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Anaesthetic considerations for management of post covid rhino-orbito-cerebral mucormycosis: Focus on challenges

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Abstract

Background and Aims: There has been increasing number of mucormycosis cases as post covid sequelae during second wave of covid pandemic. Our study focussed on challenges in anaesthetic management of surgical resection of post covid rhino-orbito-cerebral mucormycosis.

Methods: We did a retrospective case study of 60 patients posted during May-June 2020 posted for surgical resection of Rhino-orbito-cerebral mucormycosis under General Anaesthesia. All patients were operated irrespective of altered laboratory biomarkers, remnant of covid -19 disease.

Results: Demographic and clinical parameters, and laboratory biomarkers were reviewed for each patient. Patients had median age of 55 years (23-85 years). Patients belonged to ASA physical status I: II: III (10: 40:10). The most common associated co-morbidity with median elevated Fasting blood sugar level 162 (63-711) followed by hypertension (48%). 85% patients were on steroid therapy (continued from covid disease treatment). 6% were hypothyroid patients. Invasive arterial monitoring was performed in 13.3% patients with femoral central line cannulation done in 85% of cases. 21% patients were shifted to ICU intubated and the rest were shifted with NRBM as a preventive measure. 23% had revision surgery whose mallampatti score was upgraded from I to III.

Conclusions: Necessary precautions should be taken for difficult airway caused by fungal debris in oropharyngeal airway and supraglottic edema. So is the importance of Post ICU care because of co-morbidities and post covid sequelae's.

Keywords: covid-19, post covid-mucormycosis, co-morbidities, anaesthetic management

Introduction

Health infrastructure has been under unaccustomed coercion in these times of universal pandemic of SARS Coronavirus 2 (SARS-CoV-2). Owing to the pathology of the underlying disease when associated with recently emerged rhinoorbitocerebral mucormycosis, it may be abetted with hemodynamic instability, difficult airway management and any organ may be ambushed. There is speculative mortality analogous with post covid rhinoorbitocerebral mucormycosis which is a progressive pretentious, infrequent fungal infection ^[1].

When more and more patients presented with post covid rhinoorbitocerebral mucormycosis in May – June 2021 we anaesthesiologists and clinicians were always geared up to manage these severely ill and immunocompromised patients with lack of evidence in literature ^[2, 3].

Respiratory failure, cardiomyopathy, arrhythmias, renal failure counting on dialysis, liver function abnormalities, thromboembolic illness, endothelial dysfunction, and neurologic manifestations were among the disease's chief embracing clinical manifestations. However successful treatment of mucormycosis rested on four crucial principles: early diagnosis, treatment of underlying predisposing factors, surgical debridement of necrotic tissue, and administration of antifungal therapy ^[4].

Even in the presence of influencing factors such as immunodeficiency, DM, and multiple organ failure, high covid biomarkers and sepsis, surgical resection for mucormycosis was often desired. For anaesthesiologists, paramount importance was airway management since the fungal debris in the oropharyngeal region and supra-glottic edema led to difficult ventilation and endotracheal intubation ^[5].

In this study, we aimed to evaluate the anaesthetic management of patients undergoing surgical resection for rhino-orbito-cerebral (ROC) mucormycosis.

Materials and Methods

The medical records of 60 patients admitted in our Hospital between of May- June 2021 who underwent surgical resection for rhino-orbito-cerebral mucormycosis were reviewed retrospectively after obtaining an approval from local Hospital committee. All patients underwent concise preoperative examination in our hospital.

Minimum requirements prior to surgery included only resolution of COVID symptoms considering to the limited data available on the time frame of recovery.

The history and physical examination emphasized details of the patient's COVID course, signs and symptoms of potential subclinical COVID complications, determination of whether a patient had returned to their "pre-COVID" baseline health, a functional capacity assessment, and an ambulatory oxygen saturation measurement.

All the patients were monitored customary in the operating theatre which included heart rate (HR), non-invasive blood pressure (NIBP), invasive blood pressure (IBP) electrocardiogram (ECG), and peripheral oxygen saturation (SpO₂).

