



Modifying Surgical Staging and Treatment Protocols of COVID 19 Associated Mucor mycosis

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Introduction

The ROCM outbreak overwhelmed a health infrastructure already reeling under relentless pressure due to Covid-19 pandemic and became of matter of grave concern ⁽¹⁾. The rarity and heterogeneity of presentation, propensity to cause devastating and long lasting sequelae unless treated urgently constituted challenging adversities for otorhinolaryngologists who were at the forefront of the battle against ROCM.

Aggressive surgical debridement of necrotic tissue with appropriate antifungal treatment has been recommended universally as a keystone part of a multidisciplinary treatment approach and described extensively in various guidelines ^(2, 3). However, a detailed staging system based surgical interventional protocols that can be individualized as per necessity has been rather conspicuous by its absence..

The necessity to maintain uniformity of care encouraged development of surgical guidelines based on clinical, endoscopic and radiological involvement of vital anatomical structures. Accordingly, we categorized our surgical approaches; learning curve based on dexterity and potential complications to segregate each group and followed them for post operative course of disease. We present our experiences of dealing with Covid-19 associated ROCM as per our staging and surgical guidelines for academic perusal and assist otorhinolaryngologists to deal with future outbreaks of mucormycosis.

Methodology

We proposed a staging system for post Covid-19 ROCM based on clinical presentations, endoscopic and radiological findings and the patients were categorized in six different stages (TABLE 1).

Surgical Stage	Structures involved
I	*Nasal Cavity mucosa *Turbinates *Limited ethmoid sinus *Limited maxillary sinus
II	*Extensive maxillary sinus/ ethmoid involvement * Frontal and Sphenoid sinus involvement * Septum * Pterygopalatine fossa * Limited lateral spread to the ITF/ Retroantral space * Bilateral limited disease to the turbinates, sinuses , PPF and ITF
III	*Limited spread to medial, inferior orbit (extraconal spread) along with all sinuses *Infraorbital nerve & inferior orbital fissure *Involvement of lateral ITF / Zygomatic route/ masseteric space * Premaxillary / Cheek space involvement * Alveolar and palatal involvement
IV	*Intraconal spread in the orbit * " Frozen globe" *Involvement of Orbital apex/ CRAO *Anterior skull base/ cribriform area involvement * Frontal bone osteomyelitis * Sphenoid bone osteomyelitis
V	*U/L Cavernous sinus thrombophlebitis *Localized abscess (frontal/temporal) *Dural enhancement along the skull base *B/L Cavernous sinus thrombophlebitis
VI	* Diffuse Brain parenchyma involvement * Complete ICA thrombosis * Large area brain infarct

Middle turbinate centrifugal concept

Based on our classification system, we proposed a system of surgical intervention best suited for each stage of the disease presentation. We adopted and labeled this approach as "Middle Turbinate Centrifugal Approach" to guide our surgical choices (FIGURE 1). This centrifugal approach entails middle turbinate in its coronal plane as the centre of our surgical circle. As the disease involvement spreads distant from the middle turbinate; superior (intracranial), inferior (palate), lateral (orbit/masseter) or anterior (skin/premaxilla); we gradually move from endoscopic approaches to open approaches with the aim to achieve complete resection with healthy margins. There is an also intermediate zone where indications for endoscopic and open surgery overlap. The choice of decision making in this zone rests with the operating surgeon and his surgical preference. However, we utilized a combined approach; using both endoscopic and open approaches in tandem, at different stages of the procedure. The distant involvement away from the centre of the surgical circle not only influenced our surgical choices, it also signified extensive involvement, greater post operative morbidities and in general a relative poorer prognosis



Guidelines to decide the approach

Stage	Approach and Incision	Procedure
I	Endoscopic No incision	1. Removal of necrosed turbinate (Middle/Inferior) 2. Middle Meatal Antrostomy (MMA) 3. Ethmoidectomy/ Sphenoidectomy
II	Endoscopic No incision	1. Inferior/middle turbinectomy 2. Wide MMA/ Modified Denker's 3. Anterior and posterior ethmoidectomy along with frontal sinusotomy 4. Sphenoidotomy with wide opening of the sinus upto the vidian canal region 5. Removal of necrotic debris from pterygopalatine fossa, Infratemporal fossa 6. Septectomy
III	1. Endoscopic+ Open 2. Open approach • Sublabial incision • Midface degloving • Lateral rhinotomy • Weber Ferguson	1. Endoscopic + Open : Endoscopic clearance of disease from turbinates, sinuses, pterygopalatine fossa, infratemporal fossa. Sublabial small sublabial incision to perform localized alveolectomy/ palatal resection of involved area 1. Open approaches : Lateral rhinotomy Weber Ferguson approach
IV	1. Open approach	Along with above mentioned approaches: For Limited orbital involvement: Localised Orbital clearance medially, inferiorly and superiorly For Frozen Globe without Cavernous Sinus involvement - Orbital Exenteration along with disease clearance For Frontal Bone Osteomyelitis : Localized frontal craniotomy and reconstruction.
V	1. Open approach 2. Palliative approach	Along with above mentioned approaches: Craniofacial resection for frontal abscess Lateral temporal approach for temporal lobe abscess • Bifrontal craniotomy • Subtemporal incision
VI	1. Palliative approach	Prognosis very poor. Conservative medical management.

