Research

Our experience with COVID-19 related Mucormycosis: a preliminary report

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Background

India has seen, much to its dismay, a massive and baffling surge of Mucormycosis in association with COVID-19. It has been a challenging, distressing, disappointing and frustrating experience during the second wave. We have seen it during the illness, but more in the post-recovery phase. It is known to occur in patients with lowered immunity post-COVID, uncontrolled diabetes, post-transplant, post-cancer treatments, hematological disorders and AIDS. This was generally considered rather rare until the status dramatically changed recently. Geographically south east Asia has recorded a good number of cases. Infection with Mucormycosis has high morbidity and mortality rate, can cause loss of eye and may be life threatening due to the invasive nature of the fungal infection which can present as Rhinocerebral Mucor. This disease requires immediate attention and a tailored treatment plan to achieve full recovery without loss of function.

An overview of 23 patients with Mucormycosis, managed in 65 days

COVID-19, caused by the virus SARS-CoV-2 that is now becoming infamous for its frequent mutation into troublesome variants, is a highly virulent, very contagious, widely dispersed infection that has swiftly evolved into a vicious, unforgiving, pandemic. The understanding of the virus, its mode of transmission, and treatment plan emerged steadily internationally over 2020–21 and are still under research and development. COVID has the effect of immunosuppression; and the disease as well as its treatment with corticosteroids has predisposed pre-diabetic patients to develop diabetes, requiring oral hypoglycemic agents or insulin. COVID-19 thus opened the gateway to many opportunistic bacterial and fungal agents, causing infections. Mucormycosis caused by mucorales is increasingly reported in the background of COVID infection, especially in India. We at

Kauvery Hospital Chennai have treated 23 such patients in a span of 65 days during the peak of the second wave of the COVID pandemic. Mucormycosis had become an evolving epidemic at the core of this pandemic, the eye of the hurricane.

Some illustrative observations

This is a blog – like report. We shall be publishing a full and formal report as we complete our work on the patients who were impacted during this wave.

The youngest patient was a 41-year-old male, with no comorbidities, and not vaccinated. He was incidentally found to have asymptomatic Aspergillosis of lung. He presented with complaints of right sided facial pain, right periorbital swelling and tooth ache for 14 days. MRI brain and PNS with contrast and diagnostic nasal endoscopy showed evidence of pan sinusitis with T2 hypointense thickening of the right maxillary sinus with right orbital floor erosion. Enhancement left maxillary sinus mucosa, with non-enhancing central areas, extending to the left osteomeatal complex with widening of the ethmoid infundibulum with peripheral heterogeneous enhancement were also seen.

The oldest patient was a 64-year-old male, with active COVID Infection, RT PCR positive, with lung involvement. Patient was admitted in the ICU in view COVID pneumonia. On bedside diagnostic nasal endoscopy crusts and mucinous discharge were seen. Material sent for KOH mount showed features suggestive of *Aspergillus* sp.

Out of the 20 operated patients, six were female patients, none of them completely vaccinated for SARS-CoV-2, with the background history of COVID-19 infection, they had received steroids, and had the co-morbidities of diabetes mellitus and hypertension.

Out of the 20 patients we operated in our center 6 were RT–PCR positive, within the 14-day window of the infection, and with uncontrolled DM, on steroid therapy. They had signs of nasal bleeding and crusting, tooth pain, facial swelling and headaches.

Intracranial extension

Three patients had extensive disease with intracranial extension.

First was a 51-year-old gentleman who was involved of the right maxilla, right ethmoids, sphenoid, right frontal, with orbital extension, erosion of the lamina papyracea with soft tissue extension into the medial and inferior extra conus space which was infiltrating into the medial and inferior rectus muscle near the apex. Enhancement was noted in the interconus superiorly and laterally into the orbital apex

with crowding of the orbital apex compression the right orbital nerve. Hyper intensity with contrast enhancement was seen on the right pterygomaxillary fissure, with extension into the posterior periantral fat, also dural, in the anterior cranial fossa, medially over the roof of the nasal cavity and the frontal sinus.

Second patient was a 52-year-old female, with post COVID bilateral maxillary, ethmoid, sphenoid sinusitis, with patchy enhancement of mucosa with non-enhancing areas. Soft tissue thickening was noted in the left infra temporal fossa, alveolar process of left maxilla and left masticator space, with enhancement post contrast. Pachymeningeal enhancement along the left anterior temporal region was seen.

The third patient was a 51-year-aged male with dural enhancement. Unfortunately, in spite of a successful surgical outcome, the patient developed sepsis and died.

Non-diabetics

Out of the 20 patients operated 14 were male patients. Out of 20 patients four patients were non-diabetic, with a backdrop of long-standing sinusitis, untreated. Out of these four patients, three had histories of COVID infection and treatment. Only one patient was never treated or had COVID infection in the past, but could have had an asymptomatic infection, but patient never got tested or took any specific treatment.

Patients who had mixed infections: We have observed growth of both aspergillus species and mucorales in the cultures and HPE in six patients treated for invasive fungal sinusitis. The histopathology features were typically suggestive of Mucor but the cultures grew *Aspergillus* sp.

