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Covid Associated Mucormycosis

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ABSTRACT
Mucormycosis is an infection caused by a group of filamentous molds within the order Mucorales. Infections may result from ingestion of contaminated food, inhalation of spores into the nares or lungs, or inoculation into disrupted skin or wounds. In developed countries, mucormycosis occurs primarily in severely immunocompromised hosts (e.g., those with hematological malignancies, organ transplantation, neutropenia, autoimmune disorders, or other impairments in immunity). In contrast, in developing countries, most cases of mucormycosis occur in persons with poorly controlled diabetes mellitus or in immunocompetent subjects following trauma. Mucormycosis exhibits a marked propensity to invade blood vessels, leading to thrombosis, necrosis, and infarction of tissue. Mortality associated with invasive mucormycosis is high (> 30-50%), with 90% mortality associated with disseminated disease. Mortality rates are much lower, though still significant (10-30%), among patients with localized cutaneous disease.The diagnosis of mucormycosis relies upon histopathology and culture. Blood tests are of limited diagnostic value. Even with disseminated disease, blood cultures are usually negative. Mucorales have a distinct histological appearance, with irregular, nonseptate hyphae that branch at right angles. Among diabetics, rhino-orbital-cerebral mucormycosis (ROCM) is the most common clinical presentation, whereas lung involvement is uncommon. In contrast, among organ transplant recipients or patients with hematological malignancies (HemeM), pulmonary and disseminated diseases are most common. Mucormycosis can progress rapidly, and delay in initiation of treatment by even a few days markedly worsens outcomes.Due to the rarity of mucormycosis, randomized controlled therapeutic trials have not been performed. Lipid formulations of amphotericin B (LFAB) are the mainstay of therapy, but the newer triazoles, posaconazole (POSA) and isavuconazole (ISAV) (the active component of the prodrug isavuconazonium sulfate), may be effective in patients refractory to or intolerant of LFAB. Early surgical debridement or excision plays an important adjunctive role. Additional studies are required to assess the optimal duration of therapy as well as the specific roles of LFAB and the triazoles in the treatment of mucormycosis.[1]

KEYWORDS : Mucormycosis; Mucorales; Patients; Fungal infections; Amphotericin B; posaconazole; isavuconazole

I. INTRODUCTION

Coronaviruses are a large family of viruses that are known to cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).A novel coronavirus (COVID-19) was identified in 2019 in Wuhan, China. This is a new coronavirus that has not been previously identified in humans.India continues to battle the second wave of COVID-19 and has recently reported the highest number of cases . As severe COVID-19 continues to claim thousands of lives in this country, there has also been a recent cases of COVID-19-associated mucormycosis (CAM) have gained attention globally.[2]

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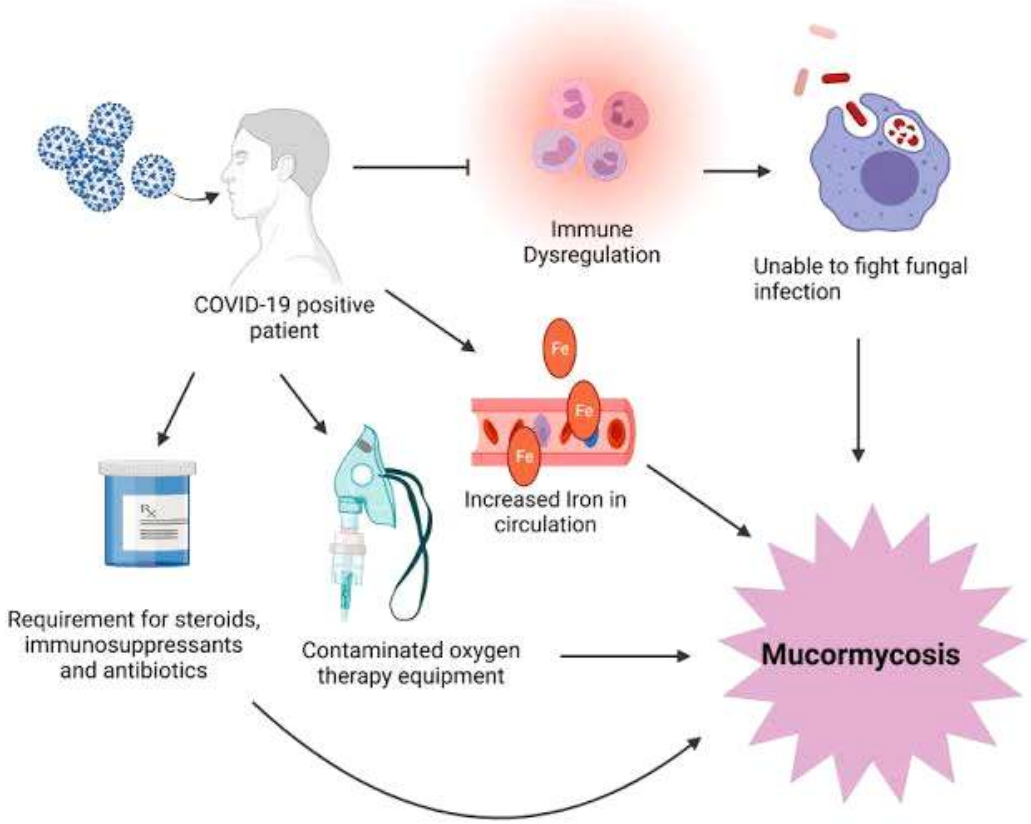