Post op protocol

Various surgical approaches and procedures undertaken in our study included endoscopic excision, lateral rhinotomy, midfacial degloving, craniofacial resection, palatal excision, orbital exenterations and neurosurgical interventions such as bifrontal craniotomy. **Our post-operative protocols included Amphotericin B for minimum 21 days followed by Posaconazole from minimum 3 months to a maximum of 6 months apart from routine post operative care and medications.** We kept a record of surgical approaches, surgical outcomes, post operative complications, time taken and other variables for every intervention undertaken as per the recommended staging system. The results were tabulated and statistically interpreted using the IBM SPSS software 22 and presented for academic perusal.

Results

Stage	Number of patients	Mean Age (in years)	Gender [n (%)]	Approaches [n (%)]	Additional Procedures	Side of Surgery (B/L, Rt, Lt)	Average Time (in min.)	Outcome [n (%)]
I	7	52.29 (±8.82)	F-2 (28.6) M-5 (71.4)	Endoscopic -7(100)	-	B/L-5(71.4) Rt-1(14.3) Lt-1(14.3)	90	Cured =7
II	52	47.96 (±13.23)	F-13(25) M-39(75)	Endoscopic-28(53.8) Endoscopic Modified Denker's - 11 (21.2) Lateral Rhinotomy-11(21.2) Weber Ferguson-1 (1.9) Combined approach- 1 (1.9)	Endoscopic Septoplasty - 1	B/L-36(69) Rt-10(19.2) Lt-6(11.5)	122.5 (±28.5)	Cured - 45 (86.5) Revision - 5 (9.6) Failure-2(3.8)
III	59	50.89 (±11.69)	F-22(37.3) M-37(62.7)	Endoscopic-6(10.2) Endoscopic Modified Denker's - 4(6.8) Lateral Rhinotomy - 28(47.5) Weber Ferguson - 11 (18.7) Midfacial Degloving- 2 (3.4) Combined - 6 (10.2)	Endoscopic Orbital Decompression- 6(10.2) Open orbital decompression - 7(11.9)	B/L-23(39) Rt-18(30.5) Lt-18(30.5)	130.7 (±40.6)	Cured-46(77.9) Revision-8(13.6) Failure-7(11.9)
IV	21	51.73 (±12.28)	F-5(23.8) M-16(76.2)	Endoscopic - 2(9.5) Endoscopic modified Denker's - 4(19) Lateral Rhinotomy-13(61.9) Weber Ferguson - 1(4.8) Combined - 1 (4.8)	Endoscopic Orbital Decompression - 4 (19) Open Orbital Decompression - 4 (19) Orbital Exenteration - 7(33)	B/L-13(61.9) Rt-2 (29.5) Lt- 6 (28.6)	153.57 (±49.37)	Cured - 15(71.4) Revision-2(9.5) Failure-4(19.04)
V, VI	4	46 (±17)	F-0 M-4(100)	Endoscopic- 1(25) Open lateral Rhinotomy + Bifrontal Craniotomy -3(75)	Frontal Lobectomy-1(25) Orbital decompression - 1(25)	B/L - 4(100) Rt- 0 Lt- 0		Cured - 1(25) Revision-0 Failure-3(75)

Discussion

The advent of endoscopic sinus surgery technologies has widened our surgical treatment options for ROCM. While open approaches have been traditionally used for ROCM, radical resection can now also be achieved with low morbidity under endoscopic guidance, which allows large resection of sinus walls to the skull base and the wide exposure of the orbital walls ⁽¹⁴⁾. Endoscopic approaches also provide the benefit of easy post operative inspection of the operated cavity endoscopically under local anesthesia for necrosis or early recurrence. An endoscopic approach is generally preferred over the open surgery in patients with early, limited disease, or with significant medical comorbidities ⁽¹⁵⁾. However, we do not recommend a blanket usage of endoscopic approach for all cases of ROCM. Selection of surgical approach has to be individualized in each case depending on the extent of anatomical involvement, structures involved, presence of comorbidities and the surgical expertise of surgeon to steer such cases. The decision making process further gets complicated in active Covid-19 positive patients where safety of healthcare personnel depends on reducing the time of potential exposure during surgery. Based on our experiences of surgically treating 143 cases of post Covid-19 ROCM, we adopted and recommend "Middle Turbinate based Centrifugal Approach" to guide our surgical choices. In spite of our best efforts and intentions, incidences of devastating complications in post Covid-19 ROCM patients is not an uncommon occurrence. Complications have been reported various case series all across the world with high mortality rates ranging from 20-50% if localized to up to 70-90% in cases of disseminated disease ⁽¹⁷⁾. We observed that complications in these patients fit in one of the following categories. (A) Complications due to primary pathology of Covid -19, mainly pulmonary involvement. (B) Complication due to mucormycosis, especially disseminated disease to eye, palate and intracranial involvement. (C) Complication due to prolonged antifungal treatment such as nephrotoxicity, hypokalemia, prolonged hospitalization and bacterial superinfection. (D) Functional disabilities or anatomical defect after debulking surgery like orbital exenteration and palate excision involving reconstructive procedures, prosthesis and rehabilitation

Conclusion

We faced unexpected challenges which often went beyond established medical protocols in absence of definite guidelines as a crisis of this magnitude was unprecedented. We formulated our treatment plans of ROCM on the basis of existing literature as well as incessantly updated the strategies in preexisting context of covid-19. Occurrence of novel adversities were dealt with and meticulous record keeping was performed to compare and reorganize our treatment approach. This study aims to share our experiences of dealing with post Covid-19 rhino-orbital-cerebral mucormycosis for academic interest and to assist otorhinolaryngologists to encounter similar healthcare emergencies in different settings around the world.

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