FRONTAL SINUS OSTEOMYELITIS: A LATE COMPLICATION IN POST COVID MUCORMYCOSIS

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ABSTRACT During the current pandemic of COVID-19, numerous manifestations and complications have developed. As seen after the Second wave, patients with COVID-19 are at high risk of fungal infections, such as mucormycosis, that may result directly from COVID-19 infection and/or as a side effect of the drugs used in the COVID-19 treatment protocol. Rhino-orbito-cerebral mucormycosis is a fungal infection that can be fatal, especially in immunocompromised patients. In this report, we described a series of 3 cases with frontal sinus osteomyelitis in post-COVID-19 diabetic patients diagnosed with mucormycosis.

KEYWORDS COVID-19, Mucormycosis, Frontal Sinus, Osteomyelitis, Diabetes mellitus

Introduction During the global Covid pandemic, there is an increase in the rate of secondary infections, among which mucormycosis is one. This is a severe, opportunistic fungal infection that can also cause fatal outcomes in several immunocompromised states, such as uncontrolled diabetes, decreased neutrophil counts, chronic use of glucocorticoid steroids, haematological malignancies, and chronic malnutrition. Organs commonly involved are lungs, sinuses, nose, brain, eyes, skin, kidneys and gastrointestinal tract. Occurrence of Vascular thrombosis leading to tissue necrosis is a remarkable sign of this disease. The most common presentation of mucormycosis is Rhino-orbital-cerebral mucormycosis (ROCM) which contributes to about two-thirds of all cases.

ROCM is a rapidly progressing disease, which can lead to grievous consequences if the diagnosis or treatment is delayed. However, the prognosis can be much better if the warning signs and symptoms are observed correctly with appropriate investigations and aggressive treatment of the disease with medical and surgical interventions.

Pott’s puffy tumour is a severe complication of ROCM. It is osteomyelitis of the frontal bone, associated with subperiosteal abscess causing oedema and swelling over the forehead and scalp.

As the cases of ROCM are increasing in incidence throughout the world after the emergence of Covid 19, we present 3 cases of post COVID mucormycosis presented at the Tertiary Care Center who developed frontal osteomyelitis and Pott’s puffy tumour as a late complication and were given surgical and medical management.

Case 1: A 37-year-old male patient complained of headaches, ptosis of the right eyelid and diminution of vision in the right eye. The patient was newly diagnosed with Type 2 Diabetes Mellitus on presenting to the hospital. The patient gave a history of COVID infection 20 days back, for which he was home quarantined. The patient was investigated with CT PNS, which was suggestive of mucosal thickening involving all sinuses and bilateral osteomeatal and left frontoethmoidal obliteration. Hence the patient was started on intravenous Amphotericin B therapy and operated on for Endoscopic sinus surgery with debridement under GA. The tissue excised from the debridement of sinuses after the histopathological examination is suggestive of mucormycosis of paranasal sinuses. The patient was managed with a transcutaneous retrobulbar Amphotericin B (TRAMB) injection for ophthalmological symptoms. Adjuvant management was given to control BSL.

After 25 days of lyophilised Amphotericin B therapy, the patient developed a unilateral frontal headache on the left side and swelling over the left frontal bone. On CT paranasal sinuses, it
suggested erosion and heterogenous enhancement in walls of left frontal sinus involving adjacent anteroinferior part of left bone and roof of left orbit suggestive of osteomyelitis changes with a collection of abscess in the lateral aspect (as shown in figure 1). The rest of the sinuses showed mild mucosal thickening overall with no evidence of bony erosions elsewhere. The patient was operated on for left-sided frontal craniotomy to remove the diseased anterior wall of the frontal sinus. The further patient completed the Amphotericin B therapy and was symptomatically relieved with clear sinuses on imaging (as shown in figure 2).

**Figure 1**

**Case 2:**
A 50-year-old male patient reported a bilateral frontal headache to the OPD for 15 days, not subsiding with medications. The patient gave a history of COVID infection one month back. He was hospitalized and received an injection of Remdesivir and steroid therapy. He was newly diagnosed as a case of Diabetes Mellitus after he was hospitalized for COVID treatment. After investigation, CT PNS suggested mucosal thickening of all sinuses and was operated for Endoscopic sinus surgery with debridement (as shown in figure 3). The tissue resected was sent for histopathological examination, which suggested mucormycosis infection. The patient was started on Amphotericin B therapy. After 1 month of treatment for mucormycosis patient developed a severe frontal headache. On MRI brain with paranasal sinuses, it was suggestive of erosion of focal lytic areas in anterior walls, roof and floor of bilateral frontal sinus along with stranding and swelling of overlying scalp likely to be osteomyelitis of frontal bone. The patient was managed medically with intravenous antibiotics and Amphotericin B for the next month, after which the patient showed healthy mucosal lining in the frontal sinus. A repeat scan showed healthy frontal bone (as shown in figure 4).

