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Anesthesia Management of Patients Posted for Resection of Rhino-orbital Mucormycosis Developed as Post-COVID Sequelae: Sharing Our Experiences

ABSTRACT

Background: Although mucormycosis is a rare life-threatening fungal infection mainly seen in immunocompromised patients, there has been increasing number of mucormycosis cases presenting as post-COVID sequelae mainly from India. Uncontrolled diabetes and overzealous use of steroid seems to be two main aggravating factors. Aggressive medical and surgical management of mucormycosis decreases mortality rate from 88% to 21%. Aim: This study is aimed to evaluate anesthetic challenges in the post-COVID patients coming for surgical clearance of mucormycosis. Demographic characteristics, associated comorbidities, procedural data, surgical details, hospital stay, and mortality rates, were reviewed in 32 patients. The mean age of our patients was 52.66 years and 96.9% had associated comorbidities. Two (6.3%) patients had Mallampati classification (MPC) IV and 12 had III (40.6%). Average anesthesia duration was 282.5 min with mean blood loss 792 ml. Twenty-one (65.6%) patients were shifted to intensive care unit out of which 15 (46.87%) were electively ventilated. Mortality was seen in two patients with mortality rate of 6.25%. **Conclusion:** Surgical resection of mucormycosis in post-COVID patients presents unique challenges – associated comorbidities, difficult airway, prolonged surgical duration, intraoperative hemodynamic instability massive blood loss, amphotericin B-related side effects mainly nephrotoxicity and hypokalemia, need for post-operative ventilation, and prolonged hospital stay. Pre-operative optimization, careful intraoperative monitoring, and post-operative management are necessary for better outcome.

Key words: Amphotericin B, Anesthesia management, COVID-19, Mucormycosis

INTRODUCTION

Mucormycosis is a rare but rapidly progressive, fulminant, opportunistic fungal infection most commonly seen in diabetics and immunocompromised individuals, such as cancer patients, organ transplant patients, or people with HIV/AIDS.[1] Immunosuppressive drugs such as steroids, neutropenia, dialysis patients on deferoxamine, malnutrition, and hematologic malignancy are also at risk of affection by the fungi.[2] Since the onset of the COVID-19 pandemic, there have been multiple reports across country of very high incidence of mucormycosis among patients with COVID-19, especially in those who are diabetic and those who have received steroids. Due to the COVID-positive status, patients were on corticosteroids which worsened the hyperglycemia and hence were more prone to invasive fungal infections.[3] Successful management depends on early diagnosis, a reversal of underlying predisposing factors, prompt and extensive surgical debridement of infected tissue, and rapid administration of systemic antifungal therapy.[4] COVID-associated mucormycosis (CAM) has been associated with high morbidity and mortality, and exorbitant treatment cost.

Due to ongoing COVID 19 pandemic, mucormycosis cases are on surge. There is lack of any study done regarding anesthesia management of CAM. Hence, in this study, we aimed to evaluate anesthesia management of patients with CAM, after obtaining Institutional Ethics Committee approval.

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MATERIALS AND METHODS

Study participants

The study included 32 patients that underwent surgical resection for mucormycosis under general anesthesia (GA).

Study design

This was a retrospective, observational, single-center study.

Pre-operative procedures

Routine monitoring including heart rate, non-invasive blood pressure, electrocardiogram, and pulse oximeter, and end-tidal CO_2 was attached. Invasive blood pressure and CVP monitoring have been done in ASA Grade III and above. Central venous cannulation (PICC line/IJV) done preoperatively in all patients.

Anesthetic management

All surgical procedures were performed under GA. Following 3 min pre-oxygenation with 100% O_2, anesthesia was induced with intravenous propofol, cisatracurium, and fentanyl. Each patient was intubated using cuffed orotracheal intubation and was mechanically ventilated. Throat packing was done and endotracheal tube secured on the left corner of mouth. Anesthesia was maintained with desflurane in a mixture of oxygen and air. Deep venous thrombosis (DVT) stockings and Flowtron pump applied. Hourly urine output monitoring was done. Intraoperative losses were replaced with adequate fluid/blood product. Depending on extent of surgical resection and chances of post-operative bleeding, some patients electively ventilated and others were reversed and extubated at the end of surgery and monitored in post-anesthesia care unit.

Post-operative management

Post-operative analgesia was provided with appropriate doses of tramadol and paracetamol.