All the patients were given general anaesthesia by adroit anaesthesiologist. Anaesthesia was given, ensuing 3 min preoxygenation and premedication with Injection glycopyrrolate 0.04mg/kg, Ondansetron 0.008mg/kg, midazolam 0.02mg/kg and fentanyl 1-2 µg/kg intravenously (Administration of anaesthetic drugs was according to ideal body weight). Anaesthesia was induced with Intravenous propofol 1-2mg/kg and injection scoline 2mg/kg was given for facilitation of endotracheal intubation with appropriately sized cuffed ETT and anaesthesia was maintained with Oxygen, nitrous oxide, sevoflurane and Atracurium using a Dräger Primus. Following intubation, the EtCO₂ value was monitored continuously. The tidal volume and the ventilation rate were adjusted to maintain the EtCO₂ value within a range of 35- 45 mmHg. In patients that had no intraoperative complications, glycopyrrolate and neostigmine were administered to reverse residual neuromuscular blockade at the end of the surgery.

The patients who attained spontaneous respiration (respiratory rate > 12/min, tidal volume > 5 mL/kg), acceptable SpO₂ levels of > 95% and who exhibited good response to verbal commands were extubated and transferred to specially designated intensive care unit (ICU). However, hemodynamically unstable patients and those who

showed no respiratory effort were transferred intubated and were ventilated in the ICU till they were able to wean. Some of the patients were also electively ventilated in which palate was surgically resected because of fungal involvement.

Results

The 60 patients comprised of 29 Males and 31 females (48%:52%) with median age of 55 yrs (range 23-85 yrs) (table 1). Patients belonged to ASA physical status 1,II and III (10:40:10) Almost all the patients had Mallampatti grade I and there was no difficulty in intubation but 23% patients who presented for revision surgery, the mallampatti grade was upgraded to III (table1). Utmost care was taken during the mask ventilation of all the patients as the nose was blocked and because of eye involvement there was disfigured face. All the patients presented with high blood sugar with average blood sugar 180±105, with a median of 162 (range 63-711) and IQR 91 and only 4 (0.06%) patients were with high serum acetone value with mean 72. (Table 2) Though only 56.6% were Diabetic precovid, 30% became diabetic post covid and only 13% who were not diabetic but presented with high blood sugar after developing mucormycosis. (table3) Out of 29 male patients 25 were active smokers and out of 31 females only 5 were smokers. (table1)

Only 4% patients were hypothyroid. 22% patients were hypertensive already and 8% patients were hypertensive with H/o IHD in past, 2% patients developed hypertension post covid whereas 52% patients were non hypertensive in the study.85% patients were on steroid therapy and 13.3% were given vasopressors perioperatively. 46% patients were on room air, 16.6% were on Ventimask, 1.6% on nasal prongs oxygen, 15% on NRBM and 20% were on BIPAP oxygen therapy when they were posted for surgical resection of mucormycosis. (Table 3)

Almost all the patients were induced with altered laboratory biomarkers. On an average HRCT score of the patient was 14.74. Patients had altered LDH, D Dimer, RBS, Blood urea with near normal electrolytes when they were posted for surgery (only 3.3% patients had Serum K⁺ above 6 meq/l which was corrected preoperatively). (Table 2) Invasive arterial monitoring was performed in 13.3% patients with femoral central line cannulation done in 85% of cases.

Table 1: Demographic data with clinical parameters

Males: females	29: 31	48%: 52%
ASA physical status= I: II: III	10:40:10	16.7%: 66.6%:16.7%
Smokers: non-smoker Males	25:4	86% smokers
Smokers: non-smoker Females	5:26	16% smokers
Live: dead post operatively	43:17	28% died , 72% shifted home
Single: revision surgery	46: 14	23% revision surgery with upgraded mallampatti score
Acetone <10:>10	56:4	0.06% acetone present with average of 72
Shifted NRBM: Intubated	43:17	21% shifted intubated

