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Case Report

# Post COVID-19 Rhinocerebral Mucormycosis Complicated by Frontal Sinus Osteomyelitis (Pott's Puffy Tumor) Reconstructed with Haddad's Flap: A Technical Note

**Qais Al sinani[1], Arif Ali Kolethekkat[2], Anwar Al Mawali [3], Suad Al-Jahdhami[4], Rashid Al Abri[5], Yahya Al Badaai[5] and Mohammed Alwashahi[6]**

*[1]ENT Resident, Oman Medical Specialty Board, Suhar Hospital, MOH, Oman*

*[2]ENT Consultant, Sultan Qaboos Hospital, Salalah, Oman*

*[3]Radiology Resident, OMSB, Oman*

*[4]Senior Consultant, Pathology Department, Sultan Qaboos University Hospital, Oman*

*[5]Senior Consultant, ENT, Department of Surgery, College of medicine &health science, Oman*

*[6]Senior Consultant, ENT, Department of Surgery, Sultan Qaboos University Hospital, Oman*

***Corresponding Author:** Mohammed Alwashahi, Senior Consultant, ENT, Department of Surgery, Sultan Qaboos University Hospital, Oman.

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## Abstract

Rhinocerebral mucormycosis in an elderly post renal transplant diagnostic and management challenge and often with poor outcome owing to an immunocompromised state. The scenario is further complicated in post-COVID-19 status. We report a case of a 73-year-old with a background of diabetes and renal transplant who had acute COVID-19 infection and subsequently developed rhinocerebral mucormycosis with frontal osteomyelitis. The diagnosis was established by clinical and radiological evaluations, which further confirmed by mycological and histopathological examinations. She was successfully treated with radical resection of the lesion by combined endoscopic and external bi-coronal frontal craniotomy and the resultant defect is reconstructed with nasoseptal "Haddad's flap with monitored systemic antifungal therapy. A follow-up until 3 years showed no recurrence.

**Keywords**: Rhinocerebral, mucormycosis, covid-19, nasoseptal, Haddad's flap

## Introduction

Invasive Rhinocerebral mucormycosis is a debilitating and fulminant disease that is often encountered in immunocompromised patients and with preexisting co-morbidities such as diabetes. The Covid19 pandemic witnessed a sharp rise in the incidence of mucormycosis due to either dysregulation of immune response or the use of corticosteroids as a treatment [1].

Fungal osteomyelitis is a rare complication of mucormycosis, most commonly reported in facio-maxillary bones, and has been recently reported with high prevalence after COVID-19 [1,3].

However, osteonecrosis of the frontal sinus co-existing with mucormycosis in the background of Covid19 is an unusual occurrence with a paucity of case reports in the literature. Therefore, we present an uncommon case of elderly female diagnosed as frontal osteomyelitis with sub-periosteal abscess due to rhino-cerebral mucormycosis in post Covid19, highlighting the treatment options with a review of literature of similar cases.

## Case Report

A 73-year-old female was referred to our tertiary hospital (Sultan Qaboos University Hospital) with complaints of headache and frontal swelling for the past 3 months, with worsening over time. There was no fever, nasal discharge, facial swelling, local skin ulceration and neurological symptoms. She was diabetic, hypertensive, and had undergone renal transplantation a few years ago. She had developed COVID19 during the pandemic for which she had been admitted and treated with steroids and immunosuppressants. Subsequently, she underwent endoscopic sinus surgery due to her headache and forehead swelling from elsewhere one month ago. She was referred for further management due to the progression of the disease. The clinical examination revealed a firm and tender

swelling localized at the midline of the forehead. An endoscopic evaluation of the nasal cavity was conducted, demonstrating minimal purulent nasal discharge in the middle meatus; however, there was no evidence of polyps, masses, or any abnormalities in the nasal mucosa.

Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) of paranasal sinus and brain showed features suggestive of bilateral frontal sinusitis with osteomyelitis and anterior epidural abscess (Figure 1A,B,C,D). She was initially treated with a combination of antibiotics (piperacillin/tazobactam, Ciprofloxacin and Ceftazidime) and an anti-fungal therapy (variconazole followed by systemic Liposomal Amphotericin B). Endoscopic debridement of both frontal sinuses was performed under general anesthesia, which revealed the presence of pus and a bone sequestrum obstructing the frontal sinus. This condition was associated with erosion of the anterior table and a thinned posterior table, with the dura being exposed. Draf II B frontal sinusotomy was done and the debrided tissue was sent for histopathological examination which showed the presence of numerous broad aseptate fungal hyphae morphologically consistent with mucormycosis and necrotic osteoporotic bone with pockets of severe acute suppurative fungal osteomyelitis. The microbiological culture isolated 'Rhizopus Oryzae'. A final diagnosis of Frontal sinus osteomyelitis (Pott's puffy tumor) with rhinocerebral mucormycosis was made in the background of post-COVID-19 (Figure 2 A,B,C). Due to the extensive nature of the disease, a further radical surgical eradication was planned after a multidisciplinary meeting by combined approach. A bi-coronal frontal craniotomy proceeded and resection of the bilateral frontal bone and sinus mucosa up to the orbital roof was performed along with endoscopic frontal sinus exploration. The dura-plasty done with artificial dura and endoscopic assisted repair of the frontal sinus floor with temporalis fascia and right-sided naso-septal flap was done and the closure of CSF leak was ensured intravenous antibacterial and antifungal treatment continued for 6 weeks based on the culture report, guided and monitored by the Infectious Disease team. The patient was discharged from the hospital and kept on oral voriconazole for one year with regular follow-up every three months. Further close evaluation revealed no recurrence for three years after surgery (Figure 3A, B, C, D).

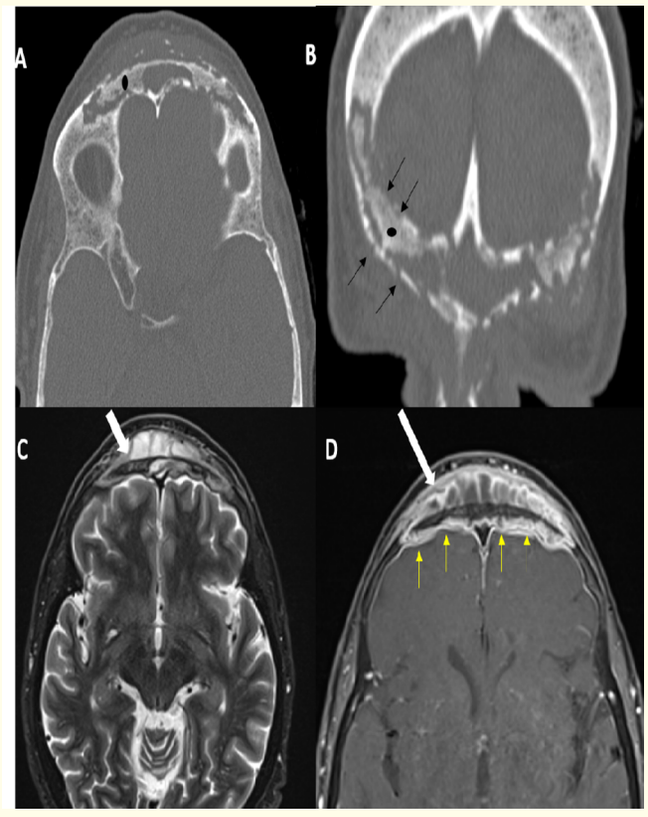


**Figure 1:** Figure 1A,B,C,D: Pre-operative CT and MRI of paranasal sinuses. Unenhanced axial and coronal CT from the frontal sinuses (A and B) shows complete opacification of frontal sinuses with destruction of the both inner and outer table of the sinus wall (Black arrows in B). Intrasinus contents show high-attenuation amorphous calcification/sequestrum (Black dot). Axial T2W MRI image (C.) shows complete opacification of frontal sinuses with the presence of T2 high-signal contents. Intrasinus T2 low signal intensity areas suggest sequestrum (small white arrow), which was seen on the corresponding CT images. A subperiosteal rim enhancing collection contiguous with the frontal sinus (long white arrow) keeping with Pott's puffy tumor. Frontal epidural pachymeningeal enhancement is also noted (Yellow arrows).

