

The aftermath of COVID-19 pandemic: Rhino-orbital mucormycosis

INTRODUCTION

Coronavirus disease (COVID)-19 causes over-activation of the innate immune response leading to multi-organ damage. In addition to affecting the major systems like respiratory, cardiovascular and gastrointestinal tract (GIT), it targets retinal vessels also causing pyogranulomatous uveitis, choroiditis and macular micro-vascular impairment.^[1] It also remains dormant in paranasal sinuses for months after acute phase infection is cured and precipitates rhino-orbital mucormycosis.

Fungal rhino-sinusitis is an ascending infection with serious life and vision-threatening consequences. We are reporting 10 such cases that were operated for functional endoscopic sinus surgery (FESS) within a period of less than 3 months after COVID-19 infection. This brief clinical overview is about the increasing cases of mucormycosis and the related anaesthesia concerns in convalescent COVID-19 patients.

These cases have highlighted the challenges before the anaesthesiologists which also emphasises the need to study the management of pandemics so that the medical fraternity would be able to manage pandemics in an efficient manner.^[2]

CASE HISTORY

The patients reported are adults (age-group 35-75 years) either known or newly diagnosed diabetics; they had history of hypertension and ischaemic heart disease (IHD) and had recently recovered from COVID-19 infection. The presenting complaints for rhinotology consultation were headache, swelling and pain in either eye and pain over face on the same side. They were receiving all medications as per physician advice. Oral hypoglycaemics were discontinued and patients were shifted to insulin regimens with strict blood glucose monitoring pre-operatively. Anti-hypertensives, statins and anti-inflammatory agents were continued. Anti-fungal regimen, either conventional or lipophilic amphotericin B was continued with monitoring of renal functions.

Pre-anaesthetic airway evaluation was done after taking due COVID-19 precautions. All routine investigations were done [Table 1]. Patients were ambulatory; six-minute walk test results were provided by chest physician. Most of the cases had anticipated difficulty in intubation due to compromised oral and dental hygiene, fungal discoloration and occasional bleeding on touch of throat and palate. Mask holding was also difficult due to pain and proptosis. Positioning for airway ease was restricted due to pain and stiffness in diabetics. Pre-operative preparation included pre- and intra-operative optimisation of blood sugar, control of hydration status due to post- COVID-19 poor general condition and inability to drink and swallow freely due to painful and/or obstructing fungal lesions and anticipated hypotension due to ongoing anti-fungal therapy.

After ensuring use of adequate personal protective equipment (PPE) including N95 masks, face shields and availability of aerosol control measures, appropriate risk consent and temperature were checked and intravenous line was accessed. Electrocardiography (ECG), pulse oximetry, non-invasive blood pressure (NIBP) monitors were connected. A difficult intubation cart was kept ready. Patients were pre-medicated with injection glycopyrrolate 4 µg/kg, injection fentanyl 2 µg/kg, intravenously. After pre-oxygenation with 100% oxygen, they were induced with injection propofol 2 mg/kg in titrated doses. The palatal perforation if present (Case no. 10) was covered with gauze and intubation performed with proper size cuffed reinforced endotracheal tube after relaxation with injection succinylcholine 1.5 mg/kg. Injection xylocard (Lignocaine Hydrochloride 2%) 1.5 mg/kg was used to attenuate laryngoscopy response. In cases of difficulty, C-MAC video laryngoscope (KARL STORZ) was used to accomplish safe intubation.

Intra-operative blood sugar monitoring was done. The patients were maintained on oxygen, nitrous oxide (50:50) and isoflurane 1% or sevoflurane with controlled ventilation. Muscle relaxation was maintained with injection atracurium 0.5 mg/kg. Intra-operative endoscopic views of the fungal infection were obtained [Figure 1]. On completion of surgery, neuromuscular blockade was reversed and after ascertaining adequate muscle power, patients were extubated and shifted to recovery with oxygen 2 L/min via Hudson-mask. The rest of the post-operative period

