Case Report
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Management and Maxillofacial Rehabilitation of COVID 19 associated Mucormycosis

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Abstract

Objectives: To study and present a management protocol formulated to treat coronavirus disease-associated invasive fungal sinusitis (mucormycosis) (CAM) and related defects. **Methods**: A prospective interventional study was conducted at a tertiary care centre over three months, involving patients with mucormycosis of the paranasal sinuses suffering from or having a history of Coronavirus Disease infection (COVID-19) who underwent debridement surgery. A protocol was formulated incorporating all the departments involved in the management of post-COVID-19 Associated Mucormycosis (CAM) patients. A separate protocol for early prosthetic rehabilitation was also developed. **Results**: Twenty patients underwent surgical and medical intervention along with prosthetic rehabilitation for CAM. All of the patients were post-COVID-19 infected and had developed acute symptoms. The maxillary sinus was affected in all these patients and 25% of the patients had involvement of the orbit along with the maxillary sinus. All patients had been administered steroids during the treatment for COVID-19-associated illness. Infrastructure maxillectomy of the right side was done in 35% of patients, bilateral maxillectomy was done in 30% of patients, and two patients underwent infrastructure maxillectomy and orbital exenteration of the right side. Six patients received a surgical obturator inserted on the second-day post-maxillectomy, 8 patients received an intermediate obturator inserted on the 10th-12th day post-maxillectomy and 6 patients received a silicone obturator inserted on the 14th-18th day after bilateral maxillectomy. **Conclusions**: Early management, prompt treatment and post-operative comprehensive rehabilitation towards an optimum Quality of Life (QOL) can be achieved for good prognosis in patients affected by CAM. The prosthetic rehabilitation protocol provided prosthesis earlier and faster to the patients that improved their QOL.

Keywords: COVID-19, Coronavirus Associated Mucormycosis, Mucorrmycosis, Maxillofacial Prosthesis, Obturator, Silicone Prosthesis

1. Introduction

The etiologic factor for Coronavirus Disease (COVID-19) is the novel beta coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. As on 18 April 2021, COVID-19 status in India reports 1801316 active cases, an increase of 12.18 %[2]. This is an unprecedented second wave that the country is experiencing. Among several treatment options for the management of COVID-19 is the use of systemic steroids with or without anti-viral medication. However, the use of high-dose glucocorticoids for a long duration may lead to increased susceptibility to bacterial and fungal infections[3–5]. Pulmonary aspergillosis complicating COVID-19 recovery has been reported while mucormycosis more rarely so[6,3].

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The combination of uncontrolled diabetes mellitus, administration of steroids and COVID-19 infection are ideal breeding grounds for fungal spores. Acute rhino-orbit-cerebral mucormycosis is often a fatal disease[7] with mortality rates ranging between 40-80% in uncontrolled diabetes. In the backdrop of long ICU stays with compromised immunity, the burden of mucormycosis infection as post-COVID sepsis is high in India[8]. In a post-mortem study of 10 patients, among other pathological processes, secondary disseminated mucormycosis was reported as a novel finding as early as March-April 2020[9]. A systematic review reported 82 cases of CAM from India, 9 cases from the USA, 3 cases from Iran and 19 cases from other parts of the world[10].

A protocol was formulated by specialities to manage cases of acute fungal rhino sinusitis, presenting as post-COVID-19 sepsis. In this prospective interventional study, we discuss in detail patients with COVID-19 Associated Mucormycosis (CAM), and palatal involvement here in the Indian setting.

2. Material and Methods

Protocols for the management of suspected post-COVID-19 associated mucormycosis (CAM) patients were formulated by a group consisting of several specialities: Ear Nose Throat (ENT), Ophthalmology, Medicine, Endocrinology, Neurology, Neurosurgery, Radiodiagnosis, Dental and prosthetic surgery, Microbiology and Pathology (Figure 1).

Details of patients suspected of CAM over a period of three months from April 2021 to June 2021 were included in this prospective interventional study. Patient demographic data, hospitalisation records, history of comorbidities, history of COVID-19 infection, history of steroid administration and duration, medical and surgical intervention and rehabilitation details were recorded. Patients with needs for prosthesis were rehabilitated according to the protocol formulated (Figure 2).