Patient with orbital involvement: Involvement of the orbit could be staged into periorbital edema, restricted eye movements, ptosis, blindness and patients needing orbital exenteration. We observed 11 patients out of 20 with involvement of the muscles of the orbit seen in all 11, periorbital swelling also seen in all 11, and unilateral ptosis seen five patients. Complete loss of vision was seen in two patients. One patient regained vision and also function soon after the surgery to near to normal.

Patients with involvement of the OMFS: We observed four patients with complaints of loose tooth, toothache, gum swelling and discoloration of the hard palate. An MRI confirmed the invasion of the floor of maxilla with invasive fungus. With the aid of our Maxillofacial surgeon the floor was partially excised and post one week, the obturator was fixed.

Oculoplastic surgeon involvement: For five patients, opinion from the oculoplastic surgeon was obtained; the debridement was planned to precision with the aim to restore function. One of the patients received intraoperative injection of Liposomal Amphotericin into the orbit at the dose of 3 mg/kg. But this did not benefit the patient as he was in a very advance stage of disease.

Neurosurgeon involvement: For two patients, opinions were obtained from neurosurgeon in view of dural enhancement. Fasica lata, fat and tissue glue were used to secure the possible area of leak.

Our approach

All 20 patients were operated endoscopically. We used sophisticated instruments for the same; about 16 patients underwent Denkers procedure, medial maxillectomy and clearance of mucormycosis. This approach aided in complete visualization of the maxillary sinus as well as helps to get access to areas easily for post-operative nasal wash and toileting.

Denkers method: Advantage is greater exposure in order to clear disease from the infra temporal fossa, maxillary artery ligation, clearance of disease from the pterygopalatine and infratemporal fossa, clear access to the skull base for clearance, easy approach to clear ethmoids, sphenoid and frontal sinus.

Our outcome

Twenty patients were operated for mucormycosis, three patients were referred in an inoperable state, with cerebral involvement and on ventilatory and inotropic supports. Three patients succumbed and had cardiac issues and sepsis, with multiorgan failure.

Discussion

Mucormycosis is an invasive fungal disease that is confirmed by the demonstration of fungi in the tissue or sterile body fluids taken from the patient and observed under direct microscopic on KOH mount, culturing the fungal in a microbiology lab, and visualization of broad ribbon-like aseptate hyphae or isolation of Mucorales. However, this could be false negative in 50% of the cases.

COVID-19 diagnosis was made in patients who tested positively for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the causative agent of COVID-19) RNA in respiratory mucosal specimens using the method of reverse transcription PCR (RT–PCR) or a positive rapid antigen test.

COVID associated mucormycosis is now a newly evolving debilitating disease with

high mortality rates, and is in a rampage. The vulnerable patient has confronted the unholy triad of COVID-19, newly diagnosed diabetes or uncontrolled diabetes with diabetes ketoacidosis in the background of receiving corticosteroids and Remdesivir/Tocilizumab. These predisposing factors prepare a fertile ground to breed fungal sinusitis, rhinocerebral and rhino orbito cerebral mucormycosis which, if not diagnosed early, would lead to a dire prognosis and death. COVID associated mucormycosis (CAM) has brought to the forefront endoscopic nasal surgery. The techniques and skills we had developed in endoscopic skull base approaches have helped us manage patients well with great outcomes, minimizing morbidity and mortality.

Challenges faced during the pandemic

Our gold standard approach for all patients was transnasal endoscopic approach, using powered instruments, micro drills, coblator, navigation system and endoscopes. These instruments where arranged specifically for the Mucor cases with special hand pieces and burrs, during the peak of the pandemic. To actually get the theatre ready and well equipped with all that's required was one of the challenges but our hospital always was supportive in providing state of the art instruments and best of care for patients, the adaptive nature of the team, hospital staff, the whole organization are truly what helped to secure fantastic outcomes.

Operating on patients with active COVID infections was supported by the magical creation of isolation wards that came up overnight, along with isolation post- op observation rooms, with protocols designed to suit this unique situation and education, and concurrent training of staff on how to manage these patients were all the agents that achieved this miracle of modern times

A great anesthetic team, with the willingness to support our teams, and with the vision to serve, support and cure, aided us pave the path to what we believe we achieved- viz: “early diagnosis and early treatment for best outcomes”.

Inj. Liposomal Amphotericin was the most scarcely available resource during the peak of the second wave of the pandemic, with government controlling the limited stock and distribution/sales. This created havoc around India where patients in dire need could not gain access to it. Fortunately, our hospital arranged timely availability of injection Amphotericin which facilitated offering the gold standard treatment, tailored for patients with advice from the Infection Diseases Physician. All our patients received one week of Inj. Liposomal Amphotericin B 5 mg/kg OD doses for one week followed by six weeks

of Tab. Posaconazole 300 mg OD. Three patients who received 10 mg/kg body weight has two had intracranial involvement and one had disseminated mucormycosis.

Counselling patients and attenders, prepping them to accept, understand and cooperate with the treatment plans, bolstered with also financial counseling to understand costs of the treatment, greatly enabled us to offer gold standard management.