Emerging mucormycosis posing threat to community: Anesthetist’s perspective in a tertiary care center

ABSTRACT
Mucormycosis has become an ever-growing threat to human health, particularly after the COVID-19 pandemic. As the number of cases of mucormycosis increased, it put a burden on anesthesiologists. Here we describe the etiopathogenesis, clinical presentation, and anesthesia management of patients suffering from mucormycosis.

Keywords: Anesthesia, coronavirus, mucormycosis

Introduction
Mucormycosis has become an ever-increasing health hazard to humans, more so in the Indian population. As the number of cases of mucormycosis was roaring high, it had burdened both the ENT surgeons and the Anesthesiologist’s community. As various states declared it an epidemic and a notifiable disease, the administrative issues added stress to doctors of these two communities regarding the arrangement of emergency operation theatres (OT) and the provision of antifungal medicines.

The number of OTs catering mucor patients had to be increased in tremendous volume round the clock 24 hourly for possible early intervention of these patients, as was the surgical requirement. Both the covid and the noncovid OTs were made functional to handle the load.

On the one hand, the medical fraternity had not been relieved of the covid stress; this emerging epidemic of mucormycosis posed another threat to the existing medical system and the dearth of the relevant antifungal drugs.

Prevalence
The prevalence of mucormycosis in India is calculated as 0.14 cases per 1000 population, amounting to 80 times more cases than in developed nations. The morbidity and mortality associated with this infection are pretty high. The reported mortality is 50%–80% due to intracerebral and intraorbital complications. The recent literature reveals that the mortality rate for rhinocerebral mucormycosis decreases to 21% with both aggressive surgical and medical treatment compared to 88% with medical intervention alone.

Etiology
The reasons for it are ethnicity, immunosuppression, or inadvertent use of drugs used to treat the existing clinical condition.

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Patients prone to mucormycosis have a history of covid, diabetes which may be uncontrolled or newly diagnosed, history of intake of steroids or immunocompromised due to some drugs or systemic illness. Patients with hematological malignancies or undergone solid organ transplants are at ever-increasing risk.

Those with severe covid infections may have lymphopenia, making them immunocompromised, thus increasing the probability of this deadly fungus.

Pathogenesis
The host response to the fungal infection is cell-mediated (decreased CD4 and CD8 cell counts) and humoral. T cells produce IL-4,10,17 and IFN-γ, which damage the fungal hyphae, thus protecting fungal invasion. It may be associated with lymphopenia, which has a poor prognosis. Any increase in lymphocyte count may improve the immune system and mount a surge in protective T cells, which might play a role in controlling invasive mucormycosis.

The patients had immunosuppression because of COVID-19 per se as an infection affecting the immune system, newly developed or preexisting diabetes, overzealous use of steroids and antibiotics in milder cases making the patients susceptible to secondary fungal infections. This was contrary to what was proposed by Randomized Evaluation of COVID-19 Therapy ('RECOVERY') Collaborative Group to administer steroids only in critically ill patients requiring oxygen or ventilator support.

Clinical presentation
As in the present scenario of the COVID-19 pandemic, the hospitals were overloaded with patients presenting with symptoms diagnosed as mucormycosis. Most of them do not respond to conservative antifungal treatment. The fungus reaches extensively at various sites like lung, kidney, skin or soft tissue, and even intracranial and intraorbital extensions. The surgeries are quite debilitating and compromise the quality of life. They land up into extensive surgeries involving vital organs like the eye, also with intracranial extensions.

People are infected through inhalation of fungal spores affecting nasal sinuses and lungs, further spreading to other vital organs. The patients may present with a constellation of symptoms like fever, redness of the periorbital area, headache, cough, dyspnea, or in extreme cases, may present with altered mental status.

