



Case Series

Perioperative management of patients recovered/recovering from COVID-19 infection with mucormycosis: A case series with practical recommendations

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ABSTRACT

Mucormycosis as a secondary fungal invasion in COVID-19 patients has been described in individual reports worldwide. However, India has declared mucormycosis epidemic in four states and one union territory. The sudden plethora of rhino-orbital mucormycosis cases in India has put the medical faculty to ponder over etiology behind such peaking graph of cases while braving it out trying to save these patients. As anaesthesiologists, the peri-operative management of these cases is a challenge due to known usual and unusual as well as yet unknown long-term multi-system derangements found in COVID-19 illness in addition to the serious nature of this aggressive fungal invasion. We are presenting a case series of six patients who underwent Functional Endoscopic Sinus Surgery along with orbital exenteration for mucormycosis.

Key Messages: Peri-operative management of mucormycosis in COVID-19 patients requires multidisciplinary evaluations, cardio-pulmonary optimisation and tight blood sugar control for better outcome. The ulterior goal should be avoiding exacerbation of post-COVID sequelae as well as extensive debridements along with Amphotericin B therapy to prevent further mucormycosis invasion.

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1. Introduction

Corona Virus Infectious Disease-19 (COVID-19) has swept the nation in the form of “second wave” causing fall off of medical infrastructure.¹ Lately number of mucormycosis cases are rising, presumably due to immunocompromised state in and beyond COVID-19. The anaesthetic concerns in such cases should target better patient outcome by catering to the manifesting complications of twin infection. We present a case series of six patients who came to our tertiary care centre in past 30 days either recovering/ recovered from COVID-19 with active mucormycosis for peri-operative management.

2. Case Description

2.1. Preanesthetic evaluation

Post-COVID team including an anaesthesiologist, medical and chest physician dealt with pre-operative optimisation. Residual cardiac dysfunction on symptomatology or clinically elicited by six minutes walk test and resting/active peripheral oxygen saturation (SpO₂) difference was assessed by cardiologists. Similarly, bedside respiratory assessment laid emphasis on physiotherapy and incentive spirometry. Features of “post-COVID” syndrome were looked for like fever, inflammation, thrombotic tendency, myalgia and depression.² Apart from routine investigations, inflammatory markers like CRP, D-Dimer and ferritin levels were sent. Anticoagulants like low molecular weight heparin (LMWH) were stopped 24 hours before surgery.

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Table 1: Brief overview of patients recovering from COVID-19 infection with active mucormycosis posted for surgical debridement

Patient's history	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (in years)	60	55	60	55	51	50
Gender	F	M	M	M	M	M
Risk factors	Diabetes+	Diabetes + Dexamethasone+	Diabetes + Dexamethasone+	Diabetes + Dexamethasone+	Diabetes+	Diabetes + Dexamethasone+
Initiation of symptoms (In days) after COVID-19 diagnosis	3	6	10	6	12	14
Diagnostic Modality	KOH preparation	KOH preparation	KOH preparation	KOH preparation	KOH preparation	KOH preparation
Investigations						
Complete Blood Count						
Hb(gm/dl)	13.7	12.5	13.2	11.2	11	13.9
Total leucocyte count(*1000/cumm)	11.6	21.2	16.2	14.3	13.3	15.3
Platelet count(*1000/cumm)	370	270	138	347	234	304
Differential Leucocyte count (DLC)	Neutrophils-75%, Lymphocytes-50%, Monocytes-10%	Neutrophils – 70%, Lymphocytes – 60%, Monocytes – 12%	Neutrophils – 80%, Lymphocytes – 45%, Monocytes – 10%	Neutrphils – 60%, Lymphocytes – 30%, Monocytes – 8%	Neutrophils – 75%, Lymphocytes – 40%, Monocytes – 10%	Neutrophils – 75 %, Lymphocytes – 40%, Monocytes- 10%
Renal Function Tests						
S.creatinine(mg/dl)	0.83	1.92	1.13	0.98	1.10	0.68
Blood urea(mg/dl)	34.1	65	75	40.4	23	26
Liver Function Tests						
Direct bilirubin/total bilirubin(mg/dl)	0.11/0.38	0.15/0.36	0.46/0.85	0.27/0.54	0.63/0.4	0.32/0.6
SGOT/SGPT/ALP(Units/Ltr)	11.3/103	17/15	75/22/41	26/37/92	34/63/98	23/25/114
Total protein/Albumin(gram/dl)	6.84/2.68	6.4/2.0	6.8/2.5	4.5/1.9	6.4/2.4	6.9/2.8
Serum Electrolytes						
Serum Sodium(mEq/L)	141	134	135	134	137	133

