Prosthodontic rehabilitation for maxillofacial defects by mucormycosis post Covid-19 pandemic

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ABSTRACT
Since the outbreak of Covid-19, with every mutation, it has posed various challenges to human life and in health sciences. Patients on corticosteroids or with comorbidities like diabetes mellitus are at increased risk of post Covid-19 infections like mucormycosis. Mucormycosis is a rare opportunistic infection, often associated with immunocompromised states. Fungal invasion of the hard palate, paranasal sinuses, orbits and brain is the commonest form of rhinocerebral mucormycosis. Among the medical professionals involved in managing patients with mucormycosis, maxillofacial prosthodontists are responsible for prosthetic treatment of lost oral and maxillofacial structures, helping patients to socialize and have an acceptable quality of life after surgical treatment. This literature review is aimed to describe maxillofacial prosthodontist challenge in rehabilitation of mucormycosis post Covid-19 infection. It is concluded that prosthodontist face many challenges in mucormycosis rehabilitation. Prosthodontist should be capable to early detection and diagnosis, carefull in planning and designing the prosthesis, wise in using of softliner material, and should always maintain long-term follow-up if any sign of lesion recurrence.
Keywords: mucormycosis, Covid-19 pandemic, maxillofacial rehabilitation

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 or (SARS-CoV2) has been declared in 6th Public Health Emergency of International Concern (PHEIC).[1] Since the outbreak of Covid-19, various mutations have occured and posed various challenges especially in health sciences. Coinfection and superinfection are common in any viral infection. Coinfection happens simultaneously, while superinfection develops after initial infection.[2] Mucormycosis is the third most common opportunistic infection after candidiasis and aspergillosis.[3] Covid-19 patients with diabetic ketoacidosis, cancer, organ transplant, neutropenia, corticosteroid usage, and hemochromatosis were predisposition factor to mucormycosis.[4]

The prevalence of mucormycosis is nearly 80 times higher in India than in developed countries.[5] Mucormycosis found in tropical and subtropical climates, such as Indonesia. Indonesia is a tropical country, warm and humid, which provides a good environment for fungi growth. Unfortunately, the prevalence of mucormycosis in some developing countries, including Indonesia, are still unclear because the cases remain undiagnosed due to difficulty in collecting tissue samples and limited facilities of mycology laboratories.[6]

Maxillofacial prosthodontist is a medical professional which involved in managing patients with mucormycosis, responsible for prosthetic restoration of lost structures in oral and maxillofacial, helping patients to socialize and have an acceptable quality of life after surgical treatment.[7] Some of the problems associated with rehabilitating extensive intraoral defects make it extremely challenging for a prosthodontist to fabricate a prosthesis. The expected outcomes are an improvement in the overall function and aesthetics after the insertion.

The purpose of this review is to describe maxillofacial prosthodontist challenges in rehabilitation of mucormycosis post Covid-19 infection.

LITERATURE STUDIES

Mucormycosis

According to WHO, mucormycosis, sometimes called zygomycosis, is a serious fungal infection but rare, caused by a group of fungi called mucormycetes.[8] Mucormycosis is a non-contagious yet aggressive and life-threatening infection. Mucormycosis mainly affects immunocompromised patients, or patients already infected with other diseases. Higher risk groups include people with diabetes (especially diabetic ketoacidosis), solid organ transplantation, neutropenia (low neutrophils, a type of white blood cells), long-term systemic corticosteroid use, and iron overload (hemochromatosis).[2,9,10] Patients on corticosteroids or with comorbidities like DM are higher risk of post-Covid infecfections like mucormycosis.[11,12]

Globally, prevalence of mucormycosis ranges 0.005-1.7 per million people. The etiologic agents mostly are *Rhizopus* spp, *Mucor* spp, and *Lichtheimia* (formerly *Absidia* and *Mycocladus*) spp.[5] Several recommendations for clinical management

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and diagnosis of Covid-19 associated mucormycosis are similar to non-Covid-19 patients.[13] The Prevention of Covid-19 associated mucormycosis needs to focus on better glycemic control and monitoring the use of systemic corticosteroids/other immunomodulating drugs in treating severe cases.[14]

Clinical manifestations of mucormycosis

The clinical features of mucormycosis depending on infection site. Generally, infection starts in the oral cavity or nose and travels to the central nervous system through the eyes.[15] Among the various clinical forms of mucormycosis, rhinocerebral is the common one, accounting for one third to half of the reported cases. It is further divided as rhino-orbitalcerebral type-1 more fatal and rhinomaxillary form type-2 less fatal, involving ophthalmic with internal carotid arteries and sphenopalatine with greater palatine arteries respectively.[16,17]

