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Mucormycosis in Post Covid Patients: A Case Series

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Abstract

Mucormycosis is a rare, fulminant, rapidly spreading fungal infection, which us ually affects patient with under-lying immune deficiency. If not managed promptly, the disease is characterized by progressive necrosis and is often fatal. Mucorales species are vasotropic, causing tissue infarctions, and the mucormycosis spectrum ranges from cutaneous, rhinocerebral, and sinopulmonary to disseminated and frequently fatal infections, especially in immunocompromised hosts. The importance of Mucorales species has grown in recent years as the number of patients with predisposing factors for mucormycosis has increased dramatically. Currently, one of the most controversial issues is the spectacular increase in the number of cases of mucormycosis in post COVID patients. The incidence rate of mucormycosis globally varies from 0.005 to 1.7 per million population. In India, prevalence of mucormycosis is estimated as 140 per million population, which is about 80 times higher than the prevalence in developed countries. In a systemic review and meta-analysis of 851 cases reports published in 2018, death was reported in 389/851 (46%) patients. Case fatality was observed to be highest among patients with disseminated mucormycosis (68%) and lowest in those with cutaneous disease (31%).

Keywords: hepatic resection, Oriental cholangio-hepatitis, left lateral segmentectomy, carcinoma gall bladder

INTRODUCTION

Mucormycosis (sometimes called zygomycosis) is an angio-invasive fungal infection caused by a group of molds called mucormycetes.

It was believed to be rare but sudden rise in post covid patients has led to it being an epidemic in few states in India. This opportunistic fungus is a normal inhabitant of human sinuses & thus has shown increased incidence in post covid immunocompromised patients. Coronavirus disease is associated with sustained lymphopenia compromising the immune system, especially in severe cases[1].

As of June 7thour country has recorded 28,252 cases of "Black Fungus" or Mucormycosis so far Out of this, 86%, or 24,370 cases, have a history of COVID-19 and 62.3%, or 17,601, have a history of diabetes 2 with Maharashtra, Gujrat, Andhra Pradesh, Madhya Pradesh and Telangana logging the highest number of rare fungal infection, according to the latest government data. 6,329 have been recorded in Maharashtra, followed by Gujarat with 5,486, and then Madhya Pradesh, Uttar Pradesh, Rajasthan, Haryana, Karnataka, Delhi, and Andhra Pradesh[2]. India has highest cases of the mucormycosis in the world. Notwithstanding, India is already having second largest population with diabetes mellitus (DM) and was the diabetes capital of the world, until recently. A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2–7 g given during the month before, predisposes immunocom promised people to mucormycosis. There are few case reports of mucormycosis resulting from even a short course (5–14 days) of steroid therapy, especially in people with DM[3]

The most important conditions predisposing to mucormycosis

include [4] -

1. Malignant haematological disease
2. Prolonged and severe neutropenia,
3. Poorly controlled diabetes mellitus with or without diabetic ketoacidosis,
4. Iron overload,
5. Major trauma,
6. Prolonged use of corticosteroids,
7. Illicit intravenous drug use,
8. Neonatal prematurity
9. Malnourishment

Commonest organ involved with mucormycosis was nose and sinus (88.9%), followed by rhino-orbital (56.7%) and ROCM type (22.2%)07[3.]

In the following article we present 3 case reports of mucormycosis showing varying involvement of maxillary sinus.

Case Report 1

A 50yr old male patient presented with the chief complaint of left cheek swelling, blurry vision & black nasal discharge for last 1 week (Fig.1a). Patient gave history COVID infection with 40% lung involvement for which he was admitted in hospital for 7 days.

During hospitalization he was gives methyl prednisolone, dexamethasone along with fabiflu & received remdesivir injection.