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Table 1 continued

Serum	3.6	4.4	4.5	4.7	4.3	4.1
Potassium(mEq/L)						
Preoperative diabetic status						
HbA1C	13	13.6	13.1	12.7	12.4	13
Urine for ketones	+	+	+	-	-	+
ArterialBlood Gases	Ph- 7.2, pCO2-30, pO2 -120, HCO3 -18, SpO2 -99%	Ph - 7.3, pCO2 - 28, pO2 - 99, HCO3 - 20, SpO2- 98%	Ph - 7.1, pCO2 - 26, pO2 - 95, HCO3- 16, SpO2- 96%			Ph- 7.4, pCO2- 35, pO2- 100, HCO3- 22, SpO2- 99%
Inflammatory Markers						
C-Reactive Protein(mg/dl)	240	208	406	115.4	85.2	178
D-dimer (nanogm/ml)	900	1250	1500	293	100	187
Ferritin (nanogm/ml)					236	236
CT/MRI findings	Left ethmoid and maxillary sinus involvement + Orbital cellulitis+ cavernous involvement+	Right frontal sinus and right anterior ethmoid sinus with extension to right frontal lobe + Orbital cellulitis+ Cavernous involvement +	Left maxillary, ethmoid and sphenoid sinus involvement + Orbital cellulitis+ Middle Cerebral Artery territory infarct in right fronto- parietal region(post-operative)	Bilateral maxillary, left ethmoid and sphenoid sinus involvement + Orbital cellulitis+ Cavernous involvement+	Bilateral maxillary, ethmoid and frontal sinus involvement+ Orbital cellulitis+	Right maxillary, frontal and ethmoid sinus+ Orbital cellulitis+ Cavernous involvement +
Intra-operative management						
Pre-operative vitals	Sinus tachycardia+ 126/min		Premature atrial ectopics (less than 6 in 2 min) difficult			
Intravenous Cannulation	Difficult	Easy		easy	easy	difficult
Central Line insertion	+	+	+	+	-	+

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Table 1 continued

Ease of intubation	Bougie, BURP 3 attempts	Stylet BURP 1 attempt	Stylet 2 attempts	1 attempt	Bougie BURP 2 attempts	1 attempt
Intra-operative events	Tachycardia upto 130 beats/minute persistent managed with injection metoprolol	Fever 101 degree Fahrenheit managed with injection paracetamol	Premature atrial and ventricular ectopics managed with injection amiodarone 300mg and injection metoprolol 3 mg	Insulin infusion and boluses due to poor glycemic control	Insulin bolus given due to intraoperative raised random blood sugar(RBS) levels	Hypertension managed with injection nitroglycerine infusion 0.01 microgram/kilogram/minute , Fever 100 degree Fahrenheit managed with injection paracetamol
Surgical field Outcome	Clear Discharged on oral posaconazole 300mg OD	Bleeding a lot Parietal abscess, confused state undergoing treatment with liposomal amphotericin b and posaconazole	clear MCA infarct, GCS 7-8, tracheostomised and discharged on follow-up	clear Discharged on follow-up	Bleeding Mucormycosis ward undergoing treatment	Bleeding Discharged on follow-up

