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Review Article

Mucormycosis – A prosthodontists perspective

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ABSTRACT

Mucormycosis, an opportunistic fungal infection commonly associated with diabetes, is now intermittent as a result of co-infection with COVID-19 and steroid use, affecting the nose and paranasal sinuses of the head and neck region, with high mortality and morbidity. It is also more common in diabetic ketoacidosis, neutropenia, cancer, organ transplantation, and/or high serum iron levels, burns, acquired immunodeficiency syndrome, indiscriminate usage of steroids, lymphoma, leukemia, poor metabolic status etc.

The most common treatment protocol for such conditions is aggressive surgical debridement, which includes resection of involved maxillofacial structures such as the maxilla, orbit, and/or nose.

Rehabilitation of such large maxillofacial defects is a Prosthodontic challenge, with many problems encountered such as lack of retention due to dislodging forces exerted by scarred postsurgical soft tissues, lack of bony base, lost structures of the posterior palatal seal area, multiple defect sites, and compromised medical status due to comorbidities, which also affects the defect's healing rate.

For patients to survive, early diagnosis and treatment are frequently required. The clinical manifestations, etiopathogenesis, and management of the dreaded fungal infection known as mucormycosis in the head and neck region will be reviewed in this paper.

1. Introduction

Mucormycosis is one of several opportunistic fungi that become invasive and pathogenic in patients with altered metabolic status or those with compromised immune systems. It is also referred to as Zygomycosis. The most common causative organisms are Rhizopus species.

Mucormycosis is classified into several types based on anatomic location, including rhinomaxillary, central nervous system (CNS), cutaneous, pulmonary, disseminated, and miscellaneous. The most common type of mucormycosis is rhino-orbito-cerebral. In clinical practise, the most common types of mucormycosis infections are paranasal sinuses (39%), lungs (24%), skin (19%), brain (9%), and gastrointestinal (7%), with other types being extremely rare.[1] The involvement of the head and neck region is frequently fatal, resulting in intracranial invasion and high mortality.

1.1. Clinical manifestations

Although patients infected with mucormycosis are uncommon in general dental practise, they may consult dentists during the early stages of the disease if their symptoms overlap with those of dental origin, such as dental pain, periorbital cellulitis, or mucosal sloughing. Palatal ulceration may be the only pathognomonic sign that leads to the diagnosis of mucormycosis in some cases.

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As a result, mucormycosis should be considered as a differential diagnosis when a patient has unilateral proptosis, swelling of the periorbital and perinasal tissues, pupil dilation and fixation, paranasal sinusitis, and cranial nerve involvement.

Rhinocerebral mucormycosis is the most common clinical form of mucormycosis, accounting for one-third to half of all reported cases. It is further subdivided into rhinoorbitalcerebral (Type 1) (more fatal) and rhinomaxillary (Type 2) (less fatal), with ophthalmic and internal carotid arteries and sphenopalatine and greater palatine arteries involved, respectively.[2]

1.2. Etiopathogenesis

The most common etiological agents of mucormycosis in humans are classified as belonging to 2 orders.

Zygomycete Mucorales and Entomophthorales are the orders (two distinct infections) Rhizopus, Mucor, Absidia, and Cunninghamella are the four Mucorales genera most closely related to disease in humans.

Conidiobolus and Basidiobolus are two genera within the Entomophthorales that are linked to human infections.[3]

These latter 2 genera are genetically and clinically distinct from the Mucorales.

Rhizopus oryzae is the single most frequently identified pathogen in mucormycosis, accounting for up to 70% of all cases.

The fungus is drawn to arteries and adheres to the arterial wall. It spreads through blood vessels and the internal elastic lamina, resulting in thrombosis, ischemia, and necrosis of the surrounding tissues.[4]

Mucorales are abundant in soil, decaying vegetables, and other places. They grow quickly in a humid environment, and the sporangiospores are released into the environment and spread as airborne propagules.

Mucormycosis in the head and neck region is not related to gender or age. Mucormycosis spores can be spread via three methods: inhalation, ingestion, and percutaneous introduction. It does not spread from one person to the next.

In India, airborne spores are more common during the transition from summer to rainy season, which may be ideal for fungal growth.

Mucorales hyphae are nonseptate, broad (5–20 m), thin-walled, right-angled branched, and twisted. It can be seen histologically with hematoxylin and eosin, the periodic acid–Schiff reaction, or Grocott-methenamine Gomori's silver nitrate staining. These fungi have a ketone reductase enzyme that allows them to grow quickly in hyperglycemic and acidic environments.

