Review Article

Mucormycosis of maxillofacial region secondary to COVID-19 infection and it's management: a narrative review

Abstract: Mucormycosis mainly affects people who have health problems or take medicines that lower the body's ability to fight germs and sickness. It most commonly affects the sinuses or the lungs after inhaling fungal spores from the air. It can also occur on the skin after a cut, burn, or other type of skin injury. The most common types that cause mucormycosis are *Rhizopus* species and *Mucor* species. Mucormycosis is a rare fungal infection with high morbidity and mortality but nowadays it is observed in many covid -19 patients therefore it is identified as a complication after covid-19. It is most commonly seen in patients with systemic illness such as Diabetes Mellitus, Neutropenia, Corticosteroid use, Organ transplantation, advanced age and also seen in patients who have stayed prolonged in ICU. This review article includes etiology, risk factors, site specificity, oral manifestations of Mucormycosis, diagnosis based on oral and maxillofacial symptoms and also management of the complications.

Key words: Dentistry, COVID-19, Diabetes Mellitus, Mucormycosis, Necrosis.

Introduction:

Mucormycosis, also known as black fungus is an opportunistic infection infection common in patients with Covid-19. It is an invasive fungal infection caused primarily by fungi from subphylum *Mucormycotina* and the order *Mucorales. Rhizopus* is predominant pathogen accounting for 90% cases of the Rhinocerebral mucormycosis.[1] The pathogens are found in soil or other organic materials such as animal faeces. Rhinocerebral and pulmonary infections are caused by inhalation of spores and cutaneous infections are caused by spores entering the skin. It can also infiltrate the blood vessels and spread to brain and other organs resulting in disseminated infections.[2] The estimated prevalence of mucormycosis in India was established at an alarming rate of nearly 70 times higher than the global data according to the Epidemiology report in 2021.[3] Dentists should be aware of the increased incidence of mucormycosis in post covid patient especially in immunocompromised individuals because of symptoms such as atypical facial or sinus pain, blackish discharge and unexpected toothache. A thorough intraoral examination is recommended in all post covid patient visiting the dental OPD. Herein we have described aetiology, spread, risk factors, site specificity, diagnosis and treatment for Mucormycosis.

Etiology, Spread, risk factors and site specification :

It is caused by fungi found in decaying food in soil or other organic matter such as animal excreta and spread through environmental factors and spores that are easily aerosolized and dispersed.[4,5]

Table no.1: Risk factors and site specification of mucormycosis.

Risk factors	Site specifications
Uncontrolled Diabetes Mellitus	Maxillary sinus
Immunocompromised individuals	Orbit and brain
Prolonged ICU stay patient	Maxillary alveolar ridge
Solid organ transplant patient	Lips
Hematopoietic stem cell transplant	Tongue
Neutropenia and Malignancies	Mandible (Rare)
Additional risk factors: -Iron overload or chelation with Desferrioxamine -Breach of skin or mucosa due to trauma and burns or surgical wounds	

Table 1 enumerates the risk factors for developing Mucormycosis along with the site specificity with decreasing frequency. Maxillary sinus is considered to be the most commonly affected followed by orbit and brain, maxillary alveolar ridge, lips, tongue and rarely affects mandible. Uncontrolled diabetes mellitus, immune compromised individuals and patients admitted in the ICU for a long time are the most prominent risk factors for Mucormycosis.[3]

Relation of Covid-19 and Mucormycosis:

There is an increased incidence of Mucormycosis recently in Covid-19 infected individuals due to diabetic patients treated with steroids, oxygen therapy and prolonged intensive care admission rates.

Dental implications:

Mucormycosis presents in various forms:

1. Rhino-orbito-cerebral
2. Pulmonary
3. Gastrointestinal
4. Cutaneous .[6]

Oral form of mucormycosis is relatively rare, the main affected area in oral and maxillofacial region is maxillary sinus and it can be present with invasion and necrosis of palate.[7] Besides

maxillary sinus mucormycosis in the alveolar bone of maxilla, lip, tongue and mandible has been reported. However cases involving mandible are very rare.[8]

Table 2. Reported cases of Mucormycosis involving the maxilla.

Authors and Year	Age, years	Sex	Predisposing diseases or risk factors
Kulendra et al (2010)[9]	59	Male	Oral hypoglycemic drugs
Ourania et al(2015)[10]	72	Female	Chronic myelomonocytic luckemia
Shastry et al(2020)[11]	52	Male	Type II diabetic and chronic smoker
Fanny M.L et al (2015)[1]	46	Female	Post extraction
Nikolaos P. et al(2010)[12]	22	Female	Type I diabetic
Dogan et al (2007)[13]	7	Male	Acute myeloid leukemia
Antonetti et al(2009)[14]	10	Male	Burns

Table 2 shows cases of Mucormycosis of Maxilla and the risk factors associated with it based on the studies done by various authors.[1,9-14] The symptoms presenting in Rhino-orbito-cerebral mucormycosis are facial pain, paraesthesia, headache, periorbital and nasal swelling, eyelid drooping, proptosis, external and internal opthalmoplegia, visual loss and blackish necrosis of palatal and nasal mucosa.[15] In the post extraction cases due to immune compromised state the fungus begins to grow on spread through blood vessels leading to formation of mucor thrombus through fibrin reaction causing vascular occlusion ischemia and infarction. This explains the formation of black necrotic eschers that form on nasal or palatal mucosa which are characteristics of Mucormycosis.[11]

Diagnosis:

The diagnosis of mucormycosis requires an in depth clinical history and an assessment of the underlying medical illness. Radiographic evaluation benefits to reveal bony erosions, extent of sinus involvement as well as presence of orbital infiltrations and intracranial involvement. CBCT shows – bony erosion, involvement of sinus and nasal cavity, mucosal thickening.[11] MDCT (multidetector computed tomography) or MRI – this imaging of choice is applicable if infection has been invaded in orbit or intracranial space.

Confirmatory diagnosis – it is based on demonstration of organism in the tissue of biopsy specimen which reveal presence of broad non septate hypae with branching at 90^0 in KOH stain.[16]

Management:

Antifungal therapy with control of predisposing risk factors and surgical management are main treatment for Mucormycosis. First line of treatment involves liposomal amphotericin B and amphotericin B lipid complex; also posaconazole and liposomal amphotericin B as a

combination therapy is also useful which is considered as second line of treatment. Antifungal treatment should be continued for atleast 4 to 6 weeks and guided by the resolution of all associated symptoms and findings.[4] Surgical approach is crucial and it should involve excision and debridement of all infected and necrotic tissue based on disease progression.[4] In some cases referral to maxillofacial surgeon is mandatory as radical resection may be required which can include partial or total maxillectomy and mandibulectomy.[4] Therefore, surgical debridement and antifungal treatment can be considered the key to controlling and eliminating mucormycosis.

Conclusion:

To conclude, mucormycosis is a disease which usually shows aggressive and an alarming mortality rate. However the actual etiopathogenesis may vary depending upon systemic conditions and diagnosing of this disease remains a challenge for the dental practitioner. The overall prognosis depends on several factors, including the rapidity of diagnosis and treatment, the site of infection, and the patient's underlying conditions and degree of immunosuppression. Due to its high mortality rate, early and prompt diagnosis, recovery from predisposing factors, early intervention with surgical debridement and therapeutic drugs are the only hopes to improve the condition from this devastating disease.

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