

Research Article



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A STUDY OF COVID-19 RELATED MUCORMYCOSIS AND ITS SURGICAL MANAGEMENT: OUR EXPERIENCE AT A TERTIARY CARE CENTER

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ABSTRACT

Background: Endoscopic sinus surgery [ESS] and its various approaches have become popular for several extended indications such as recurrent sinusitis and inverted papilloma. ESS is a suitable option for radical debridement in rhinocerebral mucormycosis.

Aims: The study aims to evaluate the role of trans-nasal endoscopic partial maxillectomy combined with the removal of devitalized tissues from various sinuses, peri-orbital spaces, infra-temporal fossa, pterygopalatine fossa in patients diagnosed with Mucormycosis during Covid-19 pandemic.

Methods: This is a hospital-based prospective observational study in which, a total of 93 cases of Mucormycosis were observed. Trans-nasal endoscopic partial maxillectomy combined with debridement of various sinuses was done.

Results: Covid-19 induced Mucormycosis commonly presented with nasal discharge, epistaxis, hemifacial pain, hemifacial swelling, proptosis, visual disturbances, and vision loss. A total of 93 patients were observed under this study out of which 91% were cured and 9% died postoperatively due to Covid-19-related MODS. Standard trans-nasal endoscopic debridement via a maxillary antrostomy does not suffice for the complete eradication of disease since access to all parts of the maxillary sinus cannot be achieved by this route.

Conclusion: The study concluded that TEPM can be a valuable surgical approach in the management of Covid-19 induced mucormycosis.

Keywords: Mucormycosis, Covid-19, trans-nasal endoscopic maxillectomy

INTRODUCTION

Mucormycosis also known as Rhino-orbit-cerebral mycosis is one of the fulminant and invasive fungal sinusitis. Diabetes Mellitus, corticosteroids, and immunosuppressant medications pre-dispose to such fatal infections although it is less frequent its clinical course is typically progressing leading to orbital involvement and eventually consequences that may be fatal. (1,2) Mucormycosis can manifest as one of the six different clinical syndromes: rhinocerebral, pulmonary (3), cutaneous, gastrointestinal CNS and disseminated. Rhino-cerebral type is the most common and is subdivided into rhinomaxillary, rhino orbital and rhino-orbito-cerebral (4). The paranasal sinuses are frequently

affected by an infection that frequently begins in the nasal mucosa through the ethmoid infection and may spread to the orbit, orbital apex, and even cavernous sinus.

This disease usually develops in patients who are immunologically compromised, but at the tissue, the level can be seen in otherwise healthy individuals (5). The number of mucormycosis cases among Covid-19 patients has increased, especially in India. This is due to the patient's favourable environment which encourages the growth of the spores. These include hypoxia, high glucose from diabetes or steroid use, the anaerobic environment caused by metabolic acidosis or diabetic ketoacidosis, high ferritin levels from inflammation, a decline in the activity and number of WBCs as well as several other underlying conditions that encourage the germination of spores and result in the disastrous scenario of mucormycosis co-infection with Covid-19. (6). Patients admitted to ICU and who require prolonged mechanical ventilation or patients with prolonged hospital stays of 50 days or longer are more likely to develop fungal co-infections. (7)

The devitalized tissue thus formed requires complete debridement of the soft tissues along with debridement of bone as well if involved as the fungus tends to spread by causing bone erosion thus leading to a breach of walls of sinuses, lamina papyracea and hard palate as well.

The goal of surgical management is to remove as much devitalized tissue as possible and establish adequate drainage of the sinuses. (8,9)

The traditional approach to maxillary sinus by a maxillary antrostomy by the widening of maxillary sinus ostia fails to offer sufficient access for exploration and debridement as in a maximum number of cases the fungus is not found limited by the walls of the sinus medical treatment with antifungals allows eradication of the fungus from circulation but has a poor local control rate if there is extensive devitalization of tissues.

Mucormycosis presents in patients already in poor health conditions, with a poor immune system, open approaches to maxillary sinus by midfacial degloving or lateral rhinotomy provide better access to such patients but at the cost of large facial scars and high morbidity and mortality in already debilitated patients.

Radical resection of infected and dead tissue has been reported to decrease mortality rate. Traditionally, radical debridement has been accomplished through an external or trans antral approach with or without orbital exenteration. To assure thorough debridement more than one procedure may be required. (10, 11)

Endoscopic sinus surgery and its expanded approaches are commonly performed for many extended indications like inverted papilloma, recalcitrant/ recurrent sinusitis etc and over years over proven better than the open technique due to visualization less functional loss and no facial scar.