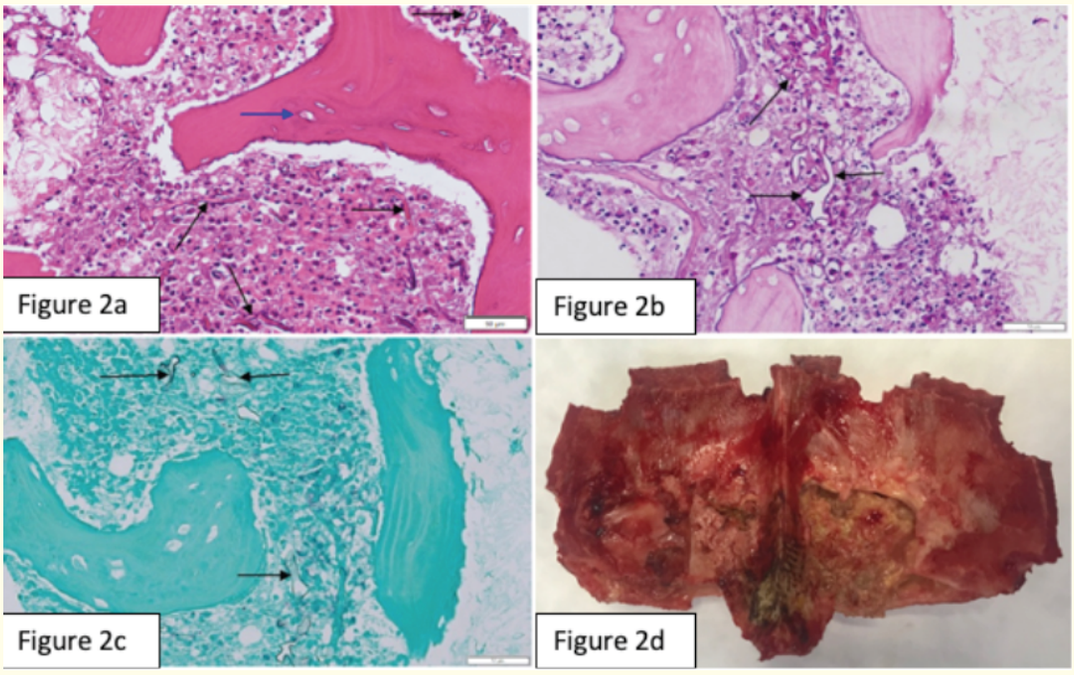


**Figure 2:** Figure 2a,b,c,d. Figure 2a. Hematoxylin & Eosin (H&E) stained section of frontal bone resection show features of osteonecrosis (necrotic bone with empty lacuna indicated by blue arrow) and severe acute suppurative osteomyelitis, with numerous neutrophils filling marrow spaces. Many fungal hyphae (black arrows) are seen within the inflammatory infiltrate of bone [x400]. Figure 2b. Periodic acid–Schiff (PAS) stain highlights strongly positive broad aseptate fungal hyphae (black arrow), some showing right angle branching; morphologically consistent with mucormycosis species [x400]. Figure 2c. Grocott methenamine silver (GMS) stain is also positive in the aseptate fungal hyphae (black arrows) [x400]. 2d, The appearance of the anterior table of the frontal bone with necrosis and pus discharge and discoloration area.