3. Statistical Analysis

Information on demographics, management, intervention and rehabilitation of patients satisfying these guidelines was gathered. Data were subjected to statistical analysis using Statistical package for social sciences (SPSS v 26.0, IBM, USA).

4. Results

A total of 20 patients underwent surgical and medical intervention along with prosthetic rehabilitation for CAM. The majority of the patients were male with a mean age of 54.75 years with a range of 42 to 78 years. All of the patients were post-COVID-19 infected and had developed acute symptoms as listed in Figure 1. The mean duration of COVID-19 infection was 13.75 days.

The chief complaint of the majority of the patients at the presentation was swelling and pain in the affected side of the face. 60% of patients did not give any history of pre-existing Diabetes Mellitus (DM), 30% gave a history of type II DM and 10% were not aware of their diabetes status. The maxillary sinus was affected in all these patients and 25% of the patients had involvement of the orbit along with the maxillary sinus. At the time of presentation, 45% of the patients had DM, 15% had both hypertension and DM, 15% had hypertension, one patient had dengue and DM and one patient had liver disease as comorbidity. No comorbidity was seen associated with 15 % of the patients. All patients had been administered steroids during the treatment for COVID-19-associated illness. Dexamethasone was administered to 45% of the patients, 30% received methylprednisolone, 5% received both dexamethasone and methylprednisolone and 10% were not aware of the administration of steroids. However, 10% of the patients did not receive any steroids. The duration of steroid administration is shown in Table 1. The maximum duration was 12 days and the minimum duration was 4 days in these patients. Of the 20 patients, 11 were hospitalized and 9 were under home quarantine. The mean duration of hospitalisation or home quarantine was 11.15 days.

Aggressive medical and surgical intervention was initiated. Radical surgical debridement of affected soft and hard tissue, till healthy viable tissue is encountered was done in all the patients (Table 2). Infrastructure