Although ESS plays only a limited role in the treatment of malignant tumours of the nose or sinuses however with expanded ESS approaches, complete resection of sinonasal lesions such as inverted papilloma is possible, and this makes it suitable for radical debridement in rhino cerebral mucormycosis (14, 15). Early diagnosis, management of the underlying disease (DM/Covid-19), amphotericin-B therapy and radical surgical debridement increase better chances of survival. This research aims to investigate the effectiveness of performing a trans-nasal endoscopic partial maxillectomy. In addition to removing necrotic tissue from the sinuses, peri-orbital regions, infra-temporal fossa, and pterygopalatine fossa in patients with Mucormycosis during the Covid-19 epidemic.

MATERIALS AND METHODS

This retrospective study was performed on 93 subjects who were operated by TEPM approach for Sino nasal Mucormycosis from July 2021 to November 2021 during the second wave of Covid 19. The information retrieved from the data dedicated to Sino nasal and skull base procedures in Department of Otorhinolaryngology and Head & neck surgery, Sri Aurobindo Medical College and Post-Graduate Institute, Indore, Madhya Pradesh. The patients were informed the surgical procedure along with the possible alternates and gave their consent. The study was conducted in line with policies approved by the local ethical committee.

Patients with Covid-19 associated fungal sinusitis were included in the study.

Patients with poor general condition on ventilator support in ICU. Patients who were unconscious, hepatic/renal encephalopathy, Patients with intracranial involvement were not included in the study. Patients with covid-19 disease who had facial swelling, proptosis, maxilla-facial pain, and dental pain were clinically suspected of fungal sinusitis and were subjected to further evaluation. They had undergone nasal swab testing for KOH stain, diagnostic nasal endoscopy, and radiological assessment (Contrast-enhanced CT scan of paranasal sinuses with orbit, MRI Brain with PNS with orbit with contrast) to ascertain the extent of disease.

Surgical Technique: All the procedures were performed under general anesthesia after proper consent. After decongestion of the nasal cavity, a 4 mm 0 degree and 45-degree endoscopes along with a high-definition camera and monitor. Debridement was performed by using Medtronic's micro-debrider to remove the devitalized necrotic tissue. Intraoperative hemorrhage was controlled by bipolar cautery and microvascular clips application of the internal maxillary artery and/or its branches if required.

Transnasal endoscopic partial maxillectomy (TEPM) was a primary procedure to address the disease in the paranasal sinuses. Various TEPM procedures were planned as per the clinical and radiological assessment of the disease. The following describes the various Trans nasal endoscopic partial maxillectomy procedures-

The orbital extension of the disease was treated by TRAM-B intra-operatively along with orbital decompression and optic nerve decompression if required. Orbital exenteration was performed in selected cases with severe proptosis, keratitis, and vision loss by oculoplastic surgeon.

Post-Operative Management

Immediate post op management of patients was done in ICU for 24 hours. Anterior Nasal packing was removed after 24 to 48 hours, and the patients were instructed to irrigate the nasal cavities regularly with saline solution. IV antibiotics are given for 1 week after surgery.

On histopathological confirmation of Mucor mycosis, Injection Amphotericin B was advised to patients according to their weight along with regular urea, creatinine, and serum electrolytes monitoring

Patients with compromised renal and cardiac functions were provided with Tablet Posaconazole 300mg twice a day on Day 1 followed by Tablet Posaconazole 300mg once a day for 3 months with regular urea, creatinine, and serum electrolytes monitoring.

RESULT

The TEPM was performed on 93 patients for the management of Covid-19 induced mucormycosis who fulfilled the inclusion criteria. Of these, 93 patients 77 were men and 16 were women. The mean age is 47.5 years with the range from 31 to 74 years. TEPM type 1 was performed in 16 cases (17.2%). TEPM type 2 was performed in 22 cases (23.6%), TEPM type 3 was performed in 43 cases (46.2%) and, TEPM type 4 was performed in 11 cases (11.8%). Treatments were administered to all 93 individuals immediately. 93 individuals who were being observed were moved to other hospitals and were lost to the study. COVID therapy and intravenous Amphotericin were part of the medical management.

TEPM was performed for the endoscopic debridement of devitalized tissue from the maxillary sinus, frontoethmoidal sinus & sphenoid sinus in all 93 patients, septum along with orbital decompression in 51 patients (54.8), pterygopalatine fossa infratemporal fossa in 15 cases (16.1%) Transcutaneous retrobulbar amphotericin-B injection was administered in 51 cases (54.8%), and orbital nerve decompression in 13 (13.9%) out of the 93 patients.