Table 1a: Case details

	1	2	3	4	5
Serial number	1	2	3	4	5
Age (years)	47	60	70	43	53
Gender (M/F)	M	M	M	M	M
Pre-operative COVID status	Positive on 12-2-21	Positive- 14.03.21 and 25.03.21	Positive in Dec 2020	Positive on 28-12-20	Negative when operated
	Negative when operated	Negative when operated	Negative when operated	Negative when operated	
Oxygen support during COVID	Via nasal prongs	On Bipap for 5 days during COVID	Via nasal prongs	Via nasal prongs	Not known
Presenting complaints-	+	+	+	+	+
Facial pain and swelling	+	+	+	+	+
Toothache and loosening	+	+	+	+	+
Orbital pain and swelling					
Duration of presenting complaints	1 week	5 days	4-5 days	1 week	5 days
Co-morbidities-					
New onset DM	+	+	+	+	+
Past H/O	IHD since 10 years	DM- 5 years. Operated CABG- 3 years HT- 3 years	DM-recent onset	DM-recent onset HT since 2 years	DM since 2 years
On Treatment-	T. Aldactone 50 mgOD T. Rosuvastatin 10 mg HS T. Digoxin 0.125 mg OD	Inj. Insulin Glargin 20 U BD T. Aspirin 75 mg OD T. Amllo 5 mg OD T. Atorvastatins 40 mg HS	Inj. Insulin (P) 10-10-8 Inj. Glargine 12 U SC BD	Insulin (P) according to glucostix T. Amlodipine 10 mg OD T. Telma 40 mg HS	T. Linezolid 600 mg BD T. Glucoryl m1 TDS T. Voglibose 0.3 mg OD
Present treatment	Heparin 5000 IU Insulin as per glucostix, T. Variconazole 200 mg BD	L. Amp B 300 mg in 5% Dextrose	L. Amp B 250 mg in 5% Dextrose	L. Amp B 250 mg in 5% Dextrose	L. Amp B 300 mg in 5% Dextrose
Investigations	Hb- 10 g/dl, RBS- 112 mg% MRI- Sinusitis with bone destruction intracranial and intra orbital with optic neuritis with right temporal lobe abscess CT Thorax- Bilateral pleural effusion with atelectasis of underlying lungs with areas of ground glass opacities. Perihilar vessel engorgement with peri bronchovascular thickening	CT Thorax- Patchy areas of Ground Glass Opacities, crazy paving appearance, subpleural fibrotic bands	MRI- Sinusitis with bone destruction intracranial and intra orbital with optic neuritis	CT Thorax- Multiple patchy confluent ground glass opacities with interstitial thickening in peribronchovascular and peripheral subpleural regions of both lungs CT brain- Hyperdense foci in both side maxillary, ethmoidal, sphenoidal sinuses with bony erosion.	CT Thorax- Multiple ground glass opacities with thin fibrolinear fibrotic changes in both lungs CT brain & paranasal sinuses- Polypoidal mucosal thickening of sphenoidal, ethmoidal and maxillary sinuses and both osteomeatal complexes widened
BP	130/86 96%	140/90	110/70	150/92	120/70
SpO2		93% on room air	97%	98%	93%
Other remarkable points in general examination if any		97% on supplementation			

Contd...

Table 1a: Contd...					
Systemic examination					
CVS/RS/CNS/PA	Normal	Fine basal crepts	Normal	Normal	Normal
Airway examination					
MO	3 fingers	3	2 fingers	2 fingers	3 fingers
MPC	3	3	3	3	3
Palate/Teeth/NE	N/upper incisors loose	Black crusts	Black crusts	Loose premolars	
Airway management plan	Video L'scope	Macintosh L'scope	Video L'scope	Video L'scope	Macintosh L'scope
Incentive Spirometry	Advised	Advised	Advised	Advised	Advised
Six min. walk test result	92%	92%	95%	97%	87%
Intraoperative events	Hypotension	Hypotension Hypoglycaemia	Hypoglycaemia	Hypertension	-
Extubated on table or ICU shifted for monitoring or ICU shifted for ventilation	Extubated	ICU-ventilated	Extubated	ICU monitoring	Extubated