Statistical analysis

Data were analyzed using SPSS V15.0 (Statistical Package for the Social Sciences, Version 15.0) package. Data were given as mean, SD, and *n* for continuous data and number and percentage for categorical data. Range of the variables was given as minimum and maximum.

RESULTS

Out of 32 patients, 26 (81.2%) were men and 6 (18.8%) were women, with a mean age of 52.66 (range, 28–68) years. Mean body weight was 70.28 (range, 56–89) kg. Twenty patients were ASA Grade II, 10 were ASA III. Fifteen (46.9%) out of 32 patients had MPC score of >III [Graph 1]. All patients had a history of COVID-19 infection in recent past. The most common comorbidity was pre-operative hyperglycemia in 31 (96.9%) patients due to diabetes mellitus (DM) or steroid treatment given during COVID period [Graph 2]. Demographic characteristics of the patients are presented in Table 1.

Blood transfusion was required in 13 (40.6%) patients [Graph 3], mean blood loss 792 (range, 100–2000) ml. Mean duration of anesthesia was 282.5 (range, 30–480) min. Twenty-one (range, 65.6%) patients transferred to ICU, 15 (range, 46.87%) patients needed ventilator support postoperatively. Invasive monitoring was done in 21 (65.6%) patients. Re-debridement required in 6 (18.75%) patients. Procedural data are presented in Table 2.

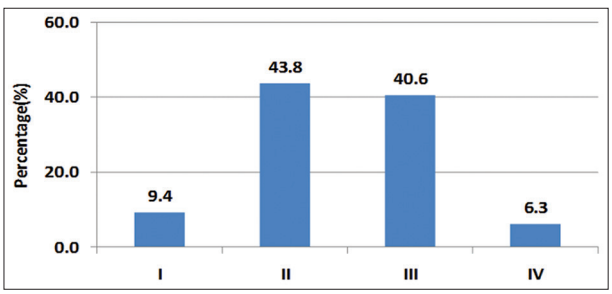
Average duration of hospital stay was 4–6 (mean, 5.2) weeks in view of prolong duration of antifungal treatment. Mortality occurred in two patients during ICU stay. Mortality rate was 6.25%.

DISCUSSION

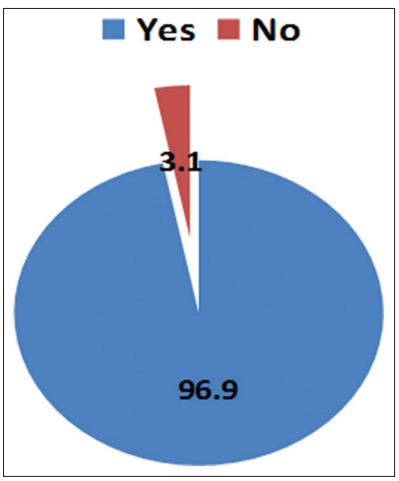
SARS-CoV-19 is an ongoing pandemic that has affected millions worldwide. It is predominantly a respiratory illness and symptoms range from a common cold to more severe disease including pneumonia. Since the onset of COVID-19 pandemic, there have been multiple reports across India of very high incidence of mucormycosis among patients with COVID-19, especially in diabetics, and those who have received steroids which worsened the hyperglycemia and hence were more prone to invasive fungal infections.[4,5]

In a recent systemic review conducted on COVID patients until April 9, 2021 by John *et al*.: COVID-associated mucormycosis typically seen in patients with DM (94%), especially the ones with poorly controlled DM (67%), while 88% were receiving corticosteroids.[6]

Treatment includes extensive surgical debridement [Figure 1, 2] with local packing of AmB soaked gauze piece,



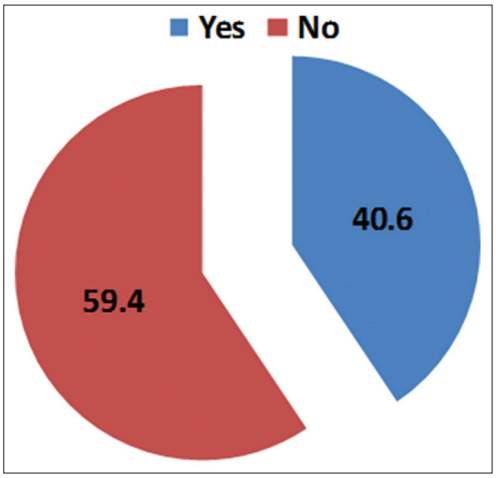
Graph 1: MPC distribution (%)



Graph 2: Diabetes (diabetes mellitus) distribution (%)

high doses of systemic AmB, control of underlying disease, strict glycemic control, and other supportive measures.