By controlling pH and glucose levels, normal body physiology frequently inhibits growth. However, in hyperglycemic and acidic states such as diabetic ketoacidosis, this environment promotes the growth of these fungi. Iron increases the pathogenicity and growth of these fungi, especially in deferoxamine patients. These fungi contain a siderophore that boosts iron uptake and tissue invasion.[5]

Mucormycosis is a risk factor for cytotoxic chemotherapy, organ transplantation, and acquired immunodeficiency syndrome. Infection spreads through sporangiospore inhalation or direct contamination of skin wounds, particularly burns. Primary mucormycosis infections in the head and neck region are most commonly found in the nasal cavity and paranasal sinuses.[1,6–8]

Thus, clinical classifications aid in the planning of appropriate surgical and prosthetic rehabilitative treatment to provide the patient with comprehensive medical care.[13]

2. Management

2.1. Prosthodontic considerations

Due to the unpredictable, indefinable progression of the fungus and the likely need for additional debridement, the post-surgical defects of mucormycosis differ markedly from those of tumour resection. In the case of mucormycosis, the surgical modifications performed in favour of prosthetic rehabilitation are not possible.

As a result, providing prosthodontic rehabilitation to mucormycosis patients is complicated, especially if they are also edentulous, because the resultant defect often cannot be used effectively to retain, support, or stabilise the obturator prosthesis, and the fact that these defects are allowed to epithelialize results in a non-keratinized membrane formation, resulting in a poor stress-bearing surface.[7]

Because the presentation of the permanent defect is determined by the healing process and scar contraction, definitive prosthodontic treatment should only be considered once the healing process is complete.[14]

The approach to reconstructive and rehabilitative treatment of the resulting defects varies greatly. As a result, classifications of maxillofacial defects that take into account the functional and aesthetic outcome, as well as indicating the most appropriate form of management, should be considered. Several classifications have been proposed, including Armany's, Spiro's, Brown et al Liverpool's classification, Cordeiro's, Okay's, Durrani's, and many more.

Durrani et al[15] (2013) 's classification of maxillary defects appears to correlate with the clinical stages of mucormycosis. The categorization is as follows:

Classification of maxillary defects: Durrani et al., (2013)

1. Alveolectomy: These defects only affect the alveolar bone.
2. Sub-total Maxillectomy: These defects cause oro-nasal or oro-antral fistulas but do not affect the maxillary orbital wall.

Table 1:

Types	Risk factors	Pathogenesis	Clinical manifestations
Rhino-orbital cerebral[9]	Diabetes mellitus, malignancies, organ transplantation	Starts in the paranasal sinuses and can spread to the palate, sphenoid sinus, and cavernous sinus.	Sinusitis, periorbital cellulitis,eye/facial pain, facial numbness, blurry vision, proptosis, headache
Pulmonary	Neutropenia, chemotherapy, HSCT with GVHD, lung transplantation	Invasion of pulmonary blood vessels by hyphal cells, resulting in haemorrhage, thrombosis, and ischemia	Prolonged high-grade fever, nonproductive cough, airway obstruction, hemoptysis
Gastrointestinal[10]	Premature neonates, malnourished children, diabetes mellitus, immunosuppression	Ingestion of spore-contaminated fermented milk and dried bread products, as well as alcoholic beverages derived from corn, primarily affected the stomach, followed by the colon and ileum.	Appendiceal, cecal, or ileac mass or gastric perforation; neutropenic patients may present with fever, typhlitis, and hematochezia
Cutaneous[11]	Trauma/burn to the skin in a susceptible host	Caused by direct inoculation of fungal spores into the skin, may lead to disseminated disease	Varies from localised disease with gradual onset to progressive, fulminant disease with gangrene and hematogenous spread; typically manifests as necrotic eschar with surrounding erythema.
Disseminated[12]	Iron overload, severe immunosuppression, profound neutropenia, acute leukemia	Mucormycosis in organs can spread hematogenously to another organ; the lung is the most frequently associated with dissemination.	Depending on the location of the disease and the degree of vascular invasion, it varies greatly.

3. Total Maxillectomy: These defects are distinguished by the absence of the entire maxilla, including the orbital floor, but the orbital contents are preserved.
4. Radical Maxillectomy: These defects are distinguished by the absence of orbital contents as well as the maxilla.
5. Composite Maxillectomy: Resection of facial skin, soft palate, and any other part of the oral cavity is required for these defects.

All of these flaws are further subdivided into Unilateral and Bilateral flaws.

Mucormycosis Prosthodontic Treatment Phases (Acquired Defects)

Prosthodontic therapy for patients with acquired surgical defects following maxillary resection is rehabilitated in three stages by an obturator prosthesis that supports the patients through various stages of healing. The treatment phases are arbitrarily divided as follows:

1. Surgical obturation
2. Interim obturation
3. Definitive obturation

2.2. Surgical obturation

Immediate surgical obturation allows for prosthesis placement during surgery. It is defined as a temporary prosthesis used immediately after surgery to restore the continuity of the hard palate. It is kept for about six days after surgery. The obturator serves as a platform for surgical dressing to be applied to.

