IJBPAS, May, 2023, 12(5): 2309-2318

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

MUCORMYCOSIS: BLACK FUNGUS INFECTION OF EYES IN POST-COVID-19 PATIENTS

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Received 09th June 2022; Revised 16th July 2022; Accepted 29th Sept. 2022; Available online 1st May 2023

https://doi.org/10.31032/IJBPAS/2023/12.5.7157

ABSTRACT

Mucormycosis or black fungus infection is a serious systemic infection caused by a group of fungi called *Mucormycetes*. The chances of getting this infection are more in COVID-19 patients after their recovery. The effects of COVID-19 infection, the use of antimicrobials, immunosuppression, and the need for ventilation during COVID-19 infection are all contributing factors to the incidence of this opportunistic infection. The pathogen can infect orofacial regions, lungs, and brain, causing multiorgan infection. Sensitive organs like eyes get infected and forced to be removed as no other alternative in saving the patient. Usually, the patients with cancer, uncontrolled diabetes, major trauma, organ transplantation, severe neutropenia, long-term corticosteroid usage, compromised immunity and who have recovered from COVID-19 are at significant risk of contracting the fungal infection as post COVID-19 infection making them blind with high mortality rates.

Keywords: COVID-19, Mucormycosis, Black fungus, CAM, CAPA, Eye

INTRODUCTION

Human beings are always under the constant threat of emerging novel viruses. Humankind is already witnessing one of the dreadful catastrophe in the form of novel Corona virus disease (COVID-19) pandemic hitting periodically in the form of first, second and third waves due to a severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and its mutants affecting nearly 10 million people; now added to it, COVID-19 associated Mucormycosis (CAM) has added fuel to the fire **[1]**. Mucormycosis commonly known as 'Black fungus' is not a new disease but an aggressive angio-invasive infection **[2-7]**. The rate of incidence ranged from 0.005-1.7 per million populations worldwide; on the contrary, its prevalence in India was appraised to be 140 per million populations. Individuals have lost their eyesight as a result of this rising pandemic disease of global catastrophe, which has also killed countless people and left many children orphaned. The novel corona virus patients can be attacked with two COVID-19 associated opportunistic fungal infections which include pulmonary Aspergillosis (CAPA) and mucormycosis (CAM) **[8-10]**. The COVID-19 associated mucormycosis (CAM) is a more complicated infection causing life-threatening situation in COVID-19 recovered patients during the B.1.617.2 Delta variant Corona virus pandemic (COVID-19 Second wave) with 31-50% mortality rates **[8, 9, 11]**. Due to its sheer magnitude of outbreak in India, all states were advised by The Indian Health Ministry to declare Mucormycosis as an epidemic **[12]**. The immunosuppressive therapy given during COVID-19 infection is an another reason for mucormycosis and other fungal infections such as Aspergillosis and Candidiasis in many countries like United States of America, India, Brazil, Italy and United Kingdom. Usually, the patients with cancer, uncontrolled diabetes, major trauma, organ transplantation, severe neutropenia, long-term corticosteroid usage, compromised immunity and who have recovered from COVID-19 are at significant risk of contracting the fungal infection as post COVID-19 infection with a mortality rate ranging between 31-50% and treating these patients is challenging task to the healthcare system **[13]**. It was reported from many places of the world with 70% of the cases being reported only from India due to high prevalence and impaired glucose tolerance **[14, 15]**. An uncontrollable sugar level is a favorable milieu for the fungal growth. The dreadful tri-combination i.e., diabetes, extensive use of

immunosuppressant steroids along with COVID-19 infection, nicknamed as 'unholy trinity' by James Kingsland **[16]** and 'triple whammy' by an expert of fungal infection, David Denning was considered to be the major cause for the surge in Mucormycotic infection **[17]**. Also, the hot and humid climates of tropical countries such as India serve as impeccable primary breeding grounds for the fungal growth. Mucormycosis, previously known as Zygomycosis was considered to be one of the rare and sevier opportunistic infection caused by the group of fungi known as *Mucorales* or *Mucormycetes* **[3, 18, 19]**. Even other fungi of the genus *Rhizopus*, *Lichthemia*, *Mucor* and *Rhizomucor* are commonly known to be associated with Mucormycosis.