The classical features of mucormycosis are angioinvasion, thrombosis, infarction, and necrosis. Hence, damage and penetration through endothelial cells lining blood vessels cause hematogenous dissemination from original site of infection to other target organs.[2] Thrombosis of vessel prevents antifungals reaching infected tissue, so the primary aim of surgery is to achieve complete debridement of necrotic tissue [Figure 3].



Graph 3: Blood transfusion needed (%)

Table 1: Demographic data and clinical characteristics. Data: Mean or number (range or %)

Variables	Patients
Age, years	52.66 (28–68)
Sex, male/female	26/6 (81.2:18.8%)
Weight, kg	70.28 (56–89)
ASA, I/II/III/IV	1/20/10/1
Difficult intubation (MPC III, IV)	15/32 (46.9%)
Associated comorbidities	31/32 (96.9%)
On anticoagulants	20/32 (62.5%)
Pre-operative hyperglycemia	31/32 (96.9)
H/O steroids treatment	24 (75.0%)

ASA: American Society of Anesthesiology – physical status classification, MPC: Mallampati classification

Table 2: Procedural data. Data: Mean or number (range or %)

Variables	Patients
Blood loss, ml	792 (100–2000)
Blood transfusion needed, number	13/32 (40.6%)
Invasive monitoring	21/32 (65.6%)
Duration of anesthesia, min	282.5 (30-480)
Post-operative ICU needed, numbers	21/32 (65.6%)
Post-operative ventilator support, number	15/32 (46.87)
Duration of ventilator support, days	1.33 (1-3)
Re-debridement done	6/32 (18.75%)

ICU: Intensive care unit

Pre-operative optimization plays a crucial role in successful management. Strict glycemic control is crucial.[7] Correction of electrolyte imbalance mainly hypokalemia is necessary. Nephropathy, coagulopathy, and septicemia are some of the key challenges in perioperative period. Many patients are started on anticoagulants since COVID is associated with prothrombotic episodes. Anticoagulants need to be stopped or continued weighing the risk and benefit ratio carefully.

Patients with ROC mucormycosis may present with difficult airway due to pain, facial edema, fungal debris in the oropharyngeal region, epiglottitis, and supraglottic edema. After primary clearance, some patients come for the second stage clearance, pack removal, or diagnostic nasal endoscopy. In these patients, there is an increased risk of difficult mask ventilation, difficult intubation due to destructed anatomy, surgical packing, edema, and fungal crust. Eckmann *et al*. evaluated a 14-year-old girl with mucormycosis and reported that they inserted tracheotomy tube since they could not perform intubation due to supraglottic edema, although the patient had been intubated with no difficulty 2 months earlier for intra-abdominal surgery.[8] In our study, we could not perform endotracheal intubation in one patient posted for emergency re-exploration for nasal bleeding 2 days after getting operated for mucormycosis clearance and emergency tracheostomy was done. So, anesthesiologist should ensure that operating theatre has difficult airway cart ready. Also, ensure proper fixation of ETT and other connections to avoid accidental tube dislodgement/disconnections. Throat packing should be done.

Extensive surgical debridement may lead to profuse blood loss requiring blood and blood product transfusion, adequate fluid replacement, and inotropic support that necessitate central venous cannulation. Karaaslan has suggested that central venous cannulation should not be performed at a location close to infected site since these patients are at increased risk of rapid development of immunosuppression, neutropenia, and thrombocytopenia.[1] PICC line can be used for antifungal administration for prolonged duration up to 6–8 weeks and can be used intraoperatively. DVT prophylaxis like mechanical compression device, DVT stockings is necessary. These patients are at increased risk of hemodynamic instability and fluid electrolyte imbalance, so invasive arterial pressure and arterial blood gas monitoring is advisable.[1] A number of volatile anesthetic drugs have been reported to show antibacterial and antifungal activity in *in vitro* studies. In a previous *in vitro* study, Barodka *et al*. reported that isoflurane inhibited the growth of albicans,[5] but the effect of these agents needs to be investigated in *in vivo* study. In our study, we used desflurane/sevoflurane as volatile anesthetic agent.