It also reduces contamination of the raw wound and aids in deglutition, allowing for early removal of the nasogastric tube. Overall, it reduces the psychological impact of surgery to some extent.[16]

Before surgery, impressions are taken and casts are placed on the articulator. Later, the operating surgeon and prosthodontist discuss the surgical margins on the cast, and the maxillary cast is altered and the prosthesis is fabricated as a result.[17]

Explicit planning of surgical margins prior to surgery may not always be possible, especially in mucormycosis cases due to its rapid progression. Nonetheless, a delayed surgical obturator can be planned in cases where emergency surgical debridement is required, which would be a lifesaving action, as well as in cases where a prosthodontist could not be consulted beforehand. It could also be considered in cases where additional debridement is required due to the fungus's uncontrollable progression.

Within a few days of surgical resection, a delayed surgical obturator is created.[18] Because the impression procedure is performed after surgery, it is necessary to handle the fresh surgical site, as well as the patient, with extreme caution, as they are prone to anxiety.

It is recommended to shorten the time between impression taking and obturator delivery because the time lag causes tissue contraction and edema, making the patient uncomfortable during obturator insertion. Another

advantage of a delayed surgical obturator is that it can be easily converted to an interim obturator, which means that the obturator's margins are not compromised until the final prosthesis is fabricated.[19]

2.3. Interim obturation

The fabrication of definitive prostheses cannot be considered until the surgical site has healed, is dimensionally stable, and, most importantly, the patient's systemic condition has stabilised, particularly in rhinocerebral mucormycosis,[20] which has a high chance of recurrence and a high mortality rate even after treatment.[14]

Interim obturators are recommended in cases where appropriate function and comfort cannot be maintained until a new prosthesis is fabricated. The interim obturator comes between the surgical and definitive obturators.[17]

2.4. Definitive obturation

A definitive obturator is usually indicated three months after surgery. Factors such as the state of healing, the dimension of the defect, the effectiveness of the previous obturator, and the remaining teeth present must all be considered when building a definitive obturator. Furthermore, the fungal infection's prognosis, as well as the patient's systemic condition, must be determined. Wound structuring and scar contracture cause dimensional changes that last at least a year and are fundamentally related to the lining soft tissues rather than the underlying bony area, necessitating periodic monitoring.[21]

The obturator prosthesis can shift by the varying amount in edentulous patients, contingent upon the shape, size, and mucosal coating of the deformity, the availability of undercuts, and the support areas that can be locked in inside and fringe to the defect. The obturator's strength and retention are enhanced by engaging the defect. The deformity edge in the posterior area is basic in the treatment planning of edentulous patients since it requires placement of implant if it extends beyond the junction of the hard and soft palate.

The status of remaining natural teeth in dentulous patients should be carefully addressed because they play a critical role in the design of the obturator prosthesis.

The diagnostic casts should be carefully examined for the presence of undercuts, as well as the location and contour of potential guide planes. To fully utilise the undercuts available in the defect, a compound path of insertion must be used. It is also suggested that multiple rests be included to improve the prosthesis's support and stability.

Additional bracing may be required to distribute lateral forces more widely among remaining dentitions in defects that extend to or beyond the midline.

3. Implants

Endosseous and maxillofacial implants that have been osseointegrated, such as zygomatic and pterygoid implants, have greatly increased the possibilities for patients with a variety of soft and hard tissue maxillofacial abnormalities to be reconstructed. Implants help to keep the prosthesis in place, provide support, and improve stability. Furthermore, prosthodontic rehabilitation with fixed prosthesis is facilitated by implant placement combined with progressive surgical restoration of significant hard tissue abnormalities.[22]

Because mucormycosis patients are systemically immunocompromised and may not be willing to take on further psychological weight as a result of surgical intervention, the decision to insert implants or not should always be carefully considered. Patients with chronic liver illness or who have had their liver transplanted are believed to have a 30% chance of developing osteoporosis, which is a cause for concern.

As a result, a team composed of a general surgeon, a physician, a maxillofacial surgeon, a prosthodontist, and the patient attendees should make the decision.

4. Conclusion

As a fulminant fungal infection, mucormycosis limits early diagnosis and treatment intervention through a collaborative approach in which the maxillofacial prosthodontist plays an important role in every step of management to improve patients overall quality of life. In mucormycosis, the defects that occur after surgical debridement differ from those that occur otherwise.[23] As a result, it is necessary to have a thorough understanding of the disease course and its nature in order to critically analyse the available anatomic structures and prostheses designs in order to achieve maximum retention, stability, and aesthetics. Maxillofacial prosthesis not only repairs the defect but also boosts self-esteem, allowing to live life to the fullest.[1,7]

5. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper

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None.

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