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MUCORMYCOSIS AND COVID-19

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Abstract

The term mucormycosis encompasses a distinctive group of infections caused by fungi belonging to genera within the taxonomic order Mucorales, usually Rhizopus, Absidia, Mortierella, and Mucor. These fungi are widespread in nature, subsisting on decaying vegetation and diverse organic materials. Mucormycosis commonly labeled as 'black fungus,' a rare but potentially fatal fungal infection, caused by the mucormycetes, a group of molds, with Rhizopus and Mucor as the most common species. The etiology of the sudden rise appears to be multifactorial in nature with several hypothesis linking mucormycosis to severe Covid-19 patients who are immune compromised and/or have associated comorbidities. Early diagnosis and prompt initiation of treatment is crucial as the condition can progress rapidly with fatal outcome. The treatment for this condition is based on a combination of antifungal medication and aggressive surgical debridement of necrotic tissue if necessary. The recommended anti-fungal drug is Liposomal Amphotericin B on a dose of 5 mg/kg/day.

INTRODUCTION: In human history, one of the most common diseases that we have faced has been a fungal infection known by the name of mycosis. Most of these result from opportunistic conditions where the host resistance impairment allows the initiation and progression of pathogenic conditions through local colonization in the oral cavity. The prevalence of these infections rises along with the use of immunosuppressive medications and immune deficiency virus diseases.[1] According to the most recent studies, there has been a marked increase in the incidence of mucormycosis in COVID-19 patients both during hospitalization and after discharge in various regions of the nation.[2]

Mucormycosis is a life-threatening deep fungal infection due to fungi of the Mucorales species first described by Paultauf in 1885 and nearly after 58 years case series was reported by Gregory et al in 1943.[3] Different myocytes such as Rhizopus, Mucor, and Lichtheimia along with 24 species of other mucorales cause Mucormycosis. These fungi are typically nonpathogenic in healthy individuals, but they can develop into opportunistic infections in patients with complex medical conditions, which can result in high rates of morbidity and even mortality. Inoculation occurs by inhalation of spores and the nose, paranasal air sinuses, and lungs are the most common sites of involvement.[4] The incidence of mucormycosis is estimated to be 1.7 cases per million people per year.[5] Often associated with compromised immunity patients, it presents with characteristic black necrotic eschar and necrosis.[6]

The infection may present as local necrotic ulceration that can result in hematogenous spread leading to fulminant infection and death. Among the several clinical forms of this disease, the rhino-orbito-cerebral form is of particular significance to the oral clinician as it can manifest in the orofacial region. The germs can be found in the head and neck, nose, sinuses, throat, and oral cavity, although pulmonary and sinus infections are the most prevalent types of infection. The fungus known as Candida is the source of the fungal infection known as white fungus.

It is an invasive fungus that can harm the mouth, heart, lungs, brain, kidneys, nails, and nails. It is significantly worse than black fungus and circulates throughout the body after entering circulation. White fungus infection, however, is not an infectious illness. An environmental Candida fungus is the responsible organism for white fungus infection. Candida mould spores enter the body of the vulnerable person through badly cleaned medical equipment, such as oxygen cylinders. This results in a white fungal illness.

MUCORMYCOSIS AND COVID-19: WHY IS THERE A CONCERN?

Mucormycosis is not a new disease and is known to occur in patients with low immunity such as in uncontrolled diabetes, post-transplant, and some cancer treatments. It occurs mainly in COVID-19 patients who have recently recovered due to COVID-19 infections because medications such as rampant overuse and irrational use of steroids, and broad-spectrum antibiotics

during the management of COVID-19 infection cause immunosuppression. Furthermore, overuse of steroids causes the development of new onset of diabetes which again is a risk factor for oral mucormycosis. The COVID-19 infection itself is linked to leukopenia and has the potential to cause immunological impairment due to suboptimal or unsuitable immune responses. Dental experts should take a past medical history before beginning any dental treatment since mucormycosis infection can happen during COVID-19 illness or after a few weeks of apparent recovery from it.[7]

CLINICAL PRESENTATION:

It is generally variable but usually, it is around 3rd week of onset of symptoms of COVID-19. Mucormycosis of the oral cavity is usually due to transpalatal extension of rhinocerebral infection, and mucormycosis localized to the periodontal tissues (i.e., gingiva and alveolar bone) (Figure 1).[8] Periodontal treatment aimed more at preserving and restoring the periodontal health rather than focusing on the aesthetic outcome of the treatment.[9]

Every infection in the oral cavity presents with a variety of clinical manifestations that can be related to some systemic infection or condition causing the periodontal changes (Figure 2).[10]