Table 1. Duration of Steroid administration

Duration of Steroid administered (days)	N = 20
>10	5
>7	5
<7	5
0	2
10	1
7	2

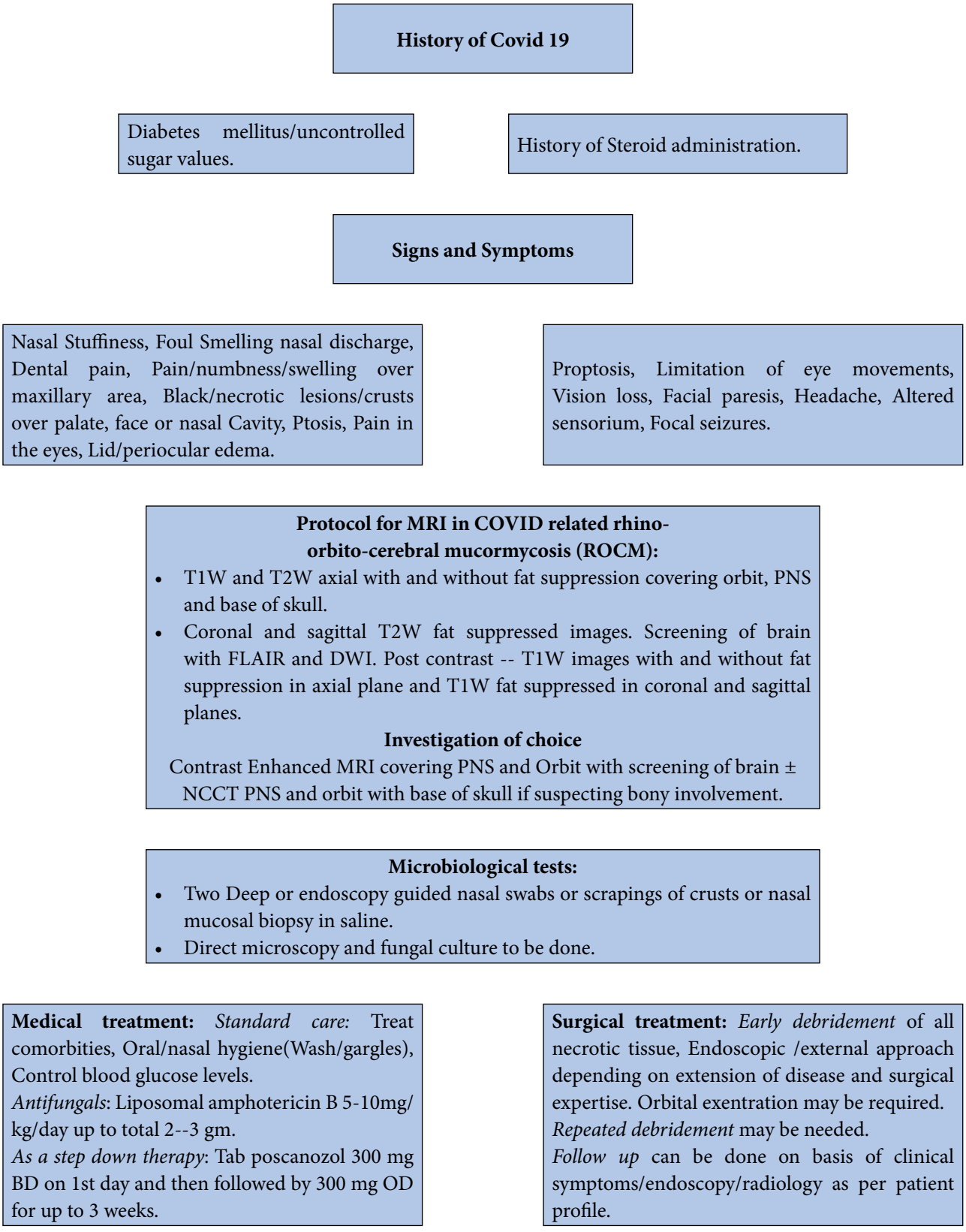


Figure 1. Protocol for management of post-COVID mucorrmycosis.

maxillectomy of the right side was done in 35% of patients and bilateral maxillectomy was done in 30% of patients. Only 2 patients underwent infrastructure maxillectomy and orbital exenteration of the right side. Amphotericin B was started as per protocol and under physician supervision.

The main aim after debridement surgery in this group of patients was to improve nutrition and start oral intake as early as possible. A protocol was formulated (Figure 2) to address this requirement. Rehabilitation with an obturator prosthesis was planned. All the obturator prosthesis was removable in nature. Impression was made in irreversible hydrocolloid (Imprint, DPI) impression material. The impressions were poured with improved dental stone (Kalstone, Kalabhai,). In cases where the contralateral arch had a considerable number of teeth, retention was obtained from the defect as well as by adapting 21 gauge stainless steel orthodontic wire (SS wire, Samit) around these teeth in the stone model obtained after impression. Autopolymerising resin (RR cold cure, DPI) was used to fabricate the obturator prosthesis. After curing the prosthesis was finished and polished following standard laboratory protocol. There were a few cases in which bilateral maxillectomy was done. Primary impression was taken with irreversible hydrocolloid (Imprint, DPI) and the model was fabricated in dental plaster (Plaster of Paris, Neelkanth). A custom tray was fabricated out of auto-polymerising resin (RR cold cure, DPI). Border moulding was done out of green stick tracing compound (Pinnacle tracing sticks, DPI) and a secondary impression was made with the addition of silicone medium viscosity (Aquasil Monophase, Dentsply) tray material after adequately blocking the defect. The master cast was made out of improved dental stone (Kalstone, Kalabhai). Modelling wax (Modeling wax, PDP) was adapted to the defect. Standard laboratory procedures were followed, dewaxing was done and the mould was obtained. Heat-curing silicone (Molloplast B, Detax,) was packed in the mould and standard curing steps were followed. The silicone obturator obtained was trimmed off the excess and inserted in the defect. All the patients were trained on how to use the obturator. Instructions on hygiene and maintenance were given.

