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POST COVIDCALAMITY-MUCORMYCOSIS: AN OVERVIEW

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ABSTRACT

Corona virus disease (Covid-19) it had declared an emergency global pandemic that cause terrible effects on respiratory system and killing more than half billion lives. Diabetes has been reported as a risk factor for Mucor mycosis in 73.5% of cases in India. People with diabetes and obesity tend to develop more severe Covid-19 infections. This means they're more expected to take corticosteroids, which are frequently used to treat Covid-19. But the corticosteroids along with diabetes increase the risk of Mucor mycosis because it has been observed that peoples are affected with Mucor mycosis due to weekend immunity. Even a short course of steroid (5-14 days) results in Mucor mycosis. Mucor mycosis, colloquially known as black fungus, is an infection from the mucoromycetes group of fungi. The virus that causes Covid-19 can damage lung tissue and blood vessels, which could also increase susceptibility to different fungal infection. brain, causing headaches or seizures. So, damage to tissue and blood vessels from Covid-19 infection, treatment with corticosteroids, high background rates of diabetes in the population most brutally affected by the coronavirus are also getting affected by life threatening fungal infection called as Mucor mycosis. Several methods have deferred the mortality but still have a challenge in curing Mucorales.

Keywords: - Covid-19; Mucor mycosis; diabetes; corticosteroids; immunity. etc.

INTRODUCTION

Wide range of unscrupulous bacterial and fungal infections accompanying COVID-19 (Coronavirus disease 2019 produced by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)).^{9,10,11} COVID-19 patients are co-infected by mainly Aspergillosis and Candida fungal pathogens.¹²

People with diabetes and obesity tend to develop more severe Covid-19 infections. This means they're more expected to take corticosteroids, which are frequently used to treat Covid-19. But the corticosteroids along with diabetes increase the risk of Mucor mycosis. Even a short course of steroid (5-14 days) results in mucormycosis.⁸

A current summary of Covid-19-associated Mucor mycosis showed 94% of patients had diabetes, and it was poorly controlled in 67% of cases.

Nowadays number of cases is now much more probable to current wave of Covid-19 infections in India.¹³ Covid-19 patients infected with black fungus which is often termed as "Mucor mycosis" are reported from India.

The disease name "Mucor mycosis" was subsequently used by the American pathologist R. D. Baker to denote a mycosis caused by certain members of Mucorales.^{14,15}

Mucormycosis, previously known as zygomycosis, is the disease caused by the numerous fungi that belong to the fungal family "Mucorales".¹⁶ Fungi in this family are regularly found in the environment in soil, for example and are often allied with decaying organic material such as fruit and vegetables. Mucorales also found in decomposing food, bird and animal excretions, water and air around construction sites, and moist environments.¹⁷ They are more common in soil than in air, and in summer and fall than in winter or spring.^{18,19}

The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators.

The pathogenic species of Mucorales cause an acute angio-invasive infection primarily in immunocompromised individuals, whereas those of Entomophthorales produce chronic and subcutaneous infection mostly in immunocompetent individuals.²⁰

The name “zygomycosis” has been progressively used instead of mucormycosis for 2 reasons: firstly, mucormycosis resonances as though the disease is caused by *Mucor* species., not the most common causes of the disease, and (2) some infections caused by the species of Entomophthorales, although rare, are clinically not distinguishable from classic mucormycosis.²¹

Infection of mucormycosis in humans occur mainly in two forms²²as superficial and visceral²³ localized and disseminated. The characteristic superficial form is seen in external ear, fingernails and skin. On the other hand, Visceral forms are manifested as pulmonary, gastrointestinal and rhino cerebral types. These spores enters either through cutaneous or respiratory route. (E.g., contamination with spores while taking soiled food or by tainted needles).²⁴Based on anatomic localization, mucormycosis can be classified as one of 6 forms: (1) rhinocerebral, (2) pulmonary, (3) cutaneous, (4) gastrointestinal, (5) disseminated, and (6) uncommon presentations.^{25,26}

Rhinocerebral (sinus and brain) mucormycosis is an infection in the sinuses that can spread to the brain. This form of mucormycosis is most common in people with uncontrolled diabetes and in people who have had a kidney transplant.^{22,23}

Pulmonary (lung) mucormycosis is the most common type of mucormycosis in people with cancer and in people who have had an organ transplant or a stem cell transplant.

Gastrointestinal mucormycosis is more common among young children than adults, especially premature and low birth weight infants less than 1 month of age, who have had antibiotics, surgery, or medications that lower the body’s ability to fight germs and sickness.^{24,27}

Cutaneous (skin) mucormycosis: occurs after the fungi enter the body through a break in the skin (for example, after surgery, a burn, or other type of skin trauma). This is the most common form of mucormycosis among people who do not have weakened immune systems.

Disseminated mucormycosis occurs when the infection spreads through the bloodstream to affect another part of the body. The infection most commonly affects the brain, but also can affect other organs such as the spleen, heart, and skin.

Generally, we inhale number of spores of fungi everyday but due to healthy immune systems and lungs prevent them causing an infection. But if the lungs are damaged and immune system is suppressed it produce different infection.

Fungi in the Mucorales family are considered devious, meaning they usually infect people with a weakened immune system, or with damaged tissue.