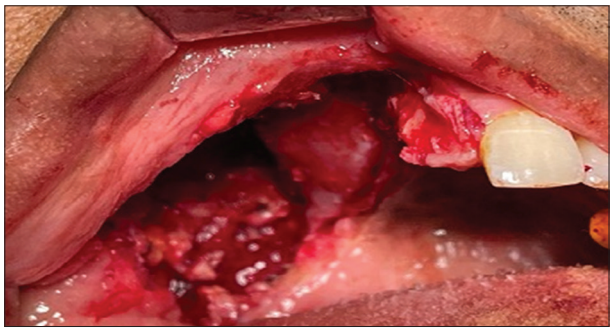


Figure 1: Surgical resection of palate

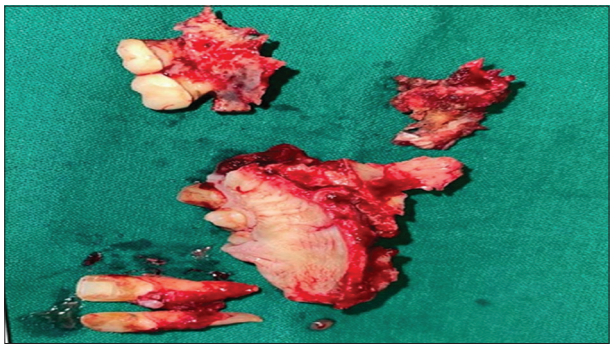


Figure 2: Surgically resected portion of palate

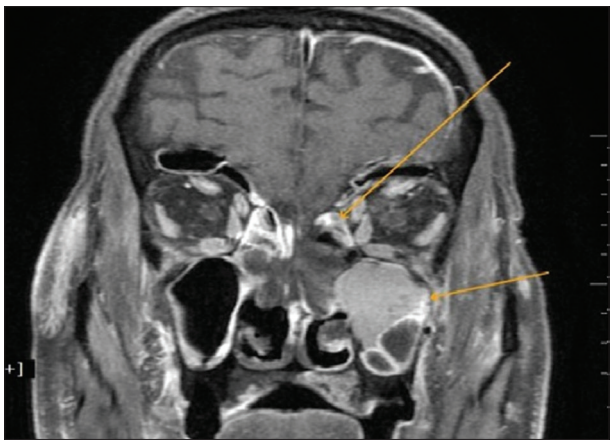


Figure 3: Magnetic resonance imaging image showing maxillary and ethmoid sinusitis

AmB remains a cornerstone of antifungal therapy for patients with opportunistic fungal infections. Antifungal drugs have poor penetration ability at the site of infection. Continuous infusion of AmB over 4–6 h has been shown to reduce incidence of nephrotoxicity and infusion-related side effects. Hypokalemia, hypomagnesemia, fever, chills, dyspnea, allergic reactions, and hypotension are common side effects of AmB. Renal function is impaired in >80% of treated patients, with 15% of patients requiring hemodialysis.[3] We have used both conventional AmB and liposomal AmB as per availability. Liposomal AmB is less nephrotoxic than conventional AmB. Continuous infusion of AmB could interact with anesthetic agents and produce adverse outcome. Kulkarni *et al*. reported that the patient had hypotension intraoperatively with arrhythmias that responded to treatment with lidocaine infusion. Hence, anesthesia providers should have heightened awareness for renal, electrolyte, coagulopathic, hemodynamic, and respiratory aberrancies when treating patients receiving AmB therapy.[3]

Literature reviews indicate that the use of aggressive medical and surgical treatment approaches in patients with ROCM has recently decreased mortality rate from 88% to 21%. Spellberg *et al*. revealed that mortality rate was 70% in patients receiving only antifungal treatment as compared to 14% in patients that underwent antifungal treatment combined with surgical debridement.[2] Jeong *et al*. reported that serum creatinine level and thrombocytopenia are most important factors affecting mortality in patients with mucormycosis.[9] In our study, mortality occurred in two patients, one patient had associated cirrhotic liver disease and other patient had extensive disease with the involvement of brain.

Delays in diagnosis and treatment of mucormycosis are associated with high morbidity and mortality. Post-operative ICU care plays a key role due to comorbidities and rapidly progressive fungal infection after surgery.

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