Mucormycosis constitutes a triad of symptoms which includes uncontrolled diabetes mellitus, periorbital infection, and meningoencephalitis. The fungus spreads to the nose, and paranasal sinuses may present in the patient as periorbital cellulitis, persistent sinusitis, blurred vision, congested conjunctiva, pain, and numbness on one side of the face. Sometimes, they present with toothache, loose tooth, or mandibular or maxillary involvement. This may worsen in the form of soft tissue swelling, necrosis of the affected area. This can progress to chemosis, proptosis, and thrombosis of prominent veins like cavernous, jugular which could be life-threatening and cause high mortality. It can lead to significant organ involvement like lungs or kidneys, and early diagnosis and treatment are crucial as they can be lethal in delayed presentation.

It may sometimes present as black eschar in the nasal cavity or hard palate.

Diagnosis
The crusts from the nasal cavity are tested by KOH stain and microscopy to confirm rhino mucormycosis. Computer tomography (CT) scans of the nose and paranasal sinuses are done to diagnose their invasion. Brain CT scans may be required to rule out intracerebral involvement. Matrix-assisted laser desorption/ionization-time of flight mass spectrometry can be used, if available.

Preanesthesia assessment
Airway assessment is an essential preoperative challenge in these patients, particularly those who are posted for redebridement.

As most of the patients were with post-covid squeal, a few specific investigations were required to rule out coagulopathy before being taken up for surgery. This may include D-dimer, CRP, fibrinogen, ferritin, and electrocardiography. These patients have a high probability of developing thrombocytopenia and raised serum creatinine levels, which correlates with poor prognoses and higher mortality.

Reverse transcriptase polymerase chain reaction (RTPCR) test is mandatory for the patient to be taken up for elective
surgery as per the protocol in our tertiary care center. Those who were covid positive were taken up for surgery in covid designated operation theatres.

**Anesthetic challenges**
The main concerns to anesthesiologists in administering general anesthesia to such patients are related to the airway. Most of the affected areas in mucor are related to nasal and paranasal sinuses, extending to orbit [Figure 2a and 2b]. The extent of debridement depends on the size of the involvement of facial structures.

These patients are very anxious as there is a possibility of extensive debridement, or they are posted for redebridement. These surgeries may lead to extensive cosmetic deformities with compromised quality of life.

The patients sometimes have difficult intubation due to fungal debris in the oropharyngeal area and supraglottic edema.\[16\]

Postoperatively, many patients are extensively debrided involving orbital exenteration, maxillary or mandibular resections. Thus, extubation of these patients becomes risky. Sometimes, these patients land up with postoperative tracheostomy as they are anticipated not to maintain their airway after extensive resection.

The greatest anesthetic challenge occurs when these patients with extensive debridement and airway compromise come for redebridement. This becomes more of an issue if the patient is not tracheostomized in the previous surgery.

The difficult airway cart should always be kept ready for patients with rhinocerebral mucormycosis. It requires various drugs and types of equipment needed for a difficult airway.\[16,17\]

**Clinical management**
A triad of adequate blood sugar control, intravenous amphotericin, and early surgical intervention remains the mainstay of successfully managing this deadly disease.\[2\]

Surgical debridement at the earliest is the best alternative to reduce the further progression of the disease.

The treatment of choice is systemic amphotericin but is associated with many unavoidable side effects like nephrotoxicity, electrolyte disturbances, fever, and hypotension.\[17\] The most dreaded complication is renal toxicity; hence, liposomal amphotericin is a better alternative. Its supply was deficient in the early days as this new scary epidemic was rising. Gradually, it has eased out now.

The rest of the supportive treatment is required for the management like adequate blood sugar control, maintenance of adequate systemic hydration, antibiotics to control secondary infections, thromboprophylaxis, and adequate nutrition.

**Conclusion**
We, as anesthesiologists are facing challenges in mucormycosis now and then in the era of COVID-19 pandemic. Thus, we need to take care and be prepared for these challenges in perioperative area in future times.

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**Conflicts of interest**
There are no conflicts of interest.

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