Ahmed et al, described oral signs of mucormycosis are often evident in the palate and may include varied degrees of mucosal staining, swelling, ulcerations, superficial necrotic regions in palatal, bone exposure, and necrosis with black eschar development.[18] Palatal ulcerations may be the first presenting symptom, demanding the patient to seek treatment. Dentist is the first clinician to identify an infection, leading to the diagnosis of mucormycosis posibilities.[19]

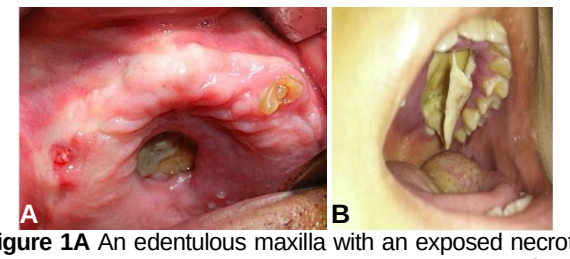

Figure 1A An edentulous maxilla with an exposed necrotic bone in palate and draining sinus in right canine region.[18] **B** ulcers in palate of mucormycosis patients.[10]

Figure 2 Sino-orbital mucormycosis.[23]

In patients with poorly regulated diabetes, dental procedures can be a risk factor for rhino-orbital cerebral mucormycosis.[20] Dental infections can lead to destructive infections of the mandible or maxilla. Headache, fever, nasal inflammation, facial pain, palatine mucosa ulceration, or dark nasal and periorbital swelling are some of the signs and symptoms of the problem.[20,21] Cellulitis, chemosis, proptosis, and blurred vision are all signs of orbital invasion.[21] Intracranial progression through direct extension or angioinvasion can happen quickly, within days. A high mortality rate is linked to brain involvement (Fig.1, Fig.2).[22]

Clinical diagnosis

An identification of host variables, quick evaluation of clinical symptoms, and a strong index of suspicion are required for diagnosis of mucormycosis. Pleuritic discomfort in a neutropenic patient or diplopia in a diabetic patient are the symptoms of mucormycosis infection that prompt the use of diagnostic imaging techniques and sample testing by microbiology, histology, and molecular modalities.[23] Other funguses such as *Fusarium* or *Aspergillus*, can cause similar clinical symptoms.[24]

Corzo-Leon et al, devised a method for detecting *rhino-orbital cerebral mucormycosis* in diabetic individuals. The following clinical manifestations must be regarded *red flags* which includes diplopia, proptosis, sinus discomfort, periorbital edema, cranial nerve palsy, palatal ulcers, and orbital apex syndrome.[25] Since the signs and symptoms are not specific, dental practitioners should be cautious if a patient has a history of COVID-19 infection, administered high-dose systemic steroids, broad anti-microbials and mechanical ventilation with any of these red-flags signs and symptoms. [17,23]

Prosthodontic considerations

The post-surgical defects of mucormycosis are remarkably different from the defects that result from tumor resection due to the unpredictable, indefinable advancement of the fungus and the probable requirement of additional debridement procedure.[17] In tumor cases, surgical modifications can be done in favour of prosthetic rehabilitation but cannot be accomplished in mucormycosis cases.[26] Therefore, provision of prosthodontic rehabilitation is worsened in mucormycosis patients especially edentulous, the resultant defect cannot be used effectively to retain, support, or stabilize the obturator prosthesis and these defects are poor in stress-bearing surface.[20,22]

The classification of maxillary defects by Durrani et al seems appropriate to correlate with the clinical stages of mucormycosis.[27] The classification is alveolectomy where the defects involve the alveolar bone alone, sub-total maxillectomy these defects cause oronasal or oro-antral fistula but do not disturb the orbital wall of maxilla, total maxillec-

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tomy these defects are characterized by absence of complete maxilla including orbital floor but the orbital contents remain intact, radical maxillectomy these defects are characterized by absence of orbital contents along with the maxilla and the last composite maxillectomy defects involve resection of facial skin, soft palate, and other part of the oral cavity.[27,28] All these defects can be further classified into unilateral and bilateral defects.