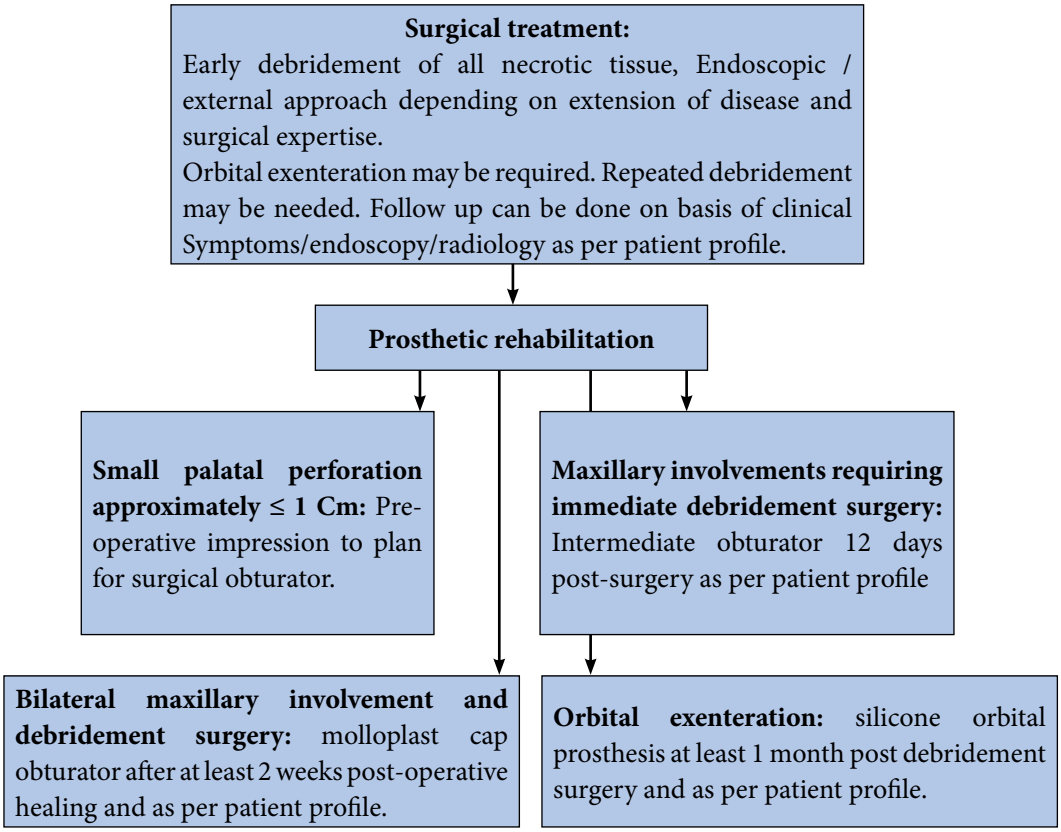


Figure 2. Protocol for rehabilitation of patients post debridement surgery for post COVID mucorrmycosis.

Table 2. Details of surgical procedures performed

Surgical Procedures	N = 20
Bilateral Maxillectomy	6
Endoscopic debridement involvement of hard palate	2
Nasal and palatal debridement	2
Infrastructure Maxillectomy	7
Infrastructure Maxillectomy and orbit exenteration	2
Sinus debridement and alveolectomy	1

Table 3. Nature of prosthesis given

Prosthesis Type	N = 20
Intermediate Obturator	8
Molloplast bulb Obturator	6
Surgical Obturator	6

Of the 20 patients six patients received surgical obturators which were inserted on second-day post-maxillectomy, 8 received intermediate obturators inserted on the 10^{th}-12^{th} day post-maxillectomy and 6 patients received silicone obturators inserted on the 14^{th}-18^{th} day after bilateral maxillectomy (Table 3) (Figures 3, 4, 5). Individual care and rehabilitation could be done after triage according to the rehabilitation protocol adopted by us (Figure 2). Intraoral rehabilitation with an obturator enabled a return to early oral intake.