[3]

Mucormycosis is an opportunistic fungal infection of the zygomycete family that can cause various types of infections. In most cases, there exist underlying conditions that predispose the hosts to the infection. As the fungi responsible are typical environmental organisms, they are usually non-pathologic in immunocompetent individuals

Mucormycosis is caused by molds belonging to the order Mucorales, which are commonly found in the soil, on plant surfaces, decaying fruits, veggies and animal manure. Most mucor molds are incapable of infecting humans because they do not grow at body temperature. However, thermotolerant species, such as those isolated from COVID-19-associated mucormycosis (CAM) cases in India, can cause opportunistic infection; and when they do, it's serious.[2]

Types of Covid Associated Mucormycosis

1. Rhino orbital cerebral mucormycosis
2. Pulmonary mucormycosis

RHINOCEREBRAL MUCORMYCOSIS

Rhinocerebral mucormycosis, commonly known as zygomycosis, is a rare fungus-related disease that affects the nose, paranasal sinuses, and brain. It's an opportunistic pathogen that thrives in immunocompromised people. The fungus grows quickly and aggressively as a result of its interaction with immunocompromised patients, generating a well-defined fulminant and life-threatening condition. To preserve lives and avoid chronic neurological consequences, early intervention is critical. In most cases, it is an acute fungal infection, although chronic presentations have been recorded as well, which are indolent and slowly progressive over several weeks. Saprophytic fungi of the class Phycomycetes, order Mucorales, and family Mucoraceae are the causal agents of rhinocerebral mucormycosis.Mucor, Rhizopus, Absidia, Cunninghamella, and Apophysomyces elegans are among these fungi. In immunocompromised people, the most common route of infection is inhalation of spores from fungus dwelling in soil or organic debris. Because it is an opportunistic infection, it benefits from a weakened host immune system and a favourable host environment, such as hyperglycemia and iron overload. It thrives in hot, humid climates and