Damaged tissue can occur after suffering or surgery due to use of drugs which suppress the immune system such as corticosteroids can lead to weakened immune function, as can a range of other immunocompromising conditions, like cancer or transplants.²¹

There are three ways humans can be affected by mucormycosis: first by swallowing spores in food or medicines, secondly by inhaling spores and last by swallowing spores in food or medicines, or when spores contaminate wounds.^{28,29} Among these three ways, inhalation is the most common.

In case of patients being treated for severe Covid-19, lungs are damaged. These spores can grow in our airways or sinuses, and occupy our bodies' tissues.

As mucormycosis can be obvious in the lungs, but the nose and sinuses are the most common site of mucormycosis infection.³⁰ From there it can spread to the eyes, possibly causing blindness, or it can also affect the skin, the intracranial involvement of mucormycosis increases the fatality rate to as high as 90%.³¹ For the many patients affected with mucormycosis, the outcome is poor. About half of patients affected will die and many will bear permanent damage to their health.

Mucormycosis can spread to the eyes, possibly causing blindness, or the brain, causing headaches or seizures. Patients arrive late, when they are already losing vision, and doctors have to surgically remove the eye to stop the infection from reaching the brain.

Steroids reduce inflammation in the lungs for Covid-19 and appear to help stop some of the damage that can happen when the body's immune system goes into overdrive to fight off coronavirus. But they also reduce immunity and push up blood sugar levels in both diabetics and non-diabetic Covid-19 patients.

If diabetes is poorly controlled, blood sugar is high and the tissues become relatively acidic is the good environment for Mucorales fungi to grow. This was identified as a risk for mucormycosis in India (where diabetes is progressively prevalent and often uncontrolled) and worldwide well before the Covid-19 pandemic.

Collectively, these findings suggest an unholy trinity of mucormycosis, diabetes and steroid in people with COVID-19.

Mucormycosis can also develop on the skin after the fungus enters the skin through a cut, scrape, burn, or other type of skin trauma.

Spread

People get mucormycosis through contact with fungal spores in the environment. For example, the lung or sinus forms of the infection can occur after someone inhales the spores

from the air. A skin infection can occur after the fungus enters the skin through a scrape, burn, or other type of skin injury.

Symptoms

Mucormycosis have the different symptoms rhinocerebral mucormycosis include discrete blackish discolouration on the bridge of the nose, pain on only one side of the face, cheekbones, with lack of sensation and bulgingsinusitis, along with clogging of the nasal tract and bloody or blackish mucus emission from the nose prominent aching in teeth, jawbone, degrading of tooth structures, objects appearing blurred or in double, with eye pain abnormal blood clotting or thrombosis of tissues, along with skin injury and damage or necrosis of dermal cells and deterioration of respiratory functions, with chest pain. Pulmonary mucormycosis comprise shortness of breath with fever, cough and chest pain. Abdominal pain, nausea, vomiting and gastrointestinal bleeding are observed due to gastrointestinal mucormycosis.

Prevention and treatment

Diagnosis and prevention as early as possible are important. This includes control of blood sugar, urgent removal of dead tissue, and antifungal drug treatment. These infections are difficult to manage for several reasons.³²If infections not diagnosed early and access to treatment is limited. This was the case in India prior to Covid-19.

Rhino-cerebral mucormycosis is the most common form in patients with diabetes mellitus,³³while pulmonary mucormycosis occurs most often in patients with hematological malignancies.³⁴

Simple preventive measures we have to take for lowering the chances of getting mucormycosis post COVID-19 recovery, like 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 do 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 by taking care this we can try to protect ourself from environment.

By taking antifungal medication mucormycosis infection can be also prevented.

Controlling these fungal infections will require increased awareness, improved tests to diagnose them early, along with a focus on controlling diabetes and using corticosteroids

wisely. Patients will need access to timely surgery and antifungal treatment. But there also needs to be more research into prevention of these infections.

Antifungal therapies include AmBDexycholate, Liposomal AmB (5-10mg/kg), AmB lipid complex, AmB colloidal dispersion, Posaconazole (400mg bid) and manage of core conditions. Second-line treatment includes combination of caspofungin and lipid AmB, mixture of lipid AmB and Posaconazole, not grouping with Deferasirox is suggested.³⁵

In case of soft tissues, cerebral disseminated, localized pulmonary lesion and rhino-orbito-types surgical treatment should be considered.³⁵

CONCLUSION

Secondary fungal infection in an immunocompromised SARS-CoV-2 infected patients a rare occurrence due to the mixed presence of *A. fumigatus* and a Mucorales species.²⁵The second wave of the COVID-19 pandemic has hit India hard.

There have been very few mucormycosis infections associated with Covid-19 in countries other than India. But here could be main factor in India is diabetes which show more possibility of mucormycosis which is colloquially known as black fungus.³⁶

A recent summary of Covid-19-associated mucormycosis showed 94% of patients had diabetes, and it was poorly controlled in 67% of cases. Expansion into the sinus or intracranial compartments can lead to neurological impairment.^{35,36}Especially the intracranial involvement of mucormycosis increases the fatality rate to as high as 90%

The virus that causes Covid-19 can damage airway tissue and blood vessels, which could also increase susceptibility to fungal infection. brain, causing headaches or seizures.

So, damage to tissue and blood vessels from Covid-19 infection, treatment with corticosteroids, high background rates of diabetes in the population most brutally affected by the coronavirus, and, importantly, more prevalent exposure to the fungus in the environment are all likely to be playing a part in the situation we're seeing with mucormycosis in India.

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