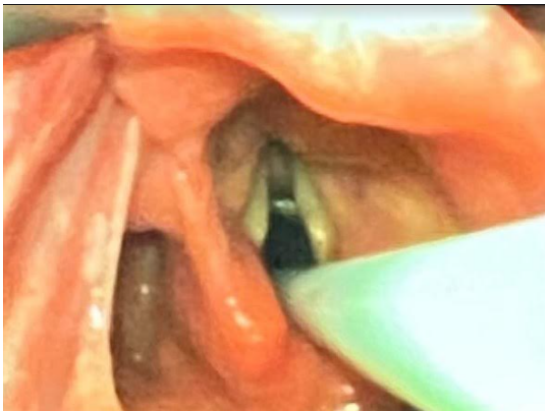


Figure 1: Preglottic edema



Figure 2: Whitish fungal growth around the vocal cords.

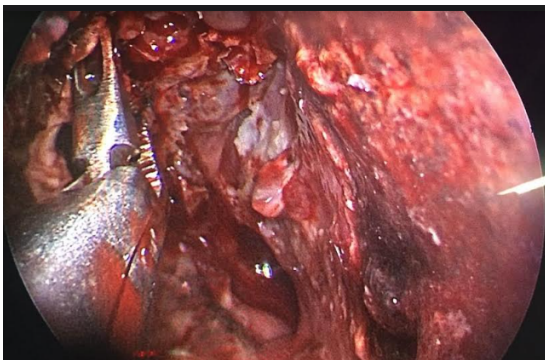


Figure 3: Black necrotic tissue inside the nasal cavity

However, as cases were taken up in emergency, many a times complete evaluations were not possible and Pulmonary Function Tests (PFTs) precluded. Written informed risk consent along with Intensive Care support and ventilatory consent were taken according to the aforesaid evaluation and the extent of surgery.

2.2. Intraoperative management

The Operation Theatre (O.T.) was prepared by 2 ± 1 anaesthesiologists clad in level 3 Personal Protective Equipment (PPE). Patient were transported with a triple-layer masks covering their nose and mouth. Vitals were attached – mainly four – lead electrocardiography (ECG), SpO₂, Non Invasive Blood Pressure (NIBP), end-tidal carbon dioxide (EtCO₂). Patients were preoxygenated with 100% O₂ and premedicated with injection fentanyl 100 microgram. Rapid sequence induction was done using injection propofol 2-2.5 milligram/kilogram(mg/kg), succinylcholine 2 mg/kg. C – Mac conventional blade was used for intubation and oropharyngeal packing, followed by maintenance with isoflurane 2 volume/volume % (V/V%) and 100% O₂. Local application of lignocaine with adrenaline pledgets inside both nares was done. However, two patients had arrhythmia/ extremely high blood pressure readings after insertion of pledgets. In those cases, pledgets soaked with plain lignocaine were kept. Injection metoprolol was given in titrated doses for bloodless field. After surgery, all patients were extubated successfully. Central line was inserted before extubation in either internal jugular / subclavian vein using ultrasound guidance. Patients were applied triple layer mask and shifted to mucormycosis ward for further management.

3. Discussion

Secondary infections after COVID-19 recovery are being witnessed due to virus induced bone marrow suppression as well as treatment modalities like tocilizumab, bartcinib, corticosteroids, broad spectrum antibiotic without clinical evidence of bacterial infection etc.^{3,4} Among fungal invasions, mucormycosis is strongly associated with poor blood glucose contro⁵ as all patients were chronic diabetics with glycosylated HbA1C ≥12. Steroids also perpetuate immunosuppression, hyperglycemia and ketone bodies formation providing favourable medium for fungal growth; found in four of our patients.⁶ Thus, indications of steroids especially in diabetics with mild COVID-19 infection should be reconsidered besides reducing dose and duration of therapy. If indicated, regular insulin can be given along with steroid dosing. We suggest using methylprednisolone rather than long-acting dexamethasone to reduce incidence of hyperglycemia. Another plausible risk factor could be augmentation mucormycosis induced thrombosis and necrosis of infected vessels with co-existing COVID-19 which demands further research.