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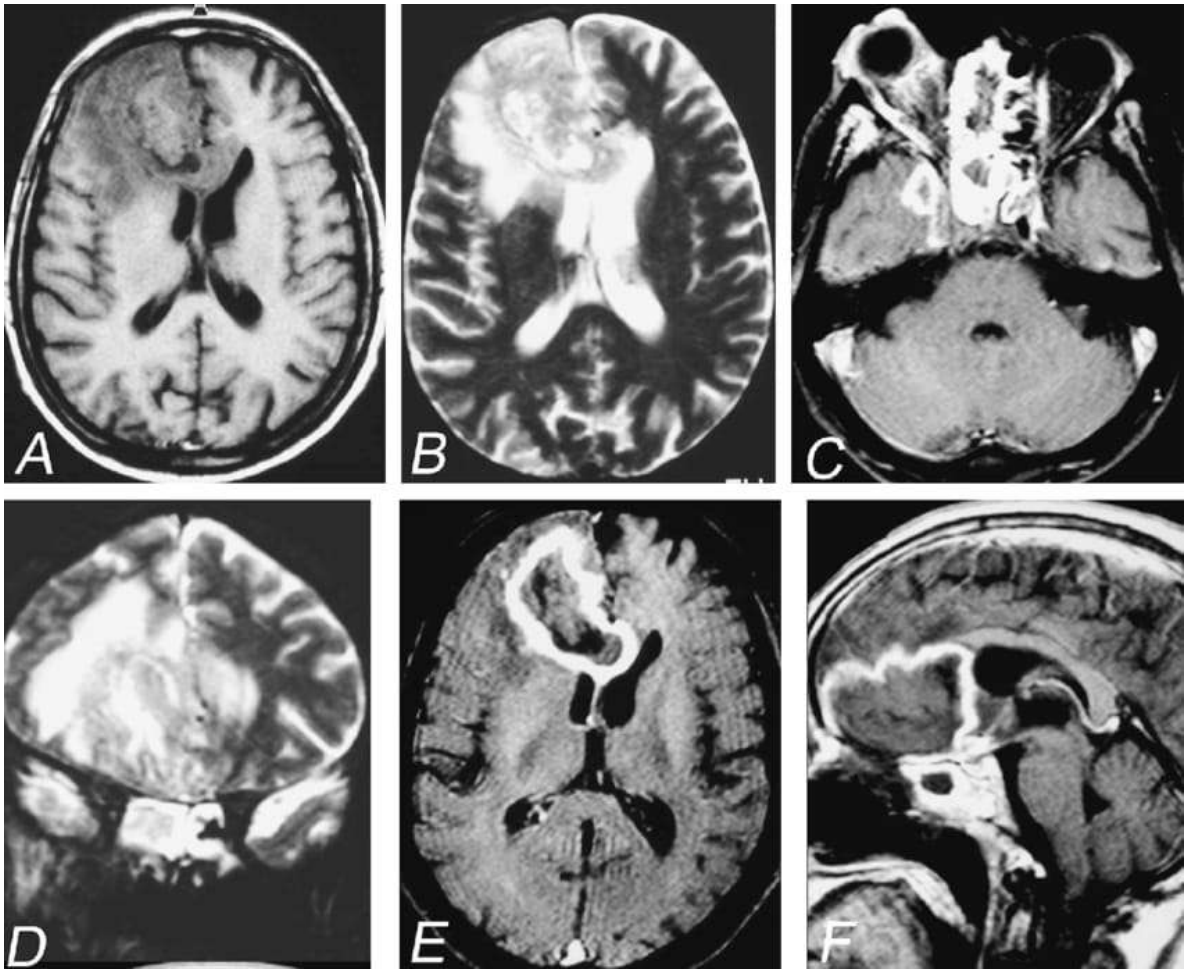
environments, particularly in tropical places and throughout the summer season.[4]



[13]

Chest computed tomography images of pulmonary mucormycosis-suspected findings in Cases 1-4. The red circles in the images of Cases 1, 2, and 4 show multiple small nodules. The red arrows in the image of Case 1 show diffuse infiltration partly surrounded by a thick, wall-like consolidation. The red circles in the image of Case 3 show two nodules with the reversed halo sign.[13]

The following are some of the symptoms of rhino orbital cerebral mucormycosis: [5]

- face edoema on one side
- Headache
- Congestion in the nose or sinuses
- Black sores on the bridge of the nose or the inside of the lips that swiftly worsen
- Fever

Diagnosis

It is important to notice that because the fungus stays predominately intravascular, a CT scan without contrast may not reveal any lesion if no mass is formed.

Imaging studies may include CT/MRI of orbit, brain and sinuses demonstrate involvement of maxillary and ethmoid sinus, orbit, cavernous sinus and less frequently involve the frontal and sphenoid sinus. In order to obtain a true diagnosis of mucormycosis, a fine needle aspiration biopsy of infected tissues must be obtained for histopathology and culture. Characteristic of this disease is aseptate hyphal elements that branch at right angles .

The most common areas to be involved are nasal cavity, maxillary sinus, ethmoid sinus and orbit.[6]

On MRI, it is common to see isointense lesions (when compared to brain) in T1-weighted

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images. Most of the patients show hypointense T2-weighted images. When cavernous sinus involvement, the cavernous sinus will show "lack of enhancement".