Based on the table 2 analysis, this research has been conducted among 93 patients whose are divided four TEPM categories. Among the 16 patients, 3 patients have done Fronto ethmoidectomy Sphenoidectomy TEPM procedure, 10 Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy TRAM-B, and 3 Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy Optic nerve decompression TRAM. On the other hand, 22 patients are encountering TEPM 2 activities. During middle meatal antrostomy, it is extended inferiorly by removing the medial maxillary wall and inferior turbinate and connecting the nasal floor to the maxillary sinus floor. Besides, 43 patients in TEPM 3 have done that mentioned procedure. Again, the medial wall of the maxilla and the pyriform aperture are both taken out Transection of the nasolacrimal duct and excision of the lacrimal bone. Moreover, 12 patients also performed surgical procedures with TEPM 4.

Follow Up

The patients were followed up for a period ranging from 1 month to 6 months. Local recurrences rates were observed in cases which were tackled by repeated debridement throughout 1-2 months post-surgery. The most common postoperative discomfort for the patients was nasal crusting necessitating regular alkaline nasal rinses and endoscopic clearances Post-procedure within 1 week 8 patients certified due to Covid-related MODS.

Patients were followed up with repeated nasal endoscopy for suction and cleaning. Several patients passed away, and 5 % of patients required admission to the intensive care unit (ICU) since they had a guarded prognosis when they arrived. In the meantime, the remaining four patients required ventilatory support even after receiving acceptable medical and surgical treatment, and they were thus moved to the intensive care unit (ICU). The duration of time spent following up with the patients ranged from one month to six months. Rates of local recurrences were reported in instances that were

treated with recurrent cleaning throughout a time of 1-2 months following surgery. The patients reported the most prevalent postoperative discomfort as being nasal crusting, which required them to regularly have endoscopic clearing as well as alkaline nasal rinses. After the operation, within one week, eight patients were certified as having COVID-related MODS.

DISCUSSION

Mucormycosis presenting as rhino cerebral mycosis is one of the most invasive fungi, showing fulminant growth in immunosuppressed individuals, starting as a local infection but turning fatal via systemic involvement in a brief time. Rhinocerebral mucormycosis is the most common type, and most easily diagnosed but turns fatal due to the propensity of the spread of the fungus to vital structures like orbit, brain, cavernous sinus etc.

Covid-19 predisposed the majority of the infected individuals to mucormycosis by severely compromising the immune status of the host. It causes devitalisation of soft tissues and bone of the affected areas as it spreads by causing thrombosis of the end arteries (endarteritis obliterans). Thus, the goal of surgical management is to remove devitalized and necrosed tissue as much as possible and to establish adequate drainage of sinuses.

Due to the introduction of new COVID virus strains, the COVID-19 epidemic swept through the country in waves. The first wave happened between March and December 2020, and the second wave reached its height in April 2021 [16]. An enormous increase in the rapid spread and contagiousness of COVIDs was seen during the second wave. The new virus was much more lethal than the original, and it quickly became a pandemic. As a result, a new trend emerged towards the unrestricted use of steroids, often through teleconsultations or OTC prescriptions. Increases in mucormycosis cases were seen in many countries as a result. Those at higher risk for contracting the disease have conditions including diabetes, immunosuppression, chemo treatment, etc [17]. Before the spread of COVID, mucormycosis was an extremely uncommon disease, with an incidence of 0.14 per 1000. Yet, after COVID, there was a significant increase in these occurrences, notably between May and July, immediately following the second peak of COVID. Inappropriate use of steroids including dexamethasone, prednisolone, and methylprednisolone has been linked to the increase observed in clinical settings. In April of 2021, we saw the beginning of the second peak, which would see an exponentially larger number of instances than the first. The sheer volume of cases swamped the medical community, leading to unrestrained and unmonitored use of Steroidal medicines, both orally and intravenously [18]. The steroid drugs caused elevated glycemic index and out-of-control diabetes. Patients on immunosuppressive treatments who developed mucormycosis also reported in considerable numbers to COVID clinics.

Sharad et al. (2022), argues that in the previous research conducted out of a total of 140 patients, 55 were found with Mucormycosis in Covid-19 patients using KOH, culture, or both methods of detection as per tertiary care hospital report. However, this study has conducted this research among 93 patients and out of 93 patients 77 were men and 16 were women. Again it has a categorised range from 31 to 74 years. In addition, TEPM type 1 was performed in 16 cases (17.2%). TEPM type 2 was performed in 22 cases (23.6%), TEPM type 3 was performed in 43 cases (46.2%) and, TEPM type 4 was performed in 11 cases (11.8%). On the other hand, the previous study found that the most prevalent isolate was *Rhizopus arrhizus*. Bloodstream infections were the most common secondary illness for those with Mucormycosis (7/15; 46.67%) while in the hospital (12/55; 21.8%). Although gram-negative (GN) organisms were more common than gram-positive (GP) ones, the most commonly isolated GP organism was *Enterococcus faecium* (5/16; 31.25%), followed by *Klebsiella pneumonia* (4/16) and *E. coli* (4/16). Moreover, COVID-19 remains a global health issue and Mucormycosis in COVID-19 patients is rising rapidly. Recent investigations have found high rates of mucormycosis in COVID-19 patients, but treatment outcomes are unknown. Our tertiary care centre manages mucormycosis in COVID-19 patients.

