

Post COVID Tsunami of Black Fungus – Anaesthetic Challenges in Management: Case Series

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Rhino-orbital-cerebral Mucor mycosis is a rare, opportunistic, fatal fungal infection most commonly seen in diabetic and immunocompromised individuals, but an outbreak of cases was seen in post COVID-19 patients during the second wave in India. Our aim is to elaborate the anaesthetic management of post COVID-19 Mucor mycosis patients scheduled for FESS (Functional Endoscopic Sinus Surgery) for debridement of involved areas. Here, we have discussed the anaesthetic challenges faced in a series of eleven patients with COVID-19 and Mucor mycosis such as uncontrolled diabetes mellitus, irrational use of steroids for the treatment of COVID-19, amphotericin B and its interactions with anaesthetic management. Preventive measures in COVID-19 patients, early detection, timely management, perioperative vigilant monitoring, multidisciplinary approach will reduce the morbidity and mortality in these patients. As limited data is available, further studies are necessary to understand aetiology and pathogenesis of Mucor mycosis in post COVID-19 for better management.

Keywords: Amphotericin B, anaesthetic management, COVID-19, FESS (Functional Endoscopic Sinus Surgery), Mucor mycosis

Introduction

COVID-19 is an infectious disease caused by the novel SARS-CoV-2 virus which has affected more than 10 million people worldwide. Rush of cases of Mucor mycosis – also called as ‘Black Fungus’ were reported during the second wave in India. It is a rare, fulminant, highly lethal, locally invasive, opportunistic fungal infection. Patients with diabetes and immunocompromised individuals are more prone as COVID-19 infection and overuse of steroids further reduce the immunity. As cases were scheduled on an emergency basis to prevent further complications, optimization of medical diseases were limited due to lack of adequate time. We faced various complications in emergency procedures like FESS (Functional Endoscopic Sinus Surgery) for debridement, enucleation, exenteration, maxillectomy and

revision FESS. Emergency surgeries in debilitated post COVID-19 patients with multiple comorbidities made anaesthetic management more challenging. Out of many cases operated in May 2021 in our institute, 11 cases with anaesthetic significance are included. The aim of this article is to provide information about possible deranged medical conditions and complications that an anaesthesiologist might face and its management.

Case series

Management of 11 cases are discussed here and specific points related to individual cases are discussed in table 1. Along with routine preoperative evaluation special attention was given to the status of COVID-19, previous and ongoing treatment, comorbidities, recent rise in blood sugar levels, cardiopulmonary status, need for oxygen support, details about the usage of amphotericin B, thromboprophylaxis and difficult airway. Patients were in American Society of Anesthesiologists physical status classification III to IV. Saturation on room air and with oxygen were recorded. Cranial nerve involvement was also assessed. Prolonged hospital and ICU stay made venous access difficult in several patients. Hypokalaemia and elevated blood sugar levels were commonly encountered. Chest x-ray, computed tomography

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and magnetic resonance imaging of paranasal sinuses showed variable involvement in each patient. Consent was taken and the patients were counselled about nasal packing and need for mouth breathing after surgery. Availability of ICU beds was ensured. Standard ASA monitoring was continued. Difficult intubation cart was kept ready. Either central venous or peripherally inserted central cannulation was done in all patients. Patients were premedicated with glycopyrrolate 0.2 mg, midazolam 1 mg, fentanyl 2 mcg/kg intravenously. After pre-oxygenation with 100% oxygen, patients were induced with intravenous propofol 2 mg/kg and they were intubated with a Portex cuffed endotracheal tube of appropriate size, after relaxation with intravenous succinylcholine 1.5 to 2 mg/kg. Patients were maintained on 50% air and oxygen, inhalational isoflurane 1% and intravenous

vecuronium 0.08 to 0.1 mg/kg. Frequent intraoperative blood sugar monitoring was done to titrate insulin infusion in patients with high blood sugar. Hypokalaemia was corrected with intravenous potassium chloride infusion. For analgesia, intravenous tramadol 0.5 to 1 mg/kg and paracetamol 1 g were given. Hemodynamically stable patients were reversed with intravenous neostigmine 0.05 mg/kg and intravenous glycopyrrolate 0.4 mg.

Spontaneously breathing patients with tidal volume above 5ml/kg, saturation greater than 95%, had a good muscle power and response to verbal command were extubated before transferring to ward or ICU. Unstable patients with poor respiratory efforts were not extubated and shifted to ICU.

Specific anaesthetic management of a series of 11 cases are mentioned in table 1.

