

Surgical Approach to Rhino-Orbital Mucormycosis using Contrast Enhanced MRI as Roadmap

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Titans Kar,¹ Arya Brata Dubey,¹ Subhradev Biswas,²

ABSTRACT

Introduction

Increase in Mucormycosis cases following COVID-19 infection was major concern due to angio-invasive nature causing necrosis. Aggressive surgical resection is necessary to combat this infection. Identifying areas of involvement like orbit, infratemporal fossa and nature of involvement (enhancing or non-enhancing) is best assessed by MRI. Hence, we decided to use MRI as surgical roadmap for disease clearance.

Materials and Methods

All post-COVID suspected mucormycosis cases based on clinical suspicion underwent MRI and nasal endoscopic biopsy. In MRI we evaluated T1 with contrast and T2 with fat suppression. Once Mucormycosis was confirmed by biopsy, Amphotericin B was started with monitoring of biochemical parameters. Surgical resection till level of viable tissue was reached was done based on MRI findings. Post-operatively patients underwent nasal douching and endoscopic surveillance.

Results

Our surgical experience shows that maximum patients had to undergo unilateral FESS with modified endoscopic Denker's approach and opening of pterygopalatine and infratemporal fossa. We conclude that all patients must minimally undergo the above surgery. Endoscopic Denker's approach allows easy post-operative surveillance. The pterygopalatine and infratemporal fossa is anatomically hidden by posterior wall of maxilla. Since we found more than 50% involvement of these areas, the necessity to open and visualise the areas in our opinion is must in all cases of post-COVID rhino-orbital mucormycosis.

Conclusion

Post-COVID Rhino-Orbital Mucormycosis requires high index of suspicion. Underrated symptoms like headache, facial pain and facial swelling in post-COVID patients with associated immunocompromised state like diabetes mellitus must be thoroughly investigated by MRI nose, paranasal sinus and orbit. Surgical debridement as dictated by MRI and routine inspection of pterygopalatine and infratemporal fossa should be done.

Keywords

Mucormycosis; COVID-19; Endoscopic Sinus Surgery; Debridement; Magnetic Resonance Imaging

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with a wide range of opportunistic bacterial and fungal infections.¹ Rhino orbital Mucormycosis is a fungal infection of the orbital tissues by the fungus Mucor of the class Phycomycetes (order Mucorales). It has been described classically as an aggressive opportunistic infection occurring in the immune compromised patients.² It is well known that COVID 19 caused more severe infections in

immune compromised state such as long standing diabetes, HIV (human immunodeficiency virus), tumor, severe prolonged neutropenia. Song *et al.*³ reported fungal coinfections associated with the global COVID 19

1 - Institute of Otorhinolaryngology & Head Neck Surgery, IPGMER & SSKM Hospital, Kolkata

Corresponding author:

Dr Titans Kar
email: titaskar@yahoo.com

pandemic based on a retrospective analysis. Recently there has been increase in cases of Mucormycosis worldwide, including India, with majority of them occurring in patients after COVID-19 infection. The reasons for acute surge in cases have been suggested to be hypoxia, high glucose, acidic medium, high ferritin, decreased phagocytic activity of WBC (steroid use) and prolonged hospitalisation with or without ventilators.⁴

This fungus is angioinvasive and causes thrombosis of vessels, with consequent black necrosis of nasal and sinus tissue. Surgery is used to remove necrotic tissue, reduce the concentration of fungal spores and facilitate the effect of antifungal drugs.^{5,6} Traditionally, some authors have recommended aggressive surgical resection of affected tissue.^{7,8} However, following wide application of nasal endoscopy in sinus surgery, other authors have reported comparable results with frequent endoscopic debridement.^{9,10} These authors have claimed that, in selected cases, this method has less morbidity, a better surgical field of vision, and comparable results.^{9,10}

Proper workup and surgical plan is essential to prevent recurrence in Mucormycosis. Imaging modalities like CT scan gives limited information about involvement of sites like orbit, optic nerve and bone, infratemporal fossa and intracranial structures. Enhancing or non-enhancing lesion (infarction, necrosis or inflammation) are best identified by MRI. A prospective study was carried out to evaluate the surgical planning for Mucormycosis cases based on few MRI sequences which helped us decide the course.