**Figure 3**

**Figure 4**

**Case 3:**
A 42-year female presented to our hospital with bilateral frontal sinus swelling and draining sinuses over the skin for 1 month. The patient gives a history of bilateral periorbital swelling 1 month back. She had a history of COVID infection 4 months ago. The patient was a newly diagnosed case of Diabetes Mellitus with uncontrolled blood sugar levels. CT PNS showed mucosal thickening with soft tissue opacification in the bilateral frontal sinus with permeative bone destruction associated with cortical break in the anterior and posterior walls of the bilateral frontal sinus and the orbital roof.

The patient was treated with bifrontal craniotomy with the removal of infected frontal bone followed by debridement and reconstruction of the frontal sinus (as shown in Figures 5, 6, and 7). Postoperatively, the patient was medically managed with Amphotericin B and monitored for nephrotoxicity. The follow-up of the patient was satisfactory.
Table 1

| Case no. | Presenting symptoms                                           | Age/Sex | Medical History                          | Surgical treatment                                     | Antifungal therapy          | Outcome                           |
|----------|---------------------------------------------------------------|---------|-----------------------------------------|--------------------------------------------------------|-----------------------------|-----------------------------------|
| 1.       | Headache, Ptosis of right eyelid, diminution of vision in right eye. | 37y/male | Uncontrolled Diabetes Mellitus, h/o COVID - 19 infection | Endoscopic sinus surgery with Left Frontal craniotomy | Liposomal Amphotericin B, Posaconazole | Satisfactory Follow up upto 3 months. |
| 2.       | Frontal headache not controlled by medication                | 50y/male | Uncontrolled Diabetes Mellitus, h/o COVID-19 infection | Endoscopic sinus surgery                               | Liposomal Amphotericin B, Posaconazole | Satisfactory Follow up upto 5 months |
| 3.       | Bilateral periorbital edema and frontal swelling              | 42y/ female | Uncontrolled Diabetes Mellitus, h/o COVID-19 infection | Bilateral Frontal Craniotomy                           | Liposomal Amphotericin B, Posaconazole | Satisfactory Follow up upto 2 months |

Discussion

Mucormycosis is a potentially fatal condition. Medical treatment alone is ineffective since drug transport to the site of infection is insufficient due to severe arterial thrombosis\(^\text{11}\). The prognosis of the underlying disease and the reversal of the predisposing state determine the ultimate fate of mucormycosis. Although greater survival rates of up to 80–85 percent have lately been reported, the mortality rate has been proven to be 50% \(^\text{12−14}\). The degree of disease, both orbital and intracranial extension in cases of rhinoorbitocerebral mucormycosis, is also a prognostic factor\(^\text{11}\).

The overall risk increases if the patient is in an immunocompromised state. Here we considered three patient’s who presented with relevant signs and symptoms, frontal headache being the common symptom among the three, and they presented with these signs and symptoms at least two weeks after COVID infection. All three patients were diagnosed with Diabetes Mellitus with poorly controlled glucose levels. One of the patients was hospitalized during a COVID infection and managed with steroids in the hospital. This could be a contributing factor along with uncontrolled glucose levels in this patient. However, all patients were managed both medically and surgically. Liposomal Amphotericin B and Posaconazole is the
pharmacological therapy given to these patients. They are highly effective and are evident by their outcome. In addition, endoscopic sinus surgery with frontal craniotomy was performed on this patient. Here it is to be emphasized that pharmacological and surgical therapies are necessary in complicated cases of frontal osteomyelitis to achieve optimum outcomes. All three patients were monitored for at least three months post-surgery, and the outcome was satisfactory.

According to Marx et al., a thorough workup of blood glucose levels, electrolytes, and blood gases is required if a patient has diabetes\(^{15}\). Aggressive correction of hyperglycemia and acidemia, along with debridement, is necessary. Medical management with antifungals, injectables, and oral therapy play an important role in prognosis. The overall approach needs to promptly diagnose and treat with all accessible modalities.

**Conclusion**

A diabetic patient with a history of COVID-19 infection and sinusonal symptoms should alert the clinician to a possible mucormycotic infection in the current scenario. Sinonasal variety is the most common type of mucormycosis, so early identification, triaging, and a proper multidisciplinary management approach are imperative. Prompt and aggressive treatment is required to ensure a favourable outcome.

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**Conflict of interest**

There are no conflicts of interest to declare by any of the authors of this study.

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