Table 1: Specific anaesthetic management of series of eleven cases with *Mucor mycosis*

| No | Age Sex ASA | Comorbidities | Diagnosis and procedure | Preoperative findings | Intraoperative events | Postoperative events |
|----|-------------------|---|---|--|---|---|
| 1. | 45 M III E | Hypertension Uncontrolled diabetes | Rhino orbital Mucormycosis For FESS | Restricted mouth opening with a large swelling over the right side of face. Blood sugar-302mg/dl | Bougie guided intubation | Extubated. After two weeks he developed numbness over right cheek again posted for Revision FESS – uneventful. |
| 2. | 67 M IV E | Uncontrolled diabetes, Alcohol withdrawal syndrome | Rhino-Orbital cerebral mucormycosis with pulmonary fibrosis For FESS | Tachypnoeic, Saturation 78% (room air), 95% (oxygen 6L/m) Blackish discolouration of hard Palate. | Supraglottic oedema noted during intubation. Intraoperative hypotension. Hydrocortisone 100 mg Noradrenaline 0.05 mcg/kg/min | Not extubated due to poor respiratory effort and inadequate tidal volume and shifted to ICU. Death on the same day. |
| 3. | 62 F III E | Hypertension Diabetes | Rhinoorbital mucormycosis with orbital apex syndrome For FESS with debridement and orbital enucleation | Buck teeth with loose upper incisor. Saturation on air-90%. Haemoglobin 6.9g%, transfused. | Sudden bradycardia (40/min due to oculo-cardiac reflex) Paused surgery. Glycopyrrolate 0.2 mg. | Extubated. Uneventful |

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|----|-----------------|---|---|---|---|---|
| 4. | 50 F IIIE | Polycystic kidney disease, Hypertension, Acute kidney injury (blood urea 154 mg/dl, creatinine 6.9 mg/dl) | Rhinoorbital mucormycosis FESS with debridement | Blood urea and serum creatinine decreased to 137 mg/dl and 5.0 mg/dl. | Isoflurane 1% and atracurium. Avoided Nephrotoxic drugs. Cautious IV fluid. | Post op day 5, developed periorbital edema and proptosis. Revision endoscopic debridement with right optic nerve decompression done -uneventful. |
| 5. | 50 M IVE | Diabetes Ischemic heart disease on warfarin and aspirin) | Rhinoorbital mucormycosis FESS with debridement | Severe left ventricular dysfunction with multiple hypokinetic segments. EF-30% INR - 1.13 | Etomidate 0.3 mg/kg. Intraoperative noradrenaline 0.05mcg/kg/min | Developed ACS on same day, thromboprophylaxis started. Later developed an ischemic stroke. |
| 6. | 73 F IVE | Past pulmonary tuberculosis, hypothyroidism, diabetes hypertension | Rhinoorbital mucormycosis with palatal involvement Left-modified Denker's with FESS, orbital exenteration with debridement | Blackish discoloration of hard palate Left sided facial palsy. Potassium - 2.9 mmol/L | Ventricular premature beats (6 beats/m) IV lidocaine 1mg/kg, potassium, magnesium 1g | Poor respiratory efforts and shifted to ICU. Patient expired on postoperative day 1. |
| 7. | 50 M IIIE | Diabetes | Rhinoorbital mucormycosis FESS with debridement | Potassium - 2.8 mmol/L. | Intraoperative ischemic changes in ECG | Thromboprophylaxis started. Acute infarct of cerebellar peduncle and pons. Three weeks later developed loss of vision left eye and facial pain. Repeated for orbital exenteration-uneventful. |
| 8. | 45 M IIIE | Diabetes | Rhinoorbital mucormycosis with maxillary involvement FESS with right sided partial maxillectomy with debridement | Multiple loose teeth Potassium-2.4 mmol/L | During intubation, damage to loose upper incisor and gum. Teeth extracted and intubated. [figure1:a & b]. Fungal debris and supraglottic oedema were found. | Revision FESS with debridement. Uneventful. |
| 9 | 43 M IIIE | uncontrolled diabetes | Rhinoorbital mucormycosis FESS with debridement | HbA1c-14% | Blood sugar-401mg/dl. Insulin infusion. | Extubated uneventfully. Revision FESS after two weeks. |

| | | | | | | |
|----|------------------|----------|--|--|---|-------------------------|
| 10 | 70 M III E | Diabetes | Rhinoorbital mucormycosis FESS with debridement | Potassium-3.1mmol/L | Ventricular premature beats (3 beats/ minute). Potassium was corrected. | Extubated uneventfully. |
| 11 | 62 F III E | Diabetes | Rhino orbital mucormycosis FESS with debridement and orbital decompression. | Blood sugar - 386 mg/dl Potassium-2.5mmol/L | Oculocardiac reflex | Uneventful |