Materials and Methods

Our Institute is a tertiary health care centre having facility for treatment of COVID patients and follow-up clinic. Following the steep rise of post-COVID Mucormycosis from March 2021, our Institute created a Mucormycosis Board consisting of Neurosurgeon, Internal Medicine, Ophthalmology, Otorhinolaryngology, Plastic Surgery and Critical Care Specialists. This was a prospective study carried out on patients admitted between April 2021 and October 2021. Suspected patients based on clinical symptoms were referred to the Board.

Detailed history was taken regarding onset of COVID symptoms (date of COVID positive & date of COVID negative), use of steroids, oxygen, onset of Mucormycosis and associated comorbidities. Clinical examination was done by individual department representatives in Mucormycosis Board. All patients underwent contrast enhanced MRI nose, paranasal sinus & orbit. Out of all sequences, we as ENT surgeons evaluated 2 sequences specifically – T1 with contrast and T2 with fat suppression. We analysed individual sites in nose and paranasal sinuses keeping in mind the surgical plane of approach based on above two sequences. To diagnose Mucormycosis, all patients underwent Diagnostic Nasal Endoscopy and biopsy. The biopsy was sent for both microscopy and culture (usual waiting period was 3-4 days). Our study included those patients where either microscopy or culture proved Mucorales species. In few cases where patients were critical and the index of suspicion was very high based on the clinical features, we did not wait for culture report and the surgery was done at earliest. We excluded patients with intracranial extension from the present study. Once Rhino- Orbital Mucormycosis was confirmed then surgical planning was discussed and approved in Board meeting. All patients received intravenous Amphotericin B at a dosage of 1mg/kg/day after proper testing for hypersensitivity. Biochemical parameters like complete blood count, renal function test, d-dimer, CRP were sent on alternate days.

All patients were operated between April 2021 and October 2021. In all cases, non-involved side was evaluated endoscopically and mucosa with suspicious features was sent for biopsy and culture at the beginning of surgery. Surgical debridement included removal of necrotic tissue until level of viable tissue. All materials obtained were sent for biopsy. After completion of surgery nasal packing was done with Amphotericin B. The pack was removed the next day and patients underwent endoscopic suction clearance twice weekly. Post-operatively alkaline nasal douching was advised. The patients received Amphotericin B for 2 weeks followed by Posaconazole (300 mg) daily. The patients

Table I: Patient Demographics

PARAMETERS	NUMBER
Duration of COVID treatment at hospital	Mean 17.3 ± 6.14 days
Duration of onset of Mucormycosis after COVID RTPCR negative	Mean 6.5 ± 3.13 days
Use of steroids	27 (61.36%)
Use of Oxygen Number 21 (47.77%) Days of Oxygen use	Mean 9.2 ± 3.42 days
Comorbidities	
Known Diabetics	15
Diabetes diagnosed during COVID treatment	11
Hypertensive	5
No comorbidities	4

were discharged after 2 weeks of surgery and followed up twice weekly. In each visit after discharge, endoscopic monitoring of cavity was done.

Results

A total of 44 patients were included in this study. Age range was 21 to 67 years with mean age of 35.12 years. Out of 44 patients, 12 (27.27%) were females and 32 (72.73%) were males. The mean duration of COVID treatment was 17.3 days. The use of steroids, oxygen and comorbidities are shown in Table I.

Among clinical features Headache (68%), facial pain (52%), facial swelling (44%), periorbital swelling (28%) (Fig 1) were major complaints. Other features were diplopia (15.90%), complete loss of vision (6.81%), ptosis (6.81%), partial loss of vision (22.72%), loosening of teeth (4.54%), palatal ulcer/necrosis (11.36%).

The spectrum of symptoms in rhino-orbital Mucormycosis is shown in Fig. 2.