Because the fungus is primarily intravascular, a CT scan without contrast may not identify any lesion if no mass has developed.

CT/MRI scans of the orbit, brain, and sinuses reveal involvement of the maxillary and ethmoid sinuses, orbit, and cavernous sinus, with the frontal and sphenoid sinuses being less commonly involved. A fine needle aspiration biopsy of infected tissues for histopathology and culture is required for a proper diagnosis of mucormycosis. Aseptate hyphal components branching at right angles are a feature of this disease.[6]

Nasal cavity, maxillary sinus, ethmoid sinus, and orbit are the most commonly affected locations.

In T1-weighted MRI scans, isointense lesions (when compared to the brain) are prevalent. The majority of the patients have T2-weighted pictures that are hypointense. When the cavernous sinus is involved, there will be a "lack of augmentation" in the cavernous sinus.

A study of patients with mucormycosis in the midface and skull base found the following signs.

- There is no damage to the sinus walls.
- Changes in inflammation
- Involvement of the carotid artery with the cavernous sinus
- Only the hard palate has been isolated (one patient)

Finally, biopsies and cultures are the gold standard diagnostic method. H+E (hematoxylin and eosin), PAS (periodic acid-Schiff), and GMS (Grocott-methenamine Gomori's silver) were used for histopathological confirmation. [6]

Risk factors

Uncontrolled diabetes, especially with acidosis or ketoacidosis, steroid therapy, solid organ or hematopoietic stem cell transplant patients, chemotherapy, hematologic dyscrasias, retroviral illness, and malnourishment are all risk factors for rhino-orbital cerebral mucormycosis.

Patients on deferoxamine medication, iron overload, and intravenous drug usage all have a higher prevalence[7]

Treatment

Excessive surgery, systemic antifungal treatment with amphotericin B (AmB), posaconazole, and terbinafine, as well as hyperbaric oxygen, were all beneficial in treating rhino orbital cerebral mucormycosis (ROCM).

Infected regions are removed both extracranially and intracranially.

Endoscopic sinus and skull base surgery with local AmB implantation and an Ommaya reservoir for 114 intrathecal AmB administrations were performed.[8]

PULMONARY MUCORMYCOSIS

Pulmonary mucormycosis (PM) is a rare fungal infection that most commonly affects immunocompromised people. The fungus feeds on decomposing food, dirt, and animal waste. Inhalation of spores is the most common way for patients to become infected. Diabetes, hematologic malignancy, and solid organ or stem cell transplant are the most common risk factors. At imaging, PM can appear to be generic. Early imaging, for example, may reveal peribronchial ground-glass opacity. Consolidation, nodules, or masses develop later in the disease's progression. Because the majority of patients are immunocompromised. Due to rapid local progression and extensive angioinvasion, this infection has a high death rate (40–76%) and severe morbidity in some cases. Depending on the immunological condition of the host, the clinical appearance might range from acute to subacute.[9]