Table 1b: Case details					
Serial number	6	7	8	9	10
Age (years)	42	54	41	59	31
Gender (M/F)	M	F	M	F	M
Pre-operative COVID status	Negative when operated	Positive in Feb21	Negative when operated	Positive on 17.3.21	Negative when operated
		Negative when operate		Negative on 22.3.21 Negative when operated	
Oxygen support during COVID	Not known	Via nasal prongs	Not known	Via nasal prongs	Via nasal prongs
Presenting complaints-	+	+	+	+	Presented and operated acute pancreatitis 3 months back. Black colouration with hole in palate since 2 months
Facial pain and swelling	+	+	+	+	
Toothache and loosening	+	+	+	+	
Orbital pain and swelling					
Duration of presenting complaints	1 week	10 days	10 days	1 week	15 days
Co-morbidities-					
New onset DM	+	+	+	+	+
Past H/O	DM since 1 year	DM-recent onset	DM-recent onset	IHD HT	DM-recent onset HT since 8 months
On Treatment-	Inj. Insulin Glargine 20 U SC HS Inj. Insulin (P) 8-6-4 SC	T. Glimepiride 2 OD Inj. Insulin NPH 8-0-8 Inj. Insulin (P) 6-6-4	Inj. Insulin NPH 6-0-6 Inj. Insulin (P)- as per glucostix	Inj. Meropenem 500 mg U HS T. Aspirin 75 mg OD T. Atorvastatin 40 mg HS	Insulin Glargine 14 units SC T. Telmisartan 40 mg
Present treatment	L. Amp B 150 mg in 5% Dextrose	L. Amp B 300 mg in 5% Dextrose	L. Amp B 300 mg in 5% Dextrose	L. Amp B 150 mg in 5% Dextrose	L. Amp B 300 mg in 5% Dextrose

Contd...

Table 1b: Contd...

Investigations	MRI brain- Pan sinusitis, left orbital cellulitis with left optic nerve extension CT neck, thorax- Signs of aspiration pneumonitis with mucormycosis with right emphysema.	CT brain- Non enhancing soft tissue thickening in maxillary, sphenoid, ethmoidal sinuses suggesting fungal sinusitis	CT brain- Invasive fungal sinusitis with bony erosion with intra orbital and intra cranial extension	CT brain and paranasal sinuses- Soft tissue density in pansinuses with left orbital cellulitis. CT Thorax- Multiple patchy areas of resolving Ground Glass Opacities with fibrotic change in lung fields with multiple subpleural bands.	CT paranasal sinuses- Right Maxillary sinusitis, bony erosion, intracranial extension, intra-orbital extension. MRI brain- Mucosal thickening in right. maxillary, ethmoidal sinus. Extension in pterygopalatine fossa and orbit.
BP	110/80	100/70	100/76	130/90	140/96
SpO2	98%	96%	97%	95%	96%
Other remarkable points in general examination if any					
Systemic examination					CVS-NAD
CVS/RS/CNS/PA	Normal	Normal	Normal	Normal	RS- rhonchi occasional Scar over abdomen
Airway examination					
MO	Tracheostomy	3 fingers	3	2	3
MPC	in situ	3	3	4	3
Palate/Teeth/NE					Palate perforation
Airway management plan	-	Macintosh L'scope	Macintosh L'scope	Video L'scope	Video L'scope
Incentive	Advised	Advised	Advised	Advised	Advised
Spirometry					
Six min. walk test result	-	92%	95%	95%	-
Intraoperative events	Hypoglycaemia	Intubation attempt	-	-	Hypotension Hypoglycaemia ICU ventilated
Extubated on table or ICU shifted for monitoring or ICU shifted for ventilation	ICU monitoring	ICU monitoring	Extubated	Extubated	

M-male. F- Female. + Present. DM-Diabetes Mellitus. H/O- History of. HT- Hypertension. IHD- Ischaemic Heart Disease. CT- Computed Tomography. MRI- Magnetic Resonance Imaging. G.E- General examination. CVS- Cardiovascular system, RS- Respiratory System. PA- Per Abdomen. MPC-Mallampati Classification Score. ICU- Intensive Care Unit. COVID- Coronavirus infectious disease. SpO2- Saturation of oxygen in peripheral blood. HS- Hour of sleep. L Ampho B- Lipophilic Amphotericin B. NAD- Nothing abnormal detected. L'scope- Laryngoscope, BP-Blood pressure; MO-Mouth opening; CVS-Cardiovascular system; RS-Respiratory system; CNS-Central nervous system; PA-Per abdomen; Amlo-Amlodipine; Telma-Telmisartan

was monitored either in the ward with analgesic cover of 15 mg/kg IV paracetamol or in the intensive care unit (ICU) on elective ventilation depending upon the clinical condition [Table 1].