About the Fungi

It is a common mold of the order *Mucorales*. It is a saprophytic soil organism growing on decaying organic matter. These fungi are omnipresent in nature and frequently observed in soil, plants, decaying fruits and vegetables, manure. Generally, the source of infection is environment, from air borne spores produced by the fungi. It is spread if spores are inhaled, or consumed by contaminated air and food respectively. This opportunistic infection in immunocompromised can spread to multiple organs like nose, sinuses, eye, tissues of the facial region and brain and can be mortal if left untreated **[20]**. It is not contagious. Biopsy and culture are used to diagnose the infection. Medical imaging can help in detection and find the extent of the disease. The disease has been reported to occur during natural disasters like tsunami, tornado and recently during the COVID-19 pandemic. Many scientists have reported different types of Mucormycosis infections with their pathophysiology after an impulsive upsurge in cases due to COVID-19 pandemic including India **[21-25]**. **This review mainly focuses on post covid-19 mucormycosis affecting the eye.** These fungi usually obstruct the blood flow and kill the infected tissue, causing it to become dead, necrotic, and resulting in black discoloration (Black Eschar). There are many complications documented during and post COVID infection **[26]**. The fungus enters the body by inhalation reaches lungs, paranasal sinuses. Earlier, medical professionals were not adequately educated or trained to treat COVID -19 infections, resulting in an unstructured treatment process, medication or self-medication involving unrestrained use antibiotics and steroids etc. The untested and inappropriate medication resulted in decrease or imbalance of normal flora of the intestine

and other organs, resulting in immune suppression and onset of opportunistic infections **[27]**. The excessive use of disinfectants and sanitizers also played a major role in imbalance of the normal flora and environmental microbial balance. People inhaled or even consumed sanitizers due to a lack of awareness on how to use them safely. Both lack of awareness and alcohol addiction made people to consume sanitizers accidentally or alcohol addicts drinking sanitizers intentionally and lost their lives **[28]**. Patients who have received high doses or a broad spectrum of antibiotics, as well as those who have spent days on ventilaton and corticosteroid therapy, are at a higher risk of developing mucormycotic infection. Other Patients with chronic diseases like diabetes, chronic renal failure, asthma, obesity, arterial hypertension and heart diseases are also reported group in getting mucormycotic infection **[6]**.

Types of Mucormycosis

There are reports of different types of mucormycosis i.e., rhino-cerebral, rhino-orbital, rhino-orbito-cerebral, pulmonary, cutaneous and disseminated or gastrointestinal mucormycosis **[29, 30]**. Most common being Rhino-orbito-cerebral followed by pulmonary mucormycosis. Mucormycosis infection also reported in the maxillofacial region such as mandible, maxilla, tongue, palate and orbitomaxillary/ infra-orbital region **[31]**. Early diagnosis should be done to the patients with complaints about soft tissue necrotic lesions of orofacial area. Mucormycosis begins at maxillary bone or nose and spreads to paranasal sinus to retro-orbital tissue and infects eyes, brain, lungs and other body organs also get affected. Early diagnosis, effective medicine, and surgical procedures all play a significant role in a patient's recovery. Most of the mucormycosis was detected within 10 to 14 days in diabetic patients who have recovered after hospitalization with severe respiratory illness caused by COVID-19 infection **[32]**. COVID-19 related mucormycosis can occur several weeks after COVID-19 infection. The diagnostic reports of mucormycosis showed abnormality in kidney function, sinus, eye, brain, lungs and gastrointestinal (GI) tract with extensive illness **[15]**. Mucormycosis was also diagnosed and identified in some fatalities during post-mortem **[33]**.