5. Discussion

This study demonstrated the management and maxillofacial rehabilitation of patients diagnosed with mucormycosis as a complication of severe to

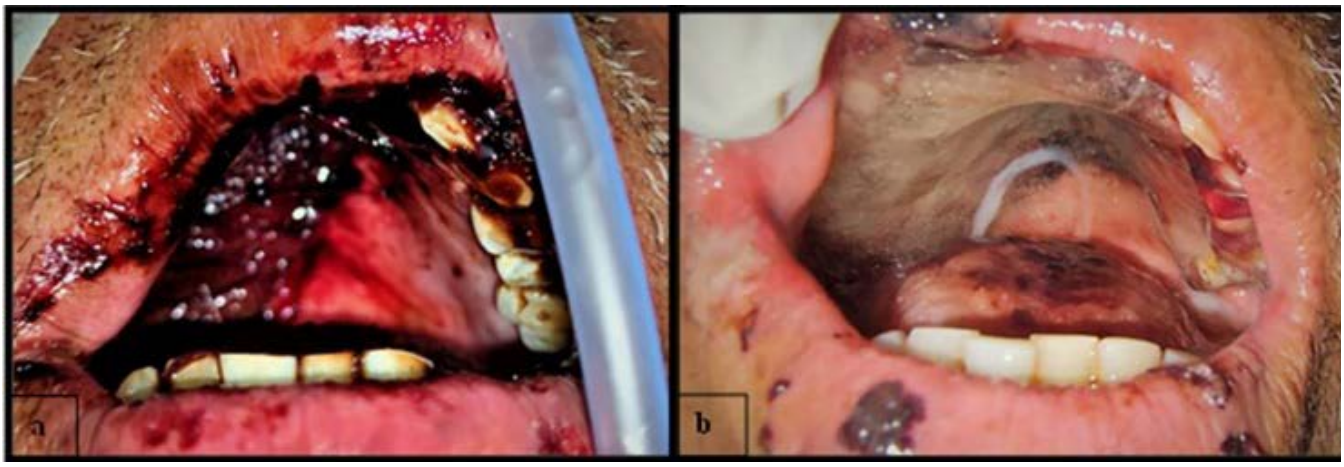


Figure 3. **(A)** Post debridement surgery (day 1). **(B)** Surgical obturator inserted post debridement surgery (day 2).



Figure 4. **(A)** Post debridement surgery day 10. **(B)** Intermediate obturator inserted post debridement surgery day 11.

moderate COVID-19 infections. Mucormycosis is an opportunistic infection of fungal origin mainly affecting immunocompromised and debilitated patient[6,11]. CAM is only emerging now as a new entity in different parts of the world[4].

Critically ill patients with prolonged hospitalization requiring a stay in ICU/mechanical ventilation, multiple comorbidities and use of corticosteroids are more likely to develop a fungal infection. It is also believed that the fungal infection may develop during the middle and later stages of COVID-19 disease especially gravely ill ones[3,4,12]. It has been postulated that a triad of pre-existing or unknown DM, COVID-19 infection and high-dose corticosteroid use initiates a cascade which increases the likelihood of contracting opportunistic fungal infection[10]. However, in this study, it was seen that some of the patients were under treatment at home quarantine after contracting COVID-19 infection. All patients developed mucormycosis after they had tested negative for COVID-19 infection.

The usual mode of entry is by inhalation of fungal spores through the nose. It then invades the blood vessels causing thrombosis and eventually necrosis hence referred to as angio-invasive fungi. The most common form is the rhino-maxillary variant, involvement of the sphenopalatine and greater palatine artery leads to avascular necrosis of the maxilla. The disease may even spread to the orbit and cranium[11]. That is why it must be recognised early and treatment started promptly to avoid morbidity and mortality[6,13]. As compared to a previous study[14], all our cases had rhinomaxillary involvement with some showing spread to orbit.

Pain and swelling in the maxillary dentition was the chief complaint in most of our cases. The first investigation of choice is usually Non-Contrast Computed Tomography (NCCT) of the paranasal sinuses[15]. If the intra-orbital or intracranial extension is suspected, gadolinium-enhanced magnetic resonance imaging is resorted to. Focal bony erosions and extra-sinus spread with the erosion of the maxillary sinus walls are strongly suggestive of the diagnosis[13,14]. This was instituted in our protocol for early diagnosis of suspected CAM at the outset. It has been reported that MRI is more sensitive than a CT scan in detecting fungal sinusitis[13,6].