During COVID treatment he gives history of hyperglycaemia for which insulin was started & is now on regular oral hypoglycemic drug after recovery. After discharge within 3-4 days he noticed extra oral swelling of left side of face with excruciating pain which only subsided with diclofenac inj. No other medically relevant history was found. On examination of nasal cavity secretions at choana was found with black crusting filling entire nasal cavity & purulent discharge at anterior end of Middle turbinates. Intra-oral examination revealed tenderness on palpitation in left upper jaw with no teeth mobility in involved teeth, no intra oral swelling or sign of necrosis was found. CT-PNS showed (Fig.1b) mucosal thickening in left frontal, ethmoidal, maxillary & sphenoid sinuses extending upto their recess. Thinning, resorption & breaks in floor & medial wall of left orbit with preseptal & paraseptal orbital fat stranding near medial & inferior rectus muscle was seen.

Based on the clinical & radiographic findings diagnosis of rhino-orbital mucormycosis was done. Patient was then started on liposomal amphotericin 20mg/kg in ringers lactate 5% slow infusion over 12 hours once daily for 2-4 weeks. Surgical debridement of left maxillary sinus was done by Caldwell-Luc approach followed by betadine & soframicin dressing. In every 3-4 days according to the level of infection dressing was changed. After oral & maxillofacial surgical intervention patient underwent functional endoscopic sinus surgery under ENT surgeons. Ophthalmic intervention included retrobulbar Amphoteric injections. Histological report of the biopsy specimen (Fig.2B) taken during surgery confirmed the diagnosis of mucormycosis.

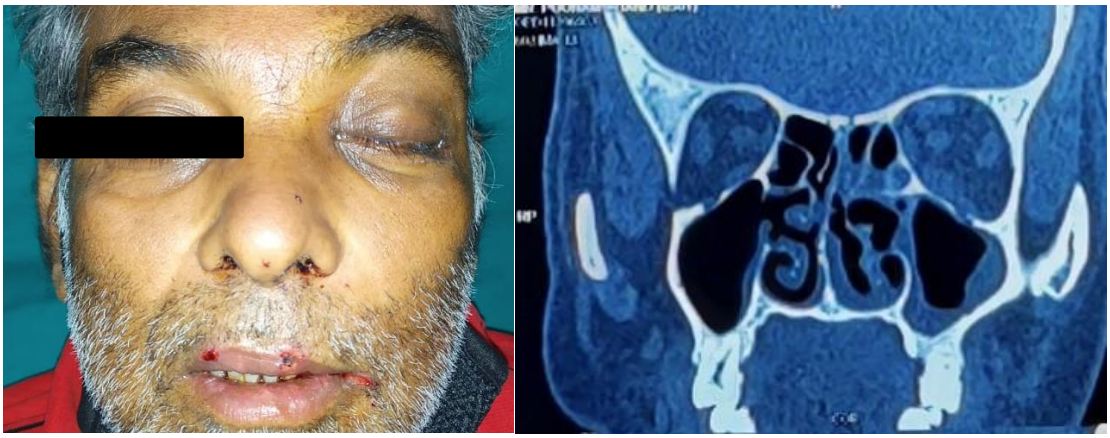

Fig.1- A: Extraoral swelling seen in left side of face including periorbital region ; B: Showing mucosal thickening of left maxillary sinus with thinning & break in floor of orbit.