Discussion

Mucor mycosis is caused by zygomycetes. It causes high mortality of about 85% even after aggressive treatment.¹ Mucor mycosis is an Angio invasive disease, which invades the walls of the arteries and veins, causing vascular thrombosis and occlusion, tissue infarction, bone invasion and subsequent intracranial spread via paranasal sinuses.² White et al reported that the incidence of invasive fungal infections is 26.7% in post COVID-19 patient.³

Anaesthesiologists must have well-versed knowledge in Mucor mycosis and its management, as well as perioperative complications, drug interactions and side effects. Considering prolonged hospital stay, need for multiple intravenous medications and inotropes, central venous access was preferred. However, proximity of internal jugular cannulation to infection site and higher chance of hematoma formation made us to consider PICC (peripherally inserted central catheter) and femoral venous cannulation.

Facial swelling, decreased mouth opening, facial palsy, palatal involvement, epiglottitis, supraglottic oedema and fungal debris in oropharyngeal region contributed to difficult bag mask ventilation and intubation [figure1: b, c and d].⁴ Difficult intubation cart along with emergency tracheotomy and protective equipment were ensured in operation theatre.^{5,6} As maxillary involvement makes teeth and gum more prone to injury, intubation should be gentle [figure1: a]. Patients with low saturation had less pulmonary reserves, however, they were managed with adequate pre-oxygenation prompt uneventful intubation.

Many in vitro studies have shown the antimicrobial effects of intravenous and

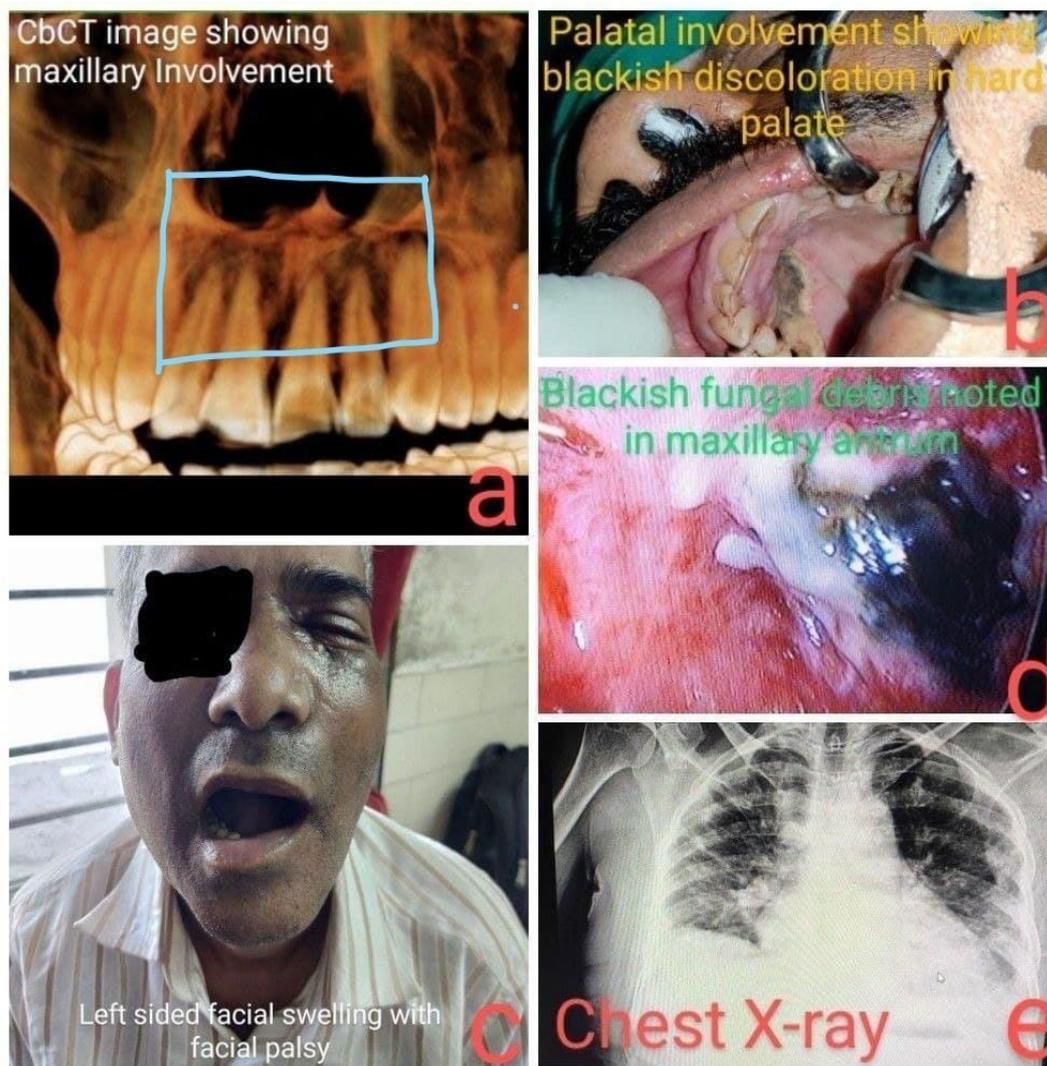
inhalational agents. Recently, isoflurane has been found to halt fungal growth in vitro and could offer future therapeutic potential for certain systemic fungal infections. Though in vivo effects have not yet been proved, isoflurane was used in all cases.⁷