Microbiologic and histopathologic confirmation of fungal spores and hyphae are diagnostic of the type of fungus. If a potential diagnosis of CAM was made based on imaging, as per recommendations and guidelines

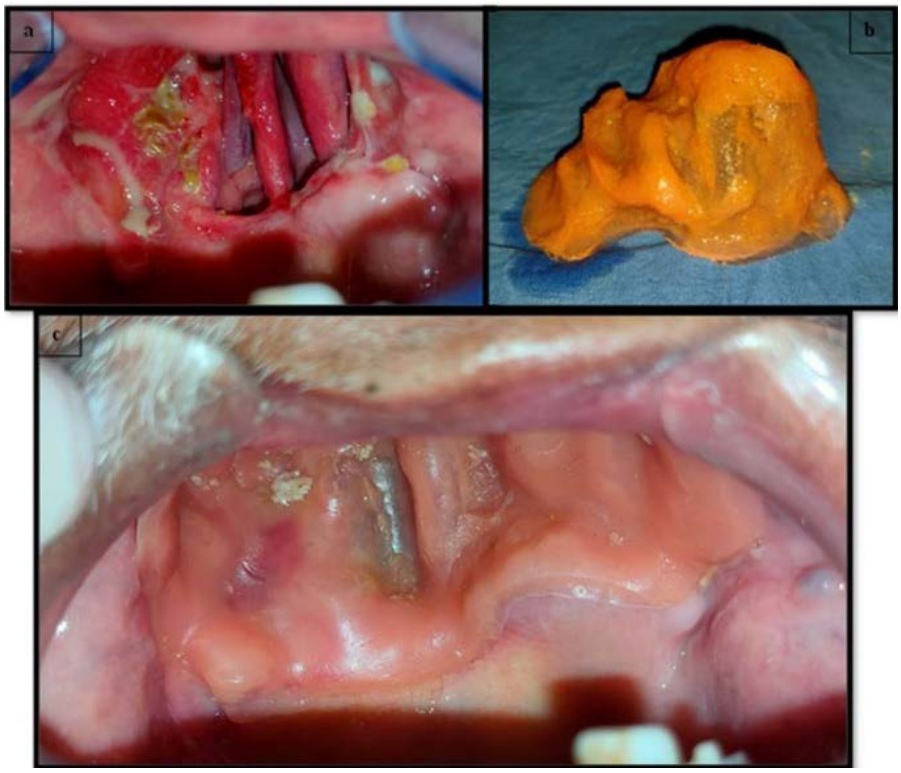


Figure 5. **(A)** Bilateral maxillectomy defect. **(B)** Silicone obturator prosthesis. **(C)** Silicone obturator prosthesis in the defect.