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Case Report 2

A 44 yr old male came to the department with chief complaint of pain, numbness, headache & swelling in maxillary teeth. Patient gave history of hospital admission for COVID infection for 90days during which he was given methyl prednisolone. During COVID treatment patient gives history of hyperglycemia for which insulin was started. No other medically relevant history was found. On oral examination no signs of tooth mobility, abscess, palatal necrosis was found. ENT examination showed no relevant finding, ophthalmic examination showed no signs of eye redness, proptosis or blurry vision.
On the basis of clinical findings patient was suspected to have rhino-sinusitis & CT & MRI was advised. CT showed polypoidal mucosal thickening of bilateral maxillary sinuses Rt>Lt with obliteration of right maxillary infundibulum, mild deviation of nasal septum towards right side & mild soft tissue swelling in right frontal, periorbital, maxillary & nasal region. MRI showed no abnormal post-contrast enhancement in brain parenchyma, mucosal thickening in bilateral maxillary, ethmoidal sinuses was seen indicating sinusitis. Patient was then started on liposomal amphotericin 20mg/kg in ringers lactate 5% slow infusion over 12 hours once daily for 2-4 weeks along with ranitidine, tramadol & metformin 500mg BD multivitamin, paracetamol (SOS). Surgical intervention included thorough debridement of sinus with Caldwell-Luc approach followed by betadine & soframycin dressing & patient was started on Posaconazole 300mg BD for 4 weeks. Histological report of the biopsy specimen taken during surgery confirmed the diagnosis of mucormycosis.

Case Report 3

A 37 yr old male came to the department with complaint of pain in left upper back tooth region since1 month. On examination no extra-oral swelling was seen, heaviness with respect to left maxillary sinus, altered sensation on left middle 1/3 of face was present. Intra-orally grade 1 mobility with 24, grade 2 mobility with 25 & vestibular tenderness with respect to 25 & 26 was present. Patient gave history of COVID infection involving 75% lung, he was hospitalized for 25days during which was administered steroids, IVIG & remdesivir. During COVID treatment hyperglycemia was observed for which insulin was given & since discharge patient is on oral hypoglycemics. CT-PNS showed (Fig.2) mild DNS to right side with right sided bony spur, soft tissue noted obliterating superior portion of left nasal cavity, nasal turbinates were unremarkable, opacified left maxillary sinus, bilateral ethmoidal air sinus & left frontal sinus with scattered hyper densities within was observed suggesting invasive fungal sinusitis with soft tissue extension & erosion Based on the clinical finding, radiographic findings & history provisional diagnosis of mucormycosis was done. Patient was started on injection amphotericin 5mg/kg in 5% ringers lactate slow infusion over 12chrs, tab metformin 500mg BD, tab glimipride 1mg BD, tab ceftriaxone along with ranitidine inj & paracetamol (SOS). Surgical debridement of left maxillary sinus with extraction of 23,24 & 25 was done followed by single dressing & closure with 3-0 silk. Nasal endoscopy pre-surgically reveals no significant finding pertaining to grade 1 findings in inferior & middle turbinate therefore no intervention was required & was advised nasal wash TDS.

Histological report of the biopsy specimen taken during surgery confirmed the diagnosis of mucormycosis.

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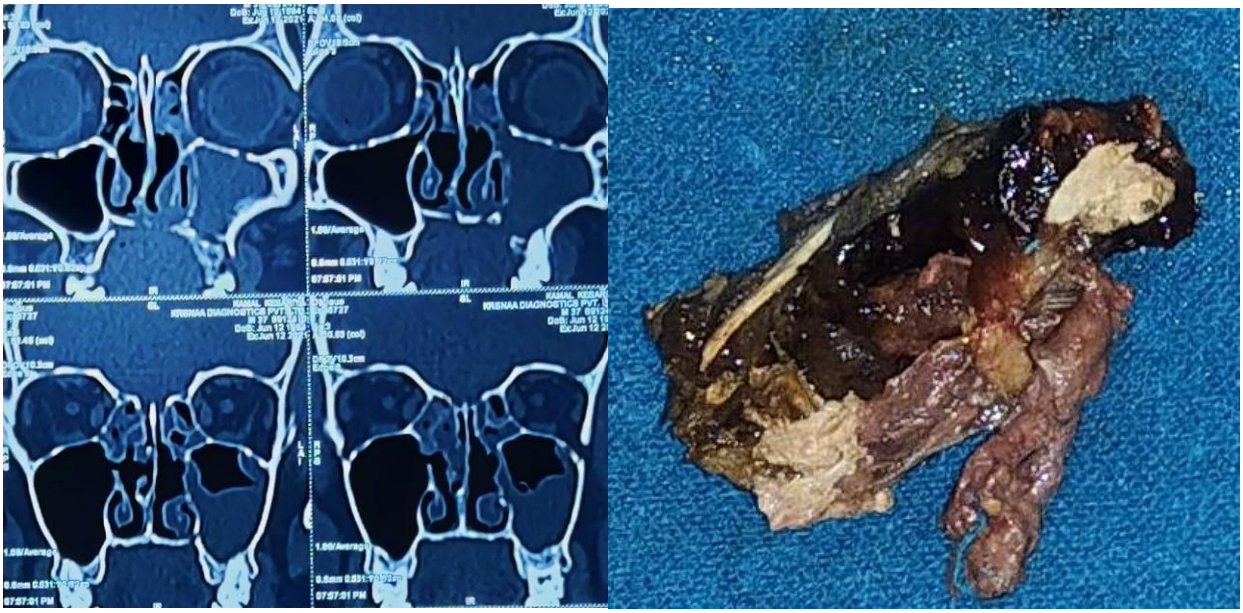