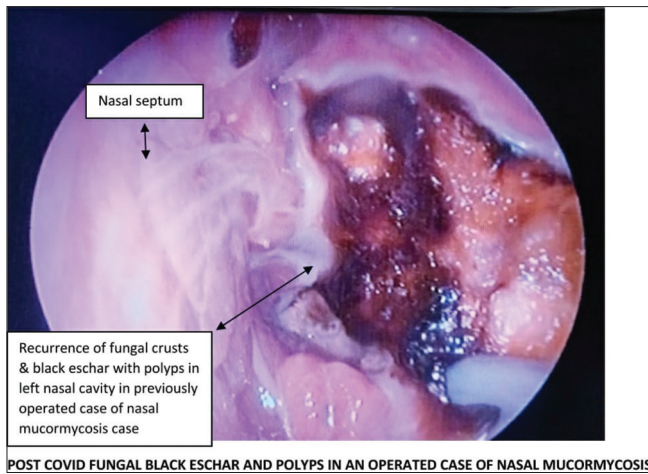
DISCUSSION

Occurrence of sinusitis, either allergic, non-allergic or infective, is commonly reported in the general population. Up to 90% cases are of fungal aetiology.^[3] In the year 2021, we noticed a steep rise (almost four times) in number of FESS cases in our institution for removal of mucormycosis, when compared to the last two years.

Chakraborty *et al.* have reported that the rational approach towards prognosis and treatment of fungal sinusitis is not yet standardised and therefore the incidence is high. They proposed the classification of fungal sinusitis as invasive and non-invasive.^[4]

Fungal rhinosinusitis is often an ascending infection affecting the orbit via vascular invasion of fungal hyphae of mucorales. It is an opportunistic infection found in immunocompromised patients.^[5]

Patients with invasive fungal infections have Cryptococci or Pneumocystis infections. The use of antifungal agents is said to change the epidemiology of *Candida albicans* to non-*albicans* *Candida* strains The



POST COVID FUNGAL BLACK ESCHAR AND POLYPS IN AN OPERATED CASE OF NASAL MUCORMYCOSIS

Figure 1: Fungal Black Eschar and Polyps

explanation for high mortality rates of such patients are due to resistance to antifungal agents, underlying serious medical diseases, seropositive status and inability to achieve early source control.^[6] Castelnovo *et al.*^[7] studied fungal sinusitis cases (1050 patients) over a period of three years and found *Aspergillus fumigatus* (76.9% cases) to be the most often occurring mycetes. They reported patients presenting with facial pain followed by nasal obstruction with computed tomography (CT) showing focal areas of non-homogeneous intensity and metal like endo-sinus calcifications in 84.4% cases.

The acute pulmonary injury in COVID-19 is due to release of pro-inflammatory cytokines like interleukin (IL-1, 2, and 6) and tumour necrosis factor (TNF)-alpha. National Health Commission of China has included tocilizumab, a novel monoclonal antibody that competitively inhibits binding of IL-6 to its receptor in COVID -19 treatment and our protocol also includes the same. Tocilizumab binds soluble as well as bound IL-6 receptors and hinders pro-inflammatory effects of the virus.^[8] Our reported cases were post- COVID and had received steroids and/or tocilizumab treatment as per department protocol.

FESS has been reported to be curative for fungal ball. In cases of fulminant invasive mycoses, surgery prevents endo-cranial complications.

High doses of systemic amphotericin B are given to control underlying disease; it is given as an infusion over 2-6 hours to reduce the severity and frequency of side effects of rapid administration. Amphotericin B is the primary antifungal therapy for patients with opportunistic fungal infections although antifungals

have poor penetration ability at the site of infection.^[9] Our patients received it in a dose of 1 mg/kg body weight titrated over 3 days. Hypokalaemia, hypomagnesemia, fever, chills, dyspnoea, and hypotension are common side effects of Amphotericin B. Allergic reactions, seizures, anaemia, and thrombocytopenia are less likely to occur but are well-documented. Renal function is also impaired, and a permanent decrease in the glomerular filtration rate is likely.

Our patients frequently had difficult airway, intraoperative hypotension with occasional arrhythmias that responded to treatment with lidocaine. We were careful about renal, electrolyte, coagulopathy, haemodynamic, and respiratory aberrancies during the anaesthetic management of these patients because of the risk associated with all major systemic functions.^[10]

CONCLUSION

Rhino-orbital mucormycosis is a serious aftermath of COVID-19, An effective multi-disciplinary approach can help to tackle this deadly disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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