ASA: American society of Anaesthesiology; NRBM: non rebreathing mask;

Table 2: Age and Laboratory Parameters

	Mean	Standard deviation	Median	Minimum	Maximum	IQR
Age (yrs) n=60	52.94	14.68	55	23	85	25
Post Covid Day	19.65	5.5	19.5	10	31	5.5
HRCT score	14.74	4.62	15	2	24	5
LDH units / litre	415.46	180.72	364.5	199	969	200.5
D- Dimer	961.92	681.52	783.5	171	3138	779
S Na+	138.6	6.40	139	110	154	6
SK+	3.71	0.78	3.6	2.2	5.6	1.2
S Cl-	103.4	7.08	103	79	126	8
RBS	180	105	162	63	711	91
Bld Urea	40.3	25.6	35.5	9	120	29
S Creatinine	1.25	0.65	1.05	0.5	3.5	0.75

Table 3: Clinical Data

Diabetes	34 (56%) already Diabetic 18 (30%) post covid Diabetic 8 (13%) presented with high blood sugar
Hypothyroid	4 (6%)
Hypertension	22(36.66%) already hypertensive 5 (8.3%) presented with HT with H/O IHD 2 (3.3%) presented with newly developed hypertension post covid 31 (52%) non hypertensives
On steroid therapy preoperatively	51 (85%) on steroid 9 (15%) not on steroid
Oxygen therapy preoperatively	28 (46%) on Room air 10 (16.6%) on Ventimask 1 (1.6%) on nasal prongs 9 (15%) NRBM 12 (20%) BIPAP
Arterial line	8 (13.3%)
Femoral line cannulation	51(85%) of cases.
Vasopressors	8 (13.3%) postoperatively

Discussion

Mucormycosis is a life-threatening fungal infection that occurs in immunocompromised patients. Diabetes, hypertension, hypothyroidism and steroids and mental stress are some identifiable risk factors which add on to the mortality of mucormycosis. Diabetes treatment posed difficulties at a time when the world was encountering an unparalleled pandemic with lockdowns, people cramped to homes with no opportunities for exercise and consistent walks, along with there was significant stress because of the unpredictability and high mortality of SARS-CoV-2 and sizable mental stress with modification in the daily groove affecting dietary intake as well [3]. All of these variables made the patients more vulnerable to complications such as invasive fungal infections. This could be one of the factors why all the patients in our study presented with high glucose levels and unveiling of the diabetes in some.

COVID-19 infection predisposed the survivors to a plethora of on-going and irreversible insults to various body systems. Recovered patients were at greater risk of having myocarditis (myocardial inflammation) and coronary thrombosis thereby accentuating the risk for perioperative cardiovascular events. The viral infection led to a prolonged hypercoagulable state, thereby increasing the chances of embolism, cerebrovascular infarcts, and deep-vein thrombosis. These aforementioned effects of the viral infection on the cardiovascular system and affixed vascular thrombosis due to mucormycosis added adverse impact on the survival [6]. In our study since patients were not completely recovered from SARS CoV-2 patients were on Oxygen therapy when posted for surgery. 16.6% were on

Ventimask, 1.6% on O2 via nasal prongs, 15% on NRBM, 20% on Bipap Oxygen therapy

The mold fungus generally reaches into the host through the respiratory tract and manifests an exceptional affinity for arteries and grows along internal elastic lamina causing thrombosis and infarction thus resulting in vascular occlusion which in turn is responsible for necrosis and ischaemia [7, 8]. There is advancement of the disease from nose and sinuses to intracranial involvement by invasion through superior orbital fissure, ophthalmic vessels, cribriform plate [9] carotid artery or possibly via a perineural route [10]. So waiting for cultures was ill considered and could lead to delay in commencement of treatment [11]. Moreover, the resultant vascular thrombosis would prevent the drugs to systemically reach the infected tissue so the principal objective was to get rid of the necrotic tissue and undergo surgical resection at the earliest possible. The drainage of paranasal sinuses with orbital exenteration was lifesaving. All the patients were operated as they came and not being worked up extensively for altered biomarkers or waiting for full resolution of covid after problems