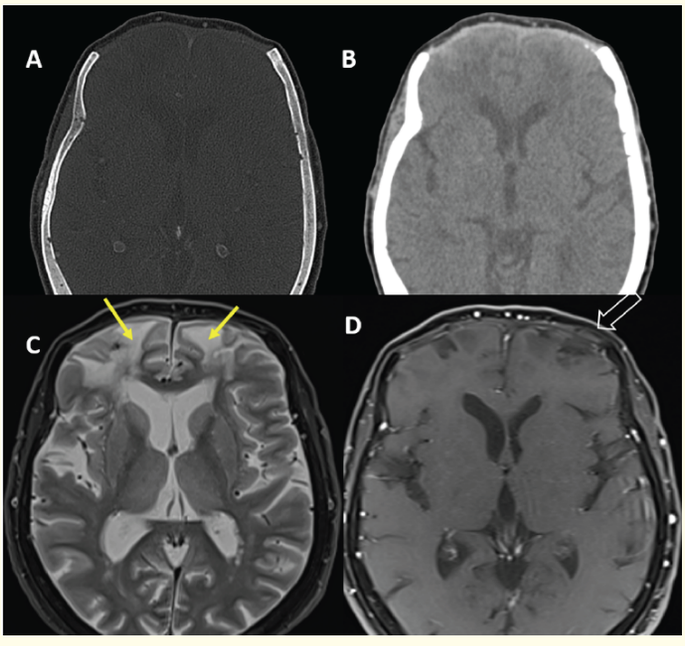


**Figure 3:** Figure 3A,B,C,D: Post-operative CT and MRI from the same level. Axial non-enhanced CT in bone and soft tissue window (A and B) - shows expected post bicoronal bifrontal creniectomy changes. No soft tissue thickening or collection at the surgical bed. Prefrontal soft tissues are normal. No intracranial collection. Axial MRI T2W and post-contrast FAT SAT T1W images (C and D) shows bifrontal gliotic changes (Yellow arrows). Prefrontal scalp soft tissues are normal. No abnormal parenchymal enhancement seen on T1W post gadolinium with fat saturation (open arrow).

## Discussion

The COVID-19 pandemic has undeniably resulted in a significant surge in mucormycosis cases. This increase is directly linked to the widespread use of corticosteroids for treatment, combined with critical underlying conditions such as uncontrolled diabetes and immunodeficiency conditions which are major risk factors for the development of this infection [3,4]. The immunosuppressive impact of COVID-19 and the immunotherapy have favored the growth of mucorales spores because hyperglycemic state leads to hyperferritinaemia and increased expression of glucose regulated protein (GRP-78) in endothelial cells that may help the entry of mucorales into tissues [3-5].

Rhino-orbito-cerebral (ROC) mucormycosis is the most common form of mucormycosis followed by pulmonary mucormycosis. Prompt detection of the disease is crucial, and starting immediate aggressive treatment, which includes maintaining strict glycemic control, discontinuing corticosteroid therapy, performing extensive surgical debridement, and administering antifungal treatment, is essential for management to lower mortality and morbidity.

Osteomyelitis of long bones has been described in trauma surgery, and maxillary bone is being the most commonly affected in covid-19 associated mucormycosis (CAM) [6,7]. Osteomyelitis of the skull is a rare clinical presentation. A typical fluctuant swelling on the forehead is seen in patients with frontal osteomyelitis [6,7].

Mucormycosis, also known as zygomycosis or phycomycosis, is an aggressive opportunistic fungal infection caused by fungi from the Mucorales group. Numerous studies have reported a link between the treatment of COVID-19 and uncontrolled diabetes mellitus (DM) with the development of mucormycosis. Other risk factors for this infection include organ transplants, malignancies, kidney failure, chemotherapy, and immunosuppressive therapy.

The occurrence of concomitant rhinocerebral mucormycosis and Pott's Puffy Tumor is extremely unusual as the involvement of the bone is not common in mucormycosis due to Angio invasiveness of the fungi. There is a scarcity of case reports in the global literature that document the co-occurrence of these two diseases in immunocompromised patients. Gupta., *et al*. reported extensive frontal bone osteomyelitis in a patient with CAM with frontal sinusitis in 2022 [8]. A study conducted in Egypt reported a total of 19 cases of frontal fungal osteomyelitis that occurred