We evaluated 2 sequences of MRI – T1 with contrast and T2 with fat suppression for planning of surgery. Diffusion-weighted MRI was used to look for optic nerve



Fig.1. Periorbital edema on left side

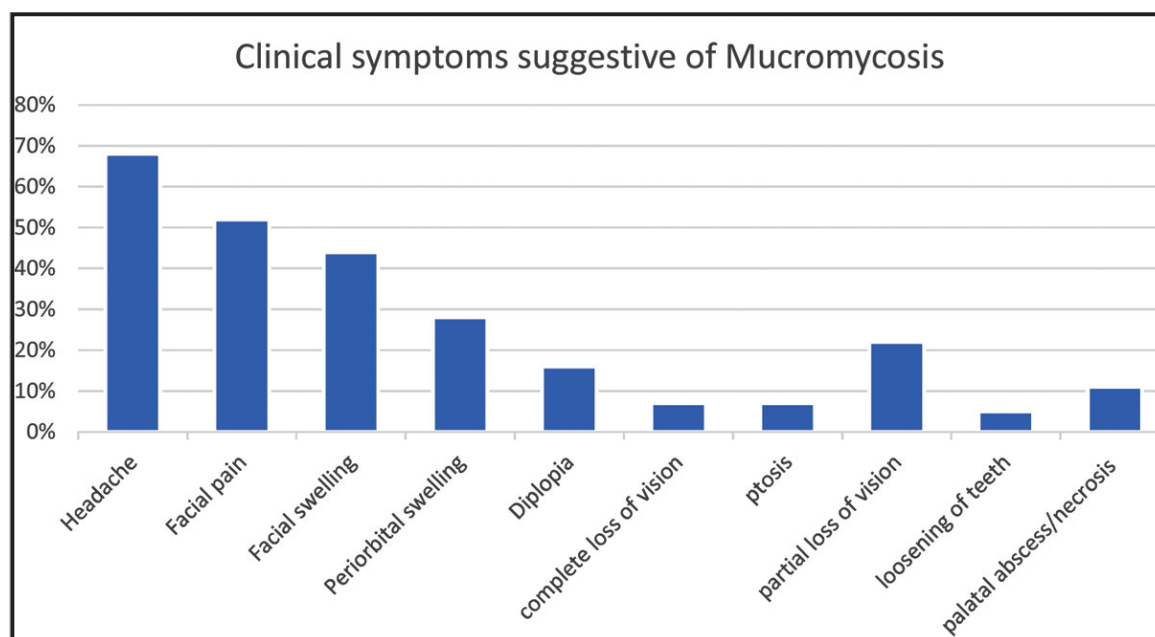


Fig 2. Spectrum of symptoms in Rhino-orbital Mucormycosis.

infarct. The involvement of various subsites in nose and paranasal sinus in T1 with contrast sequences is in 7 (15.90%) cases. The inferior turbinate was purely enhancing 15 (34.09%), non-enhancing 6 (13.63%) and

heterogenous (enhancing and non-enhancing) in 23 (52.27%) cases. The alveolus was involved in 2 (4.54%) cases and hard palate involved in 5 (11.36%) cases. The involvement of various sinus according to mode of enhancement is shown in Table II.

Table II: Involvement of various subsites in nose and paranasal sinus in T1 with contrast sequences

	T1 WITH CONTRAST		
	Enhancing	Non-enhancing	Normal
Maxillary	35 (79.54%)	9 (20.45%)	6 (13.63%)
Anterior Ethmoid	40 (90.90%)	15 (34.09%)	1 (2.27%)
Posterior Ethmoid	40 (90.90%)	10 (22.72%)	0
Sphenoid	26 (59.09%)	7 (15.90%)	11 (25%)
Frontal	23 (52.27%)	0	21 (47.72%)
Pterygopalatine Fossa	33(75%)	4 (9.09%)	7 (15.90%)
Infratemporal Fossa	24 (54.54%)	5 (11.36%)	15 (34.09%)

The T2 with fat suppression sequences was used to evaluate mainly orbital involvement. Orbital cellulitis (soft tissue inflammation) was present in 9 (20.45%), extraocular muscle involvement in 5 (11.36%), orbital apex involvement 3 (6.81%) and bony erosion of orbital wall in 4 (9.09%) cases. The DWI showed optic nerve infarct in 3 cases.