Prosthodontic treatment for mucormycosis

Prosthodontic therapy for patients with acquired surgical defect are rehabilitated in three phases through different stages of healing. The phases of treatment are arbitrarily divided as follows; surgical obturation, interim obturation and definitive obturation.[27] Immediate surgical obturation grants the placement of prosthesis immediately after surgery. It is retained about six days post-surgery.[23] The obturator acts as surgical dressing. It also decreases contamination of the wound, helps in deglutition, permitting early removal of nasogastric tube. The outline of surgical margins is discussed by maxillofacial surgeon and prosthodontist before the prosthesis is fabricated.[29]

Planning of surgical margin is not be always possible especially in mucormycosis cases since it is rapidly progressive.[30] Nevertheless, a delayed surgical obturator can be planned in situations where it necessitates emergency surgical debridement which would be a lifesaving action, and also in cases where a prosthodontist could not be consulted beforehand. It could also be considered in cases where there is requirement of additional debridement procedure due to indefinable advancement of the fungus.[31]

Interim obturator is advised in cases with large defects, where appropriate function and comfort cannot be maintained until fabrication of new prosthesis. The surgical and definitive obturators are intervened by interim obturator.[29] Fabrication of definitive prosthesis cannot be considered till the surgical site is healed, dimensionally stable and most importantly, until the patient's systemic condition becomes stable, specifically in rhinocerebral mucormycosis, which has a high chance of recurrence and high mortality rate even after treatment.[32]

Definitive obturator is commonly indicated three months after surgery. The factors such as the state of healing, dimension of the defect, effectiveness of previous obturator and the remaining teeth must be considered in construct a definitive obturator.[29] In addition, the prognosis of the fungal infection along with the systemic condition of the patient must be determined.[23] The dimensional changes occurring due to structuring of the wound and scar contracture is extended for one year and fundamentally related to the lining soft tissues rather than the underlying bony area, thereby needing periodic follow up.[28,32]

Implants

Osseointegrated endosseous and maxillofacial implant such as zygomatic and pterygoid implants have dramatically raised the potential for reconstruction of patients with varied soft and hard tissue maxillofacial defects. Implants contribute in retention, support and enhance the stability of prosthesis.[26] Furthermore, placement of implants with surgical reconstruction of extensive hard tissue defects facilitates prosthodontic rehabilitation with fixed prosthesis. The decision to place implants or not should always be evaluated specifically in mucormycosis patients due to systemically immunocompromised.[29,32]

DISCUSSION

SARS-CoV-2 can infect and replicate in the human islet cells, leading to β-cell damage and reduced endogenous insulin secretion.[33] Diabetes mellitus being a major risk factor for mucormycosis. John et al, identified 41 confirmed cases in patients with Covid-19 and noted that 93% had diabetes and 88% were receiving corticosteroids.[34] Another indirect association between the concomitant surge in Covid-19 and mucormycosis is the dissemination of fungal spores via water used in oxygen humidifiers.[14,35] The most commonly affected site was the nose and sinuses (88.9%), which is followed by rhino-orbital mucormycosis (56.7%) and rhino-orbital-cerebral mucormycosis (22.2%).[9]

Early and complete surgical treatment is recommended for mucormycosis, besides antifungal medications and correction of predisposing factors.[28] Increasing number of cases and predominant involvement of the orofacial region, can expected to encounter more patients with orofacial defects after surgical treatment of mucormycosis post Covid-19 pandemic.[7,31] Hence, there is an urgent need to provide maxillofacial prosthetic rehabilitation for patients with mucormycosis to improve their quality of life.[7] Increased awareness of morbidity is needed among medical professionals.[10,28,36]

Prosthodontist face many challenges in mucormycosis rehabilitation, not only to replace the missing teeth, but also the lost soft tissues and bone, including hard palate and alveolar ridges. Prosthodontist should be capable to early detection and

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diagnosis. Before beginning treatment for mucormycosis, the patient should be assessed by a medical specialist, ideally an endocrinologist, to ensure adequate protection with long-acting insulin and a systemic antifungal to prevent future fungal infection during and after treatment.[10] Severe ulcerative ulcers should be considered as mucormycosis, especially in post-covid patients with diabetes. Patients who have recently recovered from Covid-19 infection should be monitored carefully, regardless of whether they have a history of mucormycosis, and should be well-sterilized before delivery, especially if an immediate surgical obturator is used, because it will be contact with an open wound.[9,34] Any symptom of sinusitis should be done radiographic diagnosis.[24] Severe ulcerative ulcers, visual disturbance, or facial or orbital swelling should be considered as mucormycosis, especially in post-covid patients with diabetes.[2]

Prosthodontists have a role to determine the types of prosthetic rehabilitation needed after surgical treatment of mucormycosis and site specificity.[29] Immunocompromised states may be associated with the occurrence of mucormycosis.[7,37] The prosthesis obturators with poor bony and structures in posterior palatal seal area were dangerous retention of the prosthesis. Post surgical soft tissues are scarred and tense, exert strong dislodging forces. The prosthesis that replaces all of the missing structures will necessarily be bulky, added weight and volume also complicates retention of prosthesis.[28]