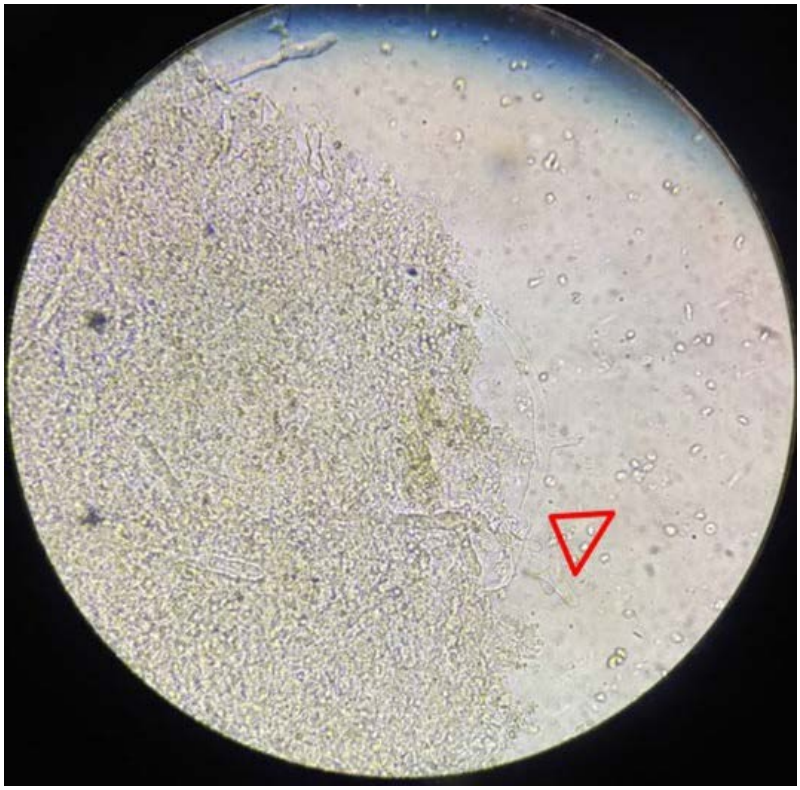


Figure 6. Fungal hyphae in KOH mount under direct microscopy.

a biopsy specimen was obtained by endoscopy. Direct microscopic evidence of fungal hyphae in Potassium Hydroxide (KOH) mounts was confirmatory of mucormycosis. (Figure 6)

There is a strong recommendation for early surgical treatment for mucormycosis. Surgery alone is not curative but provides disease control and histopathological confirmation. Repeat debridement or resection needs to be done as required[13,14]. Post-surgical treatment first-line antifungal therapy with liposomal amphotericin B 5–10 mg/kg per day needs to be started immediately. There is marginal to moderate recommendation for posaconazole oral suspension and delayed-release tablet as a suitable alternate treatment[13] Mortality rates range from 40% to 80%. High mortality rates (>80%) are reported in cases with disseminated disease or intracranial involvement. Lower mortality is reported when the early tissue-based diagnosis is feasible and surgical debridement is done[7,13]. It is worth noting that though 25% of patients had orbital involvement, 10 % underwent exenteration highlighting the effort to save the orbit and associated structures at all costs.

Radical surgery initiated early may salvage and stabilize the patient. However, it will lead to a complex oro-naso-orbital defect[16]. There are various options aimed at the reconstruction of these defects. In the early stages, surgical reconstruction will be risky as repeated debridement is required and associated comorbidities need to be managed first. The main aim of post-debridement surgery is to start oral intake as early as possible to improve the nutritional requirements of these patients. An obturator prosthesis is suitable in this situation, as it is a removable, rapid alternative to reconstruction, non-invasive, easy to manipulate, easier hygiene maintenance and economical[16,17].

A number of obturator designs have been reported in the literature for the rehabilitation of patients affected by mucormycosis[16,18–20]. In our study, surgical and intermediate obturator were used for the rehabilitation of CAM cases post-maxillectomy. A silicone obturator was used in cases with bilateral maxillectomy (Figure 5). The mode of retention for surgical and intermediate obturators was from the remaining dentition, whereas, for bilateral maxillectomy cases retention was obtained from anatomical undercuts selectively recorded during the impression procedure. Though osseointegrated dental implants or zygomatic implants could have been used for retention of the obturator, however, the conventional

mode was adopted as surveillance of the defect was of priority and any invasive procedure was postponed till complete remission of fungal infection and healing.

A number of case reports and reviews are present describing CAM[3,6,7,21]. Our data from a tertiary care teaching institute is the first comprehensive ongoing experience of CAM involving the palate over the past three months. All 20 patients have received comprehensive treatment involving various specialities for CAM. They completed two monthly follow-ups at the end of the study period. All patients had started oral feed and there was an improvement in the quality of life of the patients. To the best of our knowledge, this is the first that a protocol for the early rehabilitation of these patients was put in place. There were no mortalities.

6. Conclusion

Among the still-evolving long-term effects of COVID-19 infection, CAM is dangerous. It must be given immediate and serious attention. As the probable causal factors of uncontrolled diabetes and steroid use have been identified, multiple speciality approaches to its treatment should be sought for early management. Post-operative comprehensive rehabilitation towards an optimum quality of life can be achieved for good prognosis in patients affected by CAM.

Ethics approval and consent from participants was taken.

Consent for publication: participants consented to the collection of data and photographs for publication.

Funding: the study was not funded.

Authors' contributions: AC analysed and interpreted the patient data.SB and Su B supervised and monitored the administration of antifungal medications. MG supervised and performed debridement surgeries. AC and DB was a major contributor to writing the manuscript. All authors read and approved the final manuscript.

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