38 patients were operated within 5 days of admission. The remaining 6 patients were operated within 3 days due to intolerance to amphotericin and need for early debridement of infective focus.

The enhancing and non-enhancing middle turbinate is shown in Fig. 3.

The radiological involvement of alveolus and anterior wall of maxilla is shown in Fig. 4.

Involvement of gum causing abscess corresponding to Fig 4 is shown in Fig 5.

Depending on extension of disease according to MRI, we divided our surgery into 8 categories (A-H) as shown in Table III.

All debrided tissues were sent for biopsy. Suspicious nasal septum mucosa was removed as part of septectomy. All 44 patients received conventional amphotericin B

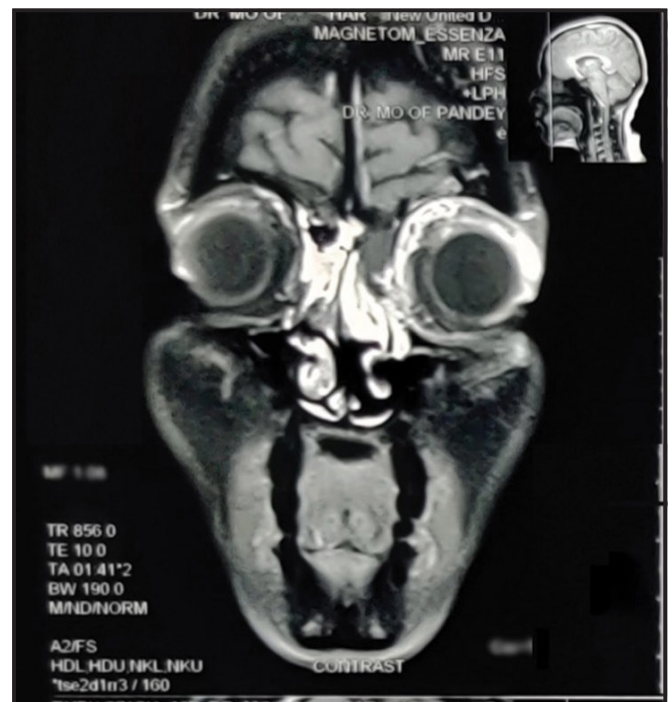


Fig 3. Coronal plane of contrast enhanced T1 weighted MRI shows dark coloured region in the middle turbinate on the left side which shows areas that has not taken up contrast.