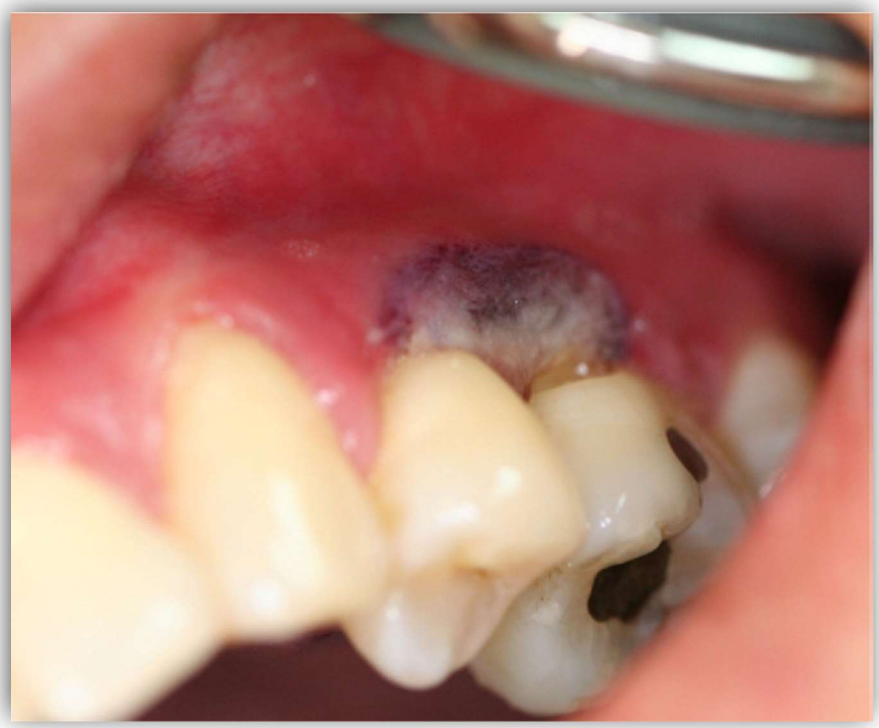

Figure: 1- Intraoral image showing Oral Mucormycotic lesion

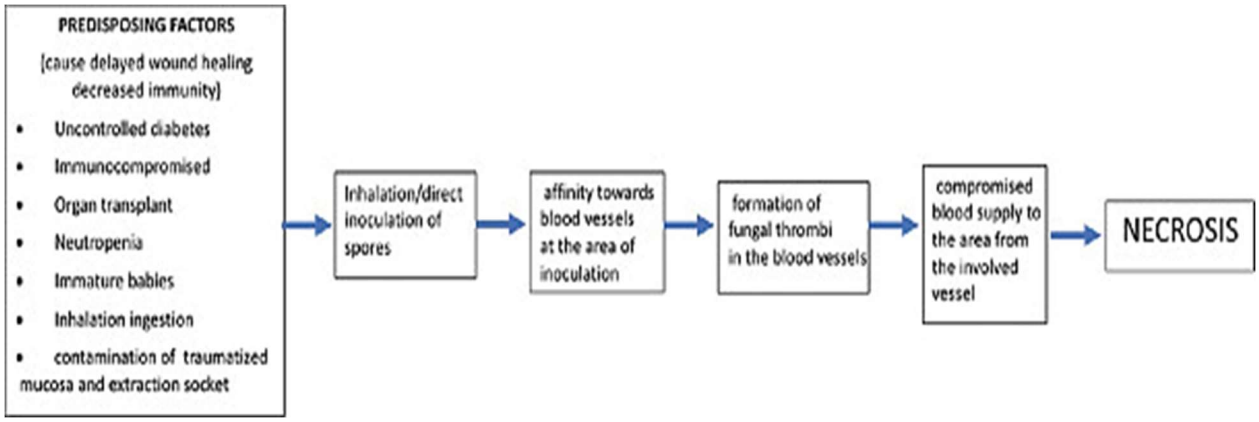

Figure 2: Predisposing factor leading to Necrosis

ORAL MANIFESTATIONS:

1. Facial pain, pain over sinuses in teeth, and gingival tissues
2. Multiple abscesses in the gingival tissues
3. Palatal ulcer
4. Loosening of teeth
5. Discoloration of the palate
6. In Severe cases, paresthesia over half of the face, periorbital swelling, and blackish discoloration of the skin over nasolabial groove/alae nasi
7. Other symptoms include blurred or double vision with pain, fever, skin lesion worsening of respiratory symptoms, hemoptysis, chest pain, alteration of consciousness, and headache.[11]

DIAGNOSIS: Clinical presentation of mucormycosis usually provides an invasive picture of perforation into bony areas. Cases have been documented with oroantral communication or perforation extending to facial tissues. Confirmation of the clinical diagnosis requires a microscopic examination of the biopsied tissue.[12] For a rapid presumptive diagnosis of mucormycosis, KOH wet mounts can be used for direct microscopy. It is applicable to all items delivered to the clinical laboratory. The ability to see the distinctive fungal hyphae is improved when KOH is combined with fluorescent brighteners like Blankophor and Calcofluor white, however, this requires a fluorescent microscope.