Fig.2 – A: showing soft tissue obliterating nasal cavity & maxillary sinus ; B – surgically removed specimen from left maxillary sinus

DISCUSSION

Mucormycosis, the third invasive mycosis in order of importance after candidiasis and aspergillosis[5], is a disease that may be caused by several species of different genera. Diabetes mellitus as a predisposing factor for mucormycosis in 36%–88% of cases. Patients with uncontrolled hyperglycemia, particularly those with ketoacidosis, are the most susceptible. Mucormycosis may be the first manifestation in some patients with undiagnosed diabetes mellitus, but it is rarely observed in those with metabolically controlled diabetes. Chronic corticosteroid-based therapy is another primary risk factor that enhances a patient's susceptibility to mucormycosis by causing defects in macrophages and neutrophils and/or steroid-induced diabetes. Therapy with DFO, an iron chelator used to treat iron and/or aluminium overload in dialysis recipients reportedly is a risk factor for Angio invasive mucormycosis. With the second wave of covid being more fatal, the guidelines of its treatment have shifted to use of steroids along with high dose antibiotics & antivirals.

In the hospital setting, there is evidence that more than half of the patients receiving high-dose steroids develop hyperglycemia, with an incidence of 86% of at least one episode of hyperglycemia and 48% of patients presenting a mean blood glucose ≥ 140 mg/dL. The main associated factors related to inpatient hyperglycemia are previous history of DM, a higher prevalence of comorbidities, prolonged treatment with steroids and older age. In most cases, the infection is rapidly progressive and results in death unless underlying risk factors (ie. metabolic acidosis) are corrected and aggressive treatment with antifungal agents and surgical excision is instituted. The most common reported sites of invasive mucormycosis have been the sinuses (39%), lungs (24%), and skin (19%)[5]. Dissemination developed in 23% of these cases. The overall mortality rate for the disease is 44% in diabetics, 35% in patients with no underlying conditions, and 66% in patients with malignancies[5]. The infection develops after inhalation of fungal sporangiospores into the paranasal sinuses. The infection may then rapidly extend into adjacent tissues. Upon germination, the invading fungus may spread inferiorly to invade the palate, posteriorly to invade the sphenoid sinus, laterally into the cavernous sinus to involve the orbits, or cranially to invade the brain. The fungus invades the cranium through either the orbital apex or cribriform plate of the ethmoid bone and ultimately kills the host. The overall mortality rate depends on clinical presentation of disease but Survival rates vary according to the focus of the infection: cutaneous isolated, 90%; sinusitis without cerebral involvement, 87%; rhino-cerebral manifestation, 45%; pulmonary forms, 36%; focal cerebral

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manifestation, 33%; disseminated disease,16%; and gastrointestinal involvement,10%.[5]

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