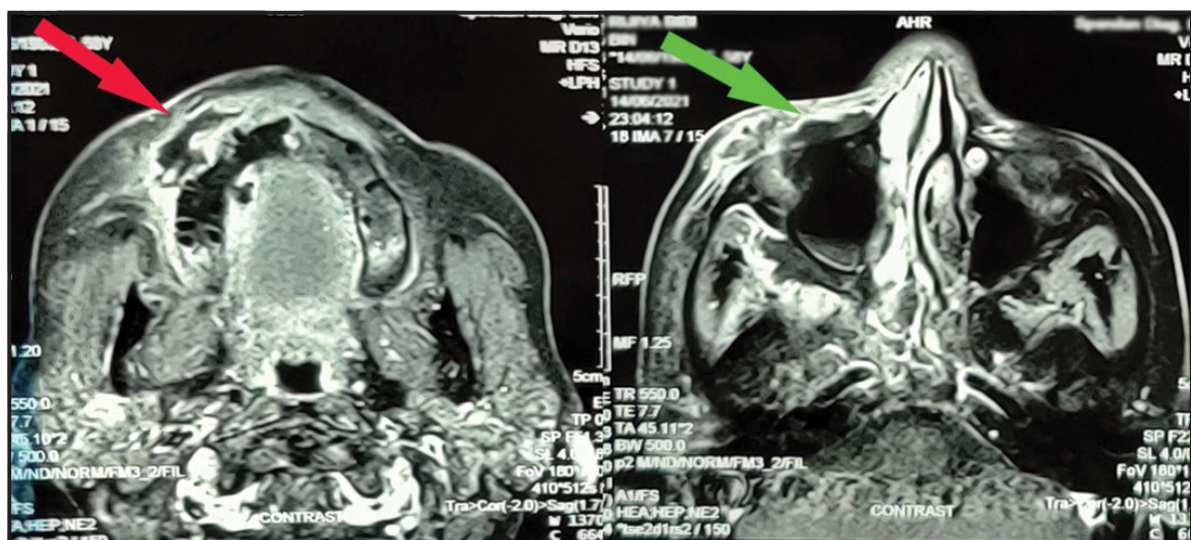


Fig. 4. Axial cut of contrast enhanced T1 weighted MRI showing gum necrosis on the right side with abscess formation (red arrow). Green arrow shows necrosed areas of the maxilla, spreading to the pterygopalatine fossa on the right side.



Fig. 5. Gum abscesses due to mucor

for 2 weeks and then Posaconazole (300 mg) administered daily. The most consistent change in biochemical parameter was low serum potassium after administration of amphotericin B (30 patients).

Revision endoscopic debridement was required in 3 cases (belonging to surgery category A & B) where both pterygopalatine fossa and infratemporal fossa had to be opened to remove necrotic tissue. Seven patients required oral prosthesis (Category F, G & H).

Unfortunately, 1 patient died due to bacterial septicemia who was intolerant to Amphotericin B and had undergone category D surgery within 3 days. This patient was newly diagnosed Diabetic during COVID treatment. Another 67-year-old patient who had undergone Category H surgery died due to cardiac arrest

The rest 42 patients were discharged and complete follow-up after discharge is available for 36 patients and

Table III: Spectrum of Surgical approach based on MRI findings

CATEGORY	SURGERY	NUMBER (%)
A	Modified Endoscopic Denker's approach + Unilateral opening of all paranasal sinus + visualisation of Pterygopalatine fossa (minimum surgery done for all patients)	2 (4.54%)
B	A+ Orbital Decompression (check periorbita and intraorbital involvement and clinically vision between 6/9-6/24)	3 (6.81%)
C	B+ Orbital Clearance (was definite involvement of intraorbital tissues)	6 (13.63%)
D	A+ Pterygopalatine fossa ± Infratemporal fossa clearance	23 (52.27%)
E	A/B/C/D + Alveolectomy (clinically loosening of teeth and MRI suggesting alveolus involvement)	2 (4.54%)
F	E+ Infrastructure Maxillectomy (hard palate involvement)	1 (2.27%)
G	Total Maxillectomy	4 (9.09%)
H	D/G + Orbital exenteration (complete loss of vision + orbital apex involvement)	3 (6.81%)

6 patients lost to follow-up. The follow-up duration after discharge ranged from 57 days to 82 days. All 36 patients are disease free in respect to last follow-up endoscopic surveillance.

Discussion

Increase in Mucormycosis in Indian context appears to be an unholy intersection of trinity of diabetes (high prevalence genetically), rampant use of corticosteroid (increases blood glucose and opportunistic fungal infection) and COVID-19 (cytokine storm, lymphopenia, endothelial damage).⁴

An early diagnosis with a prompt, well coordinated, multidisciplinary approach has been vital to save both the life and sight of the patient. Microbiological diagnosis, control of the underlying systemic condition, and antimicrobial therapy with debridement of necrotic tissue have remained the mainstay of management of rhino orbital Mucormycosis over the years. Systemic review of cases by Singh et al⁴ showed age range between 22-86 years with male predominance. Our study had age range between 21-67 years with male predominance. A study by Ravani et al¹¹ shows mean age of presentation 56.3 years with male dominance (64.5%). Singh et al reports active COVID status in 59.4% and recovered in 40.6% cases. Pre-existing diabetes was present in 80% cases and new onset diabetes was seen in 2.2% cases.⁴ However, in our study, which was exclusively based on post-COVID recovered patients, 34.09% were known diabetic and 25% were diagnosed as diabetic during COVID treatment. Use of steroids has been reported in 76.3% cases⁴ worldwide whereas our study showed 61.36%.