The histological analysis of the tissue reveals broad, nonseptate-type hyphae with the pathognomonic right-angle branching characteristic of hyphae. With a more significant connective tissue invasion, the hyphae will be seen. The Grocott-Gomori methenamine silver stain, a unique staining technique, aids in the confirmation of the nonseptate hyphae. Since not all cases of mucormycosis will exhibit the conventional diagnostic interpretation in imaging, a comprehensive clinical examination of the oral cavity is advised to make a clinical diagnosis in invasive lesions:

1. Non-contrast computerized tomography of paranasal sinuses to see bony erosion
2. High-resolution computerized tomography chest shows ≥10 nodules, reverse halo sign, and computerized tomography (CT) bronchus sign
3. CT angiography

4. Magnetic resonance imaging (MRI) brain for better delineation of the central nervous system (CNS) involvement.[12]

CT is 100% sensitive and 78% specific in the diagnosis of sinonasal mycosis. Both contrast-enhanced CT scans and CE MRI of the paranasal sinuses are helpful for the early diagnosis of mucormycosis. Histopathological examination remains the gold standard in the diagnosis of oral mucormycosis.[13]

DIFFERENTIAL DIAGNOSIS: It should be made with aspergillosis in which the filaments would be seated and bound by acute angles.

MANAGEMENT: Both medication and surgical management strategies are employed in mucormycosis cases. Patients should be advised to control diabetes and diabetic ketoacidosis. If the patient is still on the use of steroids and immunomodulating drugs, the same should be reduced with the aim to discontinue the same which should be done after consulting the concerned medical practitioner.[14]

MEDICATIONS INCLUDE: They should initiate Amphotericin B therapy on time and should ensure that the patient has controlled blood glucose while attending the dental clinic for treatment.[15]

1. Liposomal Amphotericin B initial dose of 5 mg/kg body weight (10 mg/kg body wt). If the CNS is involved, it is recommended to use isavuconazole (200 mg 1 tablet 3 times daily for 2 days followed by 200 mg daily) or posaconazole (300 mg delayed-release tablets twice a day for 1 day followed by 300 mg daily) as the alternative treatment. This treatment must be continued until a favorable response is achieved and the disease is stabilized, which may take several weeks.
2. Conventional Amphotericin B (deoxycholate) in the dose of 1–1.5 mg/kg may be used if the liposomal form is not available and renal functions and serum electrolytes are within normal limits.[16]

Following this, extensive surgical debridement should be used to remove all necrotic materials such as affected gingiva, tooth, and palatal ulcer.[17]

PREVENTION: Periodontists should ensure past medical history is taken before initiation of dental treatment and be vigilant regarding oral signs and symptoms of mucormycosis. In the event of even the slightest suspicion, they should visit the medical staff right once because, in pertinent circumstances, therapy may need to begin even before a diagnosis is made. Doctors should be counseled to use steroids and antibiotics sparingly, that is, in accordance with the approved dosage, timing, and duration. They should initiate Amphotericin B therapy on time and should ensure that the patient has controlled blood glucose while attending the dental clinic for treatment.[18]

Periodontists should counsel the patients recovered from COVID-19 infection, to keep them informed about all their co-morbidities such as diabetes, hypertension, heart disease, and any malignancy, and should tell the doctor about all medicines being taken, especially if under medication with immunosuppressant drugs for any immune-related disorder/disease.[19] They are also advised to use masks and maintain personal hygiene and immediately inform the doctor if they develop signs and symptoms of oral mucormycosis during or after their dental treatment.[20]

CONCLUSION: Oral mucormycosis is not a new fungal infection and has been diagnosed and responsibly treated by the periodontist for a long; however, with the surge of COVID-19 infection causing immunosuppression in the patients, their number has risen sharply. Although fatal sometimes when treated late, its successful treatment lies in early diagnosis. Since dental professionals are perhaps the first doctors to identify signs and symptoms, they should remain vigilant in their diagnosis so that the same can be treated and fatalities can be avoided.[21]

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