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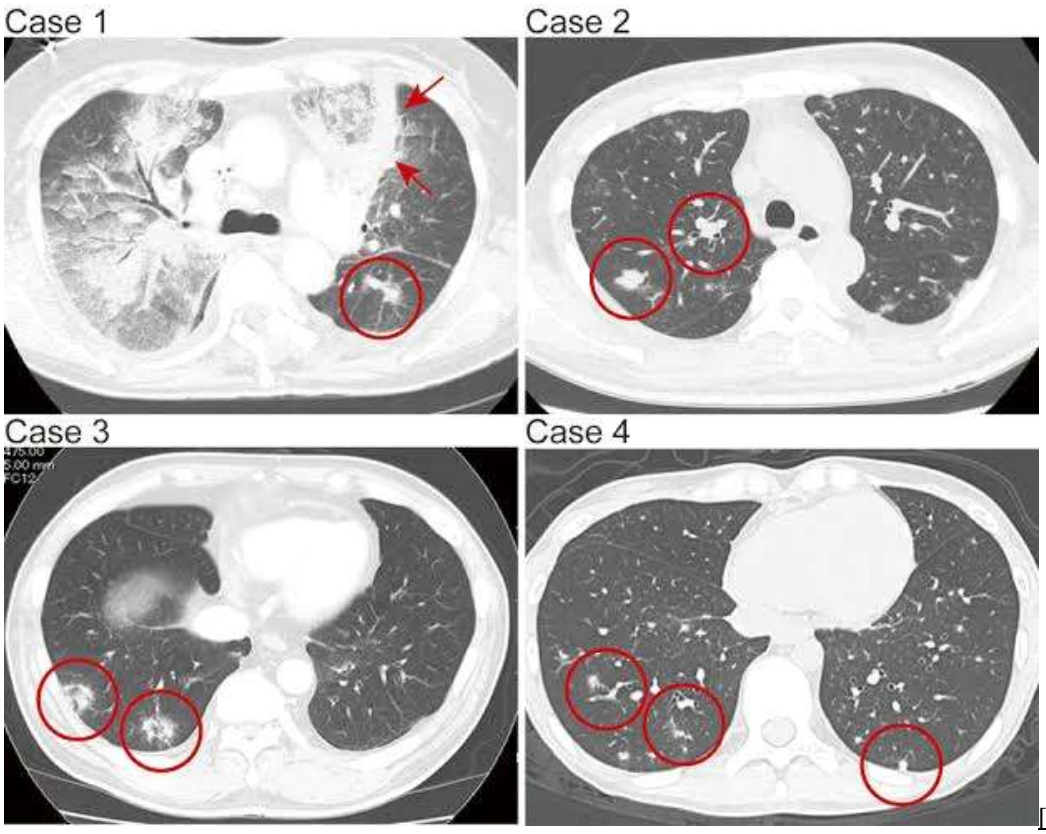

[10]

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Symptoms of pulmonary mucormycosis include the following:

- Fever(>38°C)
- Cough
- Pain in the chest
- Breathing problems [5]

Diagnosis:

Lung mucormycosis is a difficult-to-diagnose pulmonary fungal illness that has no effective treatment.

The diagnosis of pulmonary mucormycosis was made after a culture of mucus acquired by bronchoscopy.

In 474 cases of invasive lung fungal infections, the four most common diagnoses were pulmonary aspergillosis, pulmonary candidiasis, pulmonary coccidioidomycosis, and pulmonary mucormycosis, according to the Chinese Medical Association Respiratory Branch.[11]

Risk factors:

Uncontrolled diabetes, hematologic malignancy (particularly acute leukaemia), stem cell transplant, solid organ transplant, neutropenia, deferoxamine medication, and corticosteroid use are all risk factors for mucormycosis. [12]

Treatment:

Amphotericin B is a polyene antifungal medication that has been used to treat mucormycosis. Amphotericin B susceptibility varies by mucormycosis, and the drug concentration of Amphotericin B in the lung is lower than in other tissues. As a result, pulmonary mucormycosis infection need a larger Amphotericin B dose. For a total treatment term of 1–3 months, the cumulative dose can reach 30 mg/kg, and the

total dose can reach 2,500–3,000 mg. A previous study revealed that Liposome amphotericin B was safer than amphotericin B alone, with a better effect and lower accumulated dose.[11]

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Antifungal medicines such as itraconazole and voriconazole, in addition to the effective Amphotericin B, may be a clinical choice.

Posaconazole, a new triazole fungicide, is superior to voriconazole and fluconazole for those who cannot tolerate the traditional medicine or for whom the drug has no effect. Due to mucormycosis creating angiemphraxis, the antifungal drug may not reach the infection's source; hence, when the antifungal drug fails to work, pulmonary lobectomy is recommended. [11]

II. CONCLUSION:

Mucormycosis is a potentially lethal invasive and fast spreading fungal illness.Most mucor molds are incapable of infecting humans because they do not grow at body temperature. However, thermotolerant species, such as those isolated from COVID-19-associated mucormycosis (CAM) cases in India, can cause opportunistic infection; and when they do, it's serious.Here we have discussed two types of covid associated mucormycosis 1.Rhino orbital cerebral mucormycosis and 2.Pulmonary mucormycosis.

Rhinocerebral mucormycosis, commonly known as zygomycosis, is a rare fungus-related disease that affects the nose, paranasal sinuses, and brain. Pulmonary mucormycosis (PM) is a rare fungal infection that most commonly affects immunocompromised people. In this article we have discussed sign and symptoms, diagnosis, risk factors and treatment of both rhino orbital cerebral mucormycosis and pulmonary mucormycosis.

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