The use of amphotericin B in the treatment of mucormycosis led to nephrotoxicity, and hypotension chiefly, was given for 3 days preoperatively in every patient to reduce the fungal overload. Besides avoiding hypotensive attacks and achieving hemodynamic stability in the perioperative period, it was highly critical for securing adequate renal perfusion and preventing the progression of renal damage [12]. Altered renal tests were well depicted in our study (table 2). There were 13.3% patients who needed vasopressors to maintain blood pressure in perioperative

period in our study whereas 42% patients developed severe hypotension and received positive inotropic support in study done by E karaaslan [13]. It should be noted that since patients with mucormycosis and with amphotericin therapy, are at increased risk of hemodynamic instability and fluid-electrolyte imbalance, continuous monitoring of arterial pressure and arterial blood gas should be performed with invasive arterial blood pressure monitoring. Invasive arterial monitoring was performed in 13.3% patients with femoral central line cannulation done in 85% of cases in our study.

The factors which lead increased morbidity and mortality in mucormycosis patients are coexisting diffuse sepsis, multiple organ failure, immune suppression and absolute neutropenia which are by products of SARS CoV-2 [14]. Blood and blood products transfusion, fluid replacement, and intraoperative support was required in some patients in our study which necessitated central venous cannulation pre-, peri-, and post-operatively and during prolonged ICU stay. Internal jugular vein was not the primary choice for central venous cannulation due to its proximity to the infected site and, in particular, pulmonary hematoma can be associated with thrombocytopenia may result in postoperative respiratory obstruction so femoral central vein was chosen. Celebi *et al.* [15] reported that a hematoma occurred following internal jugular vein cannulation in a patient who had acute lymphoblastic leukemia (ALL) with pancytopenia and underwent surgery due to mucormycosis. E karaaslan [13] achieved central venous cannulation via femoral vein in 4 and via internal jugular vein in 1 patient.

WHO strongly recommended the use of corticosteroids (dexamethasone, hydrocortisone or prednisone) orally or intravenously for the treatment of patients with severe and critical COVID-19. While steroids were effective to reduce the infection associated with inflammation, when used responsibly and timely to avoid aggressive virus replication. Steroid use was restricted to patients with persistent fever, oxygenation impairment (breathing difficulty) or worsening cough due to airway inflammation for over 5-7 days. Steroids are believed to modulate the inflammation mediated lung injury thereby reduce progression of respiratory failure in covid -19 [16] Considering India as the diabetes capital of the world, indiscriminate use of steroids for patients with known and borderline diabetes can cause superadded infections or breakthrough fungal and bacterial infections. In our study we found that 85% of patients were still on steroid for covid -19 which could also explain high blood sugar in our patients, and newly developed hypertension (3.3%) which could also be an added factor for adverse impact on the survival [17].

The mortality rate decreased from 88% to 21% when patients received both medical and surgical treatment. [5,14,18] Spellberg *et al.* [19] revealed that the mortality rate was 70% in patients that received antifungal treatment alone as opposed to 14% in patients that underwent antifungal treatment combined with surgical treatment. E karaaslan [13] reported 25% mortality rate when both anti-fungal and surgical resection of mucor which was similar to our study, Mortality was 28% when both amphotericin and surgical resection was used to treat mucormycosis.

Conclusions

We anaesthesiologists must prepare ourselves and reframe our anaesthetic approach for this new post-COVID mucormycosis disease. Large-scale prospective studies are

needed to unfold the anaesthetic challenges in these patients.

Ethics approval and consent to participate: The study protocol was approved by the hospital Committee of LG Hospital

Availability of data and materials: The datasets generated during and/or analyzed during the current study is available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: UB, RBS, DKP and SkS contributed to the conception and design of the study. All organized the data collection, reviewed, and greatly contributed to the interpretation of results.

All authors have checked the statistical analysis and critically reviewed its comprehensive content, and finally approved the version to be submitted for publication.

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