The clinical manifestation of post-COVID Mucormycosis was limited to headache, facial pain and facial swelling in majority of cases. In our experience, any of the above symptoms with history of COVID-19 must be aggressively evaluated for Mucormycosis. Early clinical presentation of rhino-cerebral Mucormycosis are often subtle and underappreciated.⁵ CT and MR imaging are often used for diagnostic workup. However, CT findings are non-specific.¹² The role of radiology

especially MRI is indispensable. Multiplanar MRI shows anatomic involvement which helps in surgery planning.¹³ MR imaging plays important role in aiding physicians in making a diagnosis for early treatment.¹⁴ The devitalised mucosa appears on contrast sequence as contiguous foci of non-enhancing tissue.^{12,15} In DWI sequence, increased signal intensity may be seen.¹⁵

Some authors have employed a surgical protocol consisting of bilateral full house FESS with debridement at the first instance, under the rationale that invasive disease may be present in the sinuses even in those patients without clinical or radiological involvement.¹⁶ No association was found between timing of surgery and outcome.¹⁶ The need for early surgery has been emphasised by various authors.^{17,18} It would appear that reversal of predisposing factors and commencement of antifungal therapy are more effective than early surgery in improving patient prognosis.¹⁰ In our management protocol, majority patients were operated within 5 days of admission. Because of the adverse renal and hepatic effects of amphotericin B (which can cause serious complications), some researchers have used it topically during treatment.¹⁰ In our series, out of 44 patients, 39 patients had adequate surgical resection as per decision taken on pre-operative MRI, as evidenced by clinical improvement and disease-free period after follow up. 3 patients required a revision surgery as the initial surgical exercise based on our interpretation of the two MRI sequences that we chose was inadequate. 2 patients expired due to other causes.

Maxillary sinus involvement and orbital exenteration was associated with poor prognosis.¹⁷

The mortality rate in Mucormycosis has been reported as 60 %¹⁷ and 52% (90 days).¹⁹ Reports suggest that disseminated and rhino orbital (with cerebral extension) Mucormycosis, shorter duration of symptoms, shorter duration of antifungal therapy, and treatment with amphotericin B deoxycholate (vs. liposomal) were independent risk factors for mortality.¹⁹ A combined medical and surgical management was associated with better survival.¹⁹ In our study use of conventional amphotericin B was restricted to 15 days followed by switching to oral Posaconazole. Regular postoperative

debridement and surveillance of these patients while on antifungal therapy with long-term follow-up helped to improve outcomes, resulting in fewer patients requiring multiple surgeries.¹⁷ In our protocol we employed endoscopic surveillance on every post-operative visit after discharge.

Nithyanandam et al²⁰ in their study on the clinical features and treatment outcomes of rhino orbital cerebral Mucormycosis have reported that debridement of sinuses is necessary in all cases of rhino orbito-cerebral Mucormycosis.

Our surgical experience shows that maximum patients had to undergo unilateral FESS with opening of pterygopalatine and infratemporal fossa. We conclude that all patients must minimally undergo the above surgery. Endoscopic Denkers' approach allows easy post-operative surveillance. The pterygopalatine and infratemporal fossa is anatomically hidden by posterior wall of maxilla. Since we found more than 50% involvement of these areas, the necessity to open and visualise the areas in our opinion is must in all cases of post-COVID rhino-orbital Mucormycosis.

Conclusion

Post-COVID Rhino-orbital Mucormycosis requires high index of suspicion. Underrated symptoms like headache, facial pain and facial swelling in post-COVID patients with associated immunocompromised state like diabetes mellitus must be thoroughly investigated by MRI nose, paranasal sinus and orbit. Surgical debridement limits as decided by MRI sequences can be an effective tool to remove necrosed tissue and inspection of areas like pterygopalatine and infratemporal fossa must be done routinely along with judicious use of post operative antifungal drugs like Amphotericin B. Endoscopic surveillance of cavity should be routinely done post-operatively and even in follow-up.

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