Anaesthetic considerations were deliberated upon by our team and summarized into optimization of active or past COVID-19 related multi-organ sequelae along with providing perfect anaesthetic environment to prevent spread of mucormycosis. Most patients were American Society of Anaesthesiologists (ASA) Category 3, 4 taken up

under high-risk consent. Although four of our patients are discharged, many others developed post-operative cardiac, pulmonary or neurological complications to which they succumbed eventually.

Safety of the operating team was our prime concern. ASA guidelines mention use of viral transmission – related precautions with immunocompromised patients having COVID-19 illness for at least 10 and up to 15 days from onset of symptoms.⁷ As most of our patients were taken within this time frame, some even symptomatic, it was decided to use level-3 PPE in every case.

In context to COVID-19, cardiac abnormalities were screened by cardiologists and optimized before surgery. Two of our patients had dysrhythmias without any functional abnormality on routine Echocardiography. We opine that stress Echocardiography/Holter's monitoring or cardiac biomarkers like Troponin T, pro-Brain Natriuretic Peptide could have been better diagnostic modalities.⁸ COVID-19 related hypercoagulable state explains difficult vascular access in 50% of our patients.⁹ Central line was inserted in all patients except one to administer liposomal Amphotericin B therapy and long-term medication.

Post COVID-19 residual shortness of breath and restrictive pattern on pulmonary function tests was present and managed intraoperatively with lung protective ventilation.¹⁰ Neurological manifestations like stroke, intracranial haemorrhage and critical illness myopathy due to intubation and prolonged immobility necessitate avoidance of succinylcholine but we used it as none of our patients had long hospital stay.

Being a major risk factor, tight sugar control was achieved with insulin alone or in combination with oral hypoglycemics. Ketoacidosis was managed with aggressive saline therapy, insulin infusion and Arterial Blood Gas (ABG) optimization pre-operatively. Side-effects of intravenous amphotericin therapy like hypokalemia, hypomagnesemia, fever, chills, dyspnea and hypotension¹¹ were an important consideration. It was given in continuous infusion to decrease frequency and severity of side effects. Aspirin and amphotericin B therapy was also going concurrently in many patients with strict input-output monitoring in view of increased risk of nephrotoxicity.

One of our patients had intraoperative multifocal premature ventricular contractions intermixed with premature atrial contractions, rate going up to 150/min accompanied by hypotension (>20% of baseline). One litre normal saline was rushed and injection amiodarone 300mg given over 10 minutes followed by metoprolol 3mg which reverted the arrhythmias and surgery was commenced. Hence, awareness about cardiac and renal parameters including electrolytes is necessary in patients on amphotericin B therapy. Plus COVID-19 associated myocarditis and prothrombotic state could have been another possibility. This patient did not regain consciousness after surgery and had Middle Cerebral Artery

(MCA) Infarct on subsequent Computed Tomography (CT) scan. Prasad K. Kulkarni et al also reported similar episode managed with lidocaine infusion. He opined that amphotericin B therapy can cause such an adverse event.¹²

Mucormycosis rarely involves laryngeal and tracheal tissues as skip lesions or in continuity making endotracheal intubation challenging.¹¹ We performed all intubations with C-Mac videolaryngoscope to prevent airway trauma and dissemination of fungal growth. One of our patients had preglottic oedema (Fig-1a) while another had whitish growth around glottic aperture (Fig-1b) which was suctioned after inserting the endotracheal tube cautiously. Lastly hyperbaric oxygen has fungistatic effect and helps in revascularization of poorly perfused hypoxic but viable areas. As hyperbaric oxygen was not available, we gave 100% oxygen avoiding nitrous oxide. Isoflurane similarly has fungistatic effect,¹² hence given in all cases.

4. Conclusion

Rhino-orbital mucormycosis superseding COVID-19 infection requires anaesthesiologists to push at remedying the risk factors, optimizing multi-organ dysfunction, ensuring tight glucose control and intraoperative bloodless field to aid in debridement. It is a simultaneous war against two enemies and only a wholesome picture curated by perioperative physicians can save our patients.

5. Source of Funding

None.

6. Conflict of Interest

None.

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