Open approaches for debridement of sinuses traditionally were through midfacial degloving /lateral rhinotomy but these procedures in the era of Covid-19 patients suffering from mucormycosis in already weak and debilitated patients seem outdated [19]. Hence, endoscopic approaches to sinuses expand the chances of debridement and resection of disease by providing better visualization, less morbidity and easy and better access to hard-to-reach areas.

In this study, we have tried to classify the level of resections according to the structures involved to provide a comprehensive classification system [20]. Resections alone do not only suffice in such cases; therefore, it is combined with other procedures to achieve maximal debridement and local disease control. The system is adapted to provide a convenient and easy classification in order of serial anatomical exposure.

Patients show good prognosis post debulking in a majority of cases with frequent nasal clearing up to 6 months of follow-up.

CONCLUSION

The study concluded that TEPM can be a valuable surgical approach in the management of Covid-19 induced mucormycosis. The treatment was administered immediately to all patients, which is essential for the successful management of mucormycosis. TEPM type 3 was the most common type performed, indicating its effectiveness in the management of Covid-19 induced mucormycosis. Moreover, the study provides useful information regarding the surgical procedures performed along with TEPM based on its categories. The findings of this study contribute to the existing literature on the management of Covid-19 induced mucormycosis and can be used to guide future research and clinical practice. Overall, the study highlighted a clinically important condition for the future management of COVID-19.

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TABLES

PROCEDURE	STRUCTURES REMOVED
TEPM 1	Wide middle meatus antrostomy
TEPM 2	Wide MMA along with the removal of medial wall of maxillary sinus inferior turbinate
TEPM 3: Endoscopic Denker's Approach	Removal of pyriform aperture along with a medial wall of maxilla. Nasolacrimal duct transected and lacrimal bone removed
TEPM 4	The anterior wall was removed up to the zygomatic bone and superiorly up to the plane passing through inferior orbital foramen, removal of posterior wall was to approach infratemporal fossa, transection of the internal maxillary artery is involved.

Table 1: Describes TEPM procedures performed, and the various structures removed

Characteristics	Findings
Age (y)	47.5+ ₋ 31-74
Case history	
Hospital admission	4 (4.3)
Yes	15(16.1)
No	2 (2.1)
Diabetes mellitus	11(11.8)
Oxygen therapy	
Yes	17 (18.3)
No	4 (4.3)
ICU stay	
Yes	11 (11.8)
No	5 (5.37)
Duration of steroid	
2 weeks	17 (18.3)
3 weeks	6 (6.5)
Day 1 symptoms	16 (17.2)
Negative report of Covid-19 symptoms	21 (22.6)
Post-surgery Covid-19 report (1 st day)	17 (18.3)
Delay of operation post onset of symptoms	1 (1.0)
Hypertension	5 (5.37)

Table 2: Baseline characteristics of the sample in this study

	Procedure is done along with TEPM		Number of patients
TEPM 1	A	Fronto ethmoidectomy Sphenoidectomy	3
	B	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy TRAM-B	10
	C	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy Optic nerve decompression TRAM	3
TEPM 2	A	Fronto ethmoidectomy Sphenoidectomy	5
	B	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy TRAM-B	13
	C	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy Optic nerve decompression TRAM-B	4
TEPM 3	A	fronto ethmoidectomy Sphenoidectomy	11
	B	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy TRAM-B	17
	C	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy Optic nerve decompression TRAM-B	6
	D	Pterygopalatine fossa Infratemporal fossa	9
TEPM 4	A	Fronto ethmoidectomy Sphenoidectomy	3
	B	Frontoethmoidectomy Sphenoidectomy Orbital decompression Septectomy TRAM-B	2
	C	Fronto ethmoidectomy Sphenoidectomy Orbital decompression Septectomy Optic nerve decompression TRAM-B	1
	D	Pterygopalatine fossa Infratemporal fossa	6

Table 3: Surgical procedures performed along with TEPM

ATLAS



Fig: 1



Fig: 2



Fig: 3



Fig: 4



Fig: 5



Fig: 6

Fig 1: left eye proptosis, left hemifacial swelling, angle of mouth deviation

Fig 2,3 showing black crusts and fungal spores on nasal endoscopy

Fig 4 showing pre-op CT-PNS: contrast-enhanced Fig 5 showing post-op - CT PNS image

Fig 6 – Six months follow-up nasal endoscopy of a patient who underwent TEPM 4 showing absent nasal septum.