Symptoms

The clinical Symptoms of the disease include headache, cold, facial swelling and pain, appearance of black or necrotic lesions, pain in the infected area, eye discomfort, blurred vision, loss of smell, numbness, fatigue,

fever and loss of teeth. The manifestation of disease starts from oral cavity of nose and travels to the central nervous system through the eyes. In some instances, the infection starts from nose spreads to brain through sinuses **[34]**. The symptoms of mucormycosis vary depending on the location of the infection. Mucormycosis has emerged as severe post COVID complication with involvement of eye as an advanced stage after which it can affect the central nervous system and put into a life-threatening stage. Usually, the disease progresses with facial swelling, bulging of the eyes with blurred vision leading to decreased or loss of vision, black lesions in infected areas. When infection spreads to lungs symptoms such as fever, chest pain with difficulty in breathing, cough with blood were observed. Persistent respiratory symptoms can be observed for weeks and months after initial diagnosis in some patients **[35]**. Gastrointestinal infection has a clinical manifestation of stomach pain, vomiting, nausea, tissue damage at infected area and bloody diarrhea. As the mucormycosis infection also starts in maxillofacial area and its signs and symptoms are often confused with common dental problems such as dento-alveolar abscess, periodontitis, teeth mobility, edema, orofacial pain and slowly progresses towards eye causing Proptosis (bulging of eye); Ptosis (drooping of eyes); Chemiosis (swelling of tissue that lines eyelids and surface of eye), eye irritation and Ophthalmoplegia (paralysis or weakness of six extraocular muscles that controls eye movement) **[36]**. All the symptoms may combine with loss of visual activity called nystagmus. Further spread of the fungus and final progression into the cranial area with fever and headache is a dangerous situation leading to the impaired function of the cranial nerves referred as superior orbital fissure syndrome (SOFS). Early detection of the infection is essential for efficient antifungal medication treatment. However, the combined symptoms of SOFS with severe orbital involvement by the fungus involve the orbital exenteration through surgery to save the life of patient **[37]**. Invasive fungal infections in patients with immunocompromised and pre-existing co-morbidities require an early diagnosis, antifungal medication and debridement to reduce the morbidity and mortality rate **[31]**.

Treatment

Mucormycosis is a serious infection that requires antifungal medication such as amphotericin B, posaconazole, or isavuconazole. These medicines are administered intravenously (amphotericin B,

posaconazole, isavuconazole) or orally (posaconazole, isavuconazole). Many other antifungal medicines such as fluconazole, voriconazole and echinocandins are ineffective against fungi that cause mucormycosis. Often, mucormycosis requires surgery to cut away the infected tissue **[38]**. Physicians, dentists, pulmonologists and ophthalmologists must examine the patient's case history for COVID-19 infection and recovery, as well as know the specifics of their chronic infections, medications, and other therapies, before suspecting any common infections in the organs. They must thoroughly examine and diagnose suspected mucormycosis infection in order to save affected people's lives and crucial organs such as their eyes. Severe cases require high-dose of antifungal therapy for long-term involving surgical intervention which may be required to remove the infected site of the organ sometimes complete removal of the eye or both the eyes i.e., 'exenteration' **[39]**. Eye enucleation, dental extraction and removal of other infected tissue in the face are standard procedures for black fungus. There is currently no standard of treatment to aid physicians in determining when exenteration may be beneficial to a patient with mucormycosis.

CONCLUSION

Mucormycosis, an opportunistic fungal infection turned out to be a deadly disease during the COVID-19 pandemic. The occurrence of disease in Post COVID-19 recovered patients and vulnerable groups for the infection to avoid the contamination from fungal spores even after recovery from COVID-19. Inhaling spores can be avoided by taking precautions like wearing a mask in dusty environments. Wearing a hand gloves during gardening, using sanitizer and washing hands after touching soil or contaminated areas can prevent the occurrence of mucormycosis infection. It can be concluded that appropriate assessment, diagnosis, treatment and medical care must be followed in mucormycosis, a post COVID-19 infection.

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