposing risk factors. The inhalation exposure is the main cause of this infection which develops after inhalation of fungal sporangiospores into the paranasal sinuses. From the sinus, it rapidly extends into adjacent tissues. As it grows, the invading fungus may spread inferiorly to invade the palate, posteriorly to invade the sphenoid sinus, laterally into the cavernoussinus to involve the orbits, or cranially to invade the brain.[29]

Symptoms of Rhinocerebral (Sinus and Brain) Mucormycosis: [30-32]

- Headache on one side- behind the eyes and lethargy are the earlier presentation
- Nausea
- Fever
- Nasal congestion and rhinorrhea
- Epistaxis nasal hypoesthesia
- Facial pain and numbness
- Blurring of visions
- History of black nasal discharge and sinusitis
- Black lesions on the nasal bridge or upper inside of the mouth that quickly become more severe (A black necrotic eschar is the hallmark of mucormycosis)
- Eyelid edema, blepharoptosis, proptosis
- Convulsions, dizziness, altered mental status

Pulmonary Mucormycosis:

Pulmonary mucormycosis occurs due to the inhalation of fungal spores into the bronchioles and alveoli, which usually leads to the rapid progression of pneumonia or endobronchial disease. It may include end bronchial lesions and complications associated with airway occlusion. 33- 34

Symptoms of Pulmonary (lung) Mucormycosis: [35-36]

- Fever
- Cough
- Dyspnea (chest pain)
- Shortness of breath
- Hemoptysis (fatal)
- Progressive subcutaneous emphysema
- Bronchial perforation
- Pancoast syndrome, horner's syndrome

Cutaneous (skin) Mucormycosis:

It affects the skin and most common portal of entry through cuts, scrapes, burns, or any trauma in the skin. It May affects people with a strong immune system also. It looks like blisters or ulcers, and with due time the infected area may turn black due to necrosis. Other symptoms include pain, warmth, excessive redness, or swelling around a wound .[37]

Gastrointestinal Mucormycosis:

It affects the digestive tract and is more prevalent in young children than adults. The most peculiar symptoms of gastrointestinal mucormycosis includes abdominal pain, nausea and vomiting, gastrointestinal bleeding.[27, 37]

Disseminated Mucormycosis:

Disseminated Mucormycosisis a condition which occurs in people who are already sick from other medical conditions, so it can be difficult to know which symptoms are related to mucormycosis. The most commonly associated organ with disseminated mucormycosis is the lung. The infection can also spread throughout the body via the bloodstream. The infection usually attacks the brain and can leads to mental

status changes or coma. Disseminated mucormycosis can also target other organs including the spleen, heart, and skin. A metastatic skin lesion is an important hallmark in early diagnosis. [23, 37]

Alarming Signs of Mucormycosis: 38:

- Sinusitis including nasal blockage or congestion, nasal discharge (blackish/bloody), local pain on the cheekbone,
- One-sided facial pain,
- Numbness or swelling,
- Toothache, loosening of teeth, jaw involvement,
- Blurred vision or double vision accompanied with pain; fever, skin lesion; thrombosis & necrosis (eschar),
- Blackish discoloration over the bridge of nose/palate,
- Worsening of respiratory symptoms
- Chest pain, pleural effusion, hemoptysis

Conclusion:

As pandemic created conditions for the infection to thrive and spread via deadly "black fungal disease" also called mucormycosis. SARSCoV2 allowing the black fungi to take hold in the patients during or after recovery with COVID. India is a diabetic capital country and the majority of individuals who are diabetic and developed hypoglycemia due to steroids usage are affected with black fungus.High dose steroids which was used during pandemicsuppressed the immune system of an individual might be one of the major causes for other pathogens to take advantage over weakened immune system. Apart from steroids there are many hypotheses like hygiene, humidifier, oxygen line or repeated usage of moist mask may be one of the factors of fungal growth. We now know that besides hygiene, humidifier or oxygen therapy there are cases who has not received oxygen, no steroids and were at home isolation also developed mucormycosis. It might be due virus strain in second wave with prevalence of mucormycosis. It can be said that mucormycosis is one of the major complications of COVID-19 and still there are cases of black fungus which needs proper diagnosis and therapeutical intervention.

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