Prosthodontist should be careful in planning and designing of the prosthesis. The principles of prosthetic management are simple and fundamental.[7] Prosthesis design is varying with the type and expansion of the defect.[11] A prosthesis that can be easily removed has advantageous in checking for the recurrence of infection at surgery site, which could help in early diagnosis and treatment before complications develop.[35] Advanced treatment with implant is less reported in litera-ture.[9,38] It can be caused of fewer prevalence of the disease in past years. The use of implant and other options is planned with fundamental principles that can help in improving the quality of life of patients.[37]

Complex maxillofacial defect needs rehabilitation with obturator combine with orbital prosthesis.[10] In such cases achieving optimum retention for the orbital prosthesis is a challenge and usually retained by retentive attachment fixed to bulb of the obturator with magnets or buttons.[10,21] Due to absence of infraorbital bone, the obturator lacks in vertical support and stability. Attached orbital prosthesis tends to move during mastication.[23] The challenges in sino-orbital case were to achieve retention for orbital prosthesis from bulb portion obturator and passivity of retentive attachment between obturator and orbital prosthesis so movement of orbital prosthesis could be minimised during function.[17]

Large-sized maxillectomy defects often result after surgical treatment of mucormycosis, and the duration of healing is determined by the aggressiveness and postoperative care.[36] A lighter obturator improves suspension cantilever mechanics, prevents overstressing of the remaining supporting structures, and increases retention.[10,39] The open-hollow bulb design is also preferred over the closed-bulb design because it is lighter in weight, easier to fabricate, and produces noticeably better articulation.[39] Regular follow-up tends to accumulate mucous secretions, which can be a source of infection.[37] Remote implant-bone anchorage using pterygoid, zygomatic, and nazalus implants was also reported to be a more effective solution than conventional implants in improving prosthesis retention and support.[7]

Unlike other disease/defects, the choice of surgical planning for prosthesis is limited in mucormycosis.[39] The rehabilitation treatment is done after complete recovery from infection. The stability of the tissues is assessed, and prosthesis design is decided on the functional requirements.[39] Majorly nonkeratinized mucosa is observed in the defect areas, it can complicate postoperative care and prosthesis retention. The use of skin grafts or protection of raw tissues with keratinized mucosa can be supportive.[2,5]

Surgically resected cases have immediate or delayed surgical obturators without soft liners.[24,26] If soft materials such as resilient liners are used on the fitting surface of the obturator, frequent cleaning is recommended because higher risk of fungal contamination.[31] The use of soft liners in a definitive obturator has advantage of reducing pressure on defect areas by providing a cushioning effect between the prosthesis and the defect margins.[10] In addition, the flexibility of these materials allows for easier placement of the obturator into retentive undercuts.[31] However, in a patient with a history of mucormycosis, the use of soft liners in a prosthesis that contacts the nasal mucosa is not recommended.[6] This is due to their higher risk of fungal contamination compared to acrylic resins.[13]

Maxillofacial prosthodontist should always maintain long-term follow-up and visual examination for any signs of lesion recurrence.[10,18] It is crucially

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important to keep in mind that maxillectomy defects are always prone to bacterial superinfection by oral and respiratory commensals.[10] Even in rehabilitation period, a superinfection can still occur. Combined with the risk of recurrence of the primary mycosis, patients should be scheduled for long-term follow-up appointments.[31]

Proper instructions were explained about denture hygiene, placement, and removal. Disinfection of acrylic partial or complete dentures can be achieved by soaking in a denture cleanser or 0.5% solution of sodium hypochlorite (1:10 ratio with water) for 10 min.[40] In denture-related mucormycosis cases, the patients should be guided to microcrowave disinfection of acrylic-based dentures, once per week. Microwave disinfection is as effective as 14-days topical antifungal medication.[24,41] Metal denture disinfection is minimal published reports. The literature guides that metal-based dentures should be disinfected using chlorhexidine, hydrogen peroxide, and antifungal solutions.[40]

Important to follow various guidelines related to the oral health post covid-19 pandemic. These include: regular brushing twice a day with flossing and mouthwash with 1% povidone iodine, monitoring blood glucose levels for glycaemic control in diabetics, monitoring of the mucosal changes in patients wearing removable or fixed prosthesis, high protein and low sugar diet with multivitamins are advised.[40,41] Dentures are cleaned properly with tooth brush and gauze pieces. Furthermore, it is recommended to change the toothbrush in patients recovered from COVID-19. [40]

It is concluded that prosthodontist face many challenges in mucormycosis rehabilitation. Prosthodontist should be capable in early detection and diagnosis, carefull in planning and designing the prosthesis, wise in uses of softliner material, and should always maintain long-term follow-up if any sign of lession recurence.

It is suggested that increasing number of mucormycosis cases post Covid-19 is an urgent need to raise awareness. Prosthodontists need to share their experiences in prosthetic rehabilitation of mucormycosis by publication so the prosthodontist can confront the challenges together.

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