Elevated blood glucose increases perioperative complications in diabetic and nondiabetic patients. Achieving target glucose of 140 to 180 mg/dl with insulin improves clinical outcome.⁸ Aggressive management of blood glucose with insulin leads to hypokalaemia, which should be corrected simultaneously.

Nephrotoxicity (80% patients and haemodialysis in 15%), hypokalaemia, hypomagnesaemia, fever, shivering, dyspnoea and hypotension are the common but serious side effects of systemic amphotericin B. Over the years liposomal amphotericin B has emerged as an alternative drug with less nephrotoxicity. Sustaining haemodynamic is crucial to prevent progression of renal damage. Adequate peri-operative hydration has foremost importance. We observed that patients receiving both amphotericin B and high dose insulin had moderate to severe hypokalaemia with electrocardiographic changes, which was corrected intraoperatively. Amphotericin B has skeletal muscle relaxant potentiating properties. Arrhythmia, atrial fibrillation, bradycardia, cardiac arrest, cardiomegaly, haemorrhage, postural hypotension, and vasodilatation have been reported.⁹ Therefore, amphotericin B infusion was avoided intraoperatively.

Posaconazole, a newer antifungal with lower side effects and oral route of administration can be

Figure 1: a) Dental cone beam CT scan showing maxillary involvement b) Palatal involvement showing blackish discoloration in hard palate c) Left sided facial swelling with facial palsy d) Blackish fungal debris noted in maxillary antrum e) chest X-ray showing bilateral lower zone



used as a step down treatment after initial therapy with amphotericin B.¹⁰ Hyperbaric oxygen therapy increases oxygen delivery to the tissue, improves vascularity and helps in faster healing. So, it can be used as adjunctive therapy.¹¹ Consider preoperative pulmonary function test, echocardiography and continuous invasive monitoring and arterial blood gas analysis intraoperatively wherever necessary. Due to the emergency nature of surgery and lack of equipment, it was not feasible for us. It was common in males (4/11 females, 7/11 males), might be due to the high incidence of COVID-19 in males.¹² Revision surgeries were more common (5/11 cases, mortality in two cases) due to aggressive nature of disease. Stroke, myocardial ischaemia and recurrence were common in the postoperative period. Despite the patient being on thromboprophylaxis, these events had occurred which may be due to the

patient's medical conditions itself or Angio invasiveness of the disease.² So, vigilant monitoring is mandatory in the postoperative period even after recovery.

Conclusion

One can anticipate intraoperative complications like airway difficulty, chances of traumatic intubation, hypotension, hyperglycaemia, hypokalaemia, arrhythmias, oculocardiac reflex and excessive bleeding during management of Mucor mycosis. Intraoperatively PICC line, avoidance of amphotericin B infusion, strict control of sugar, correction of hypokalaemia, maintaining renal perfusion should be considered. Judicious use of steroids and antibiotics, strict glycaemic control, preventive measures like nasal hygiene, early detection by vigilant monitoring and prompt treatment on time may decrease morbidity and mortality due to Mucor mycosis.

Multidisciplinary approach is necessary to improve the patient's perioperative outcome. As it is evolving disease further research is needed to know about pathogenesis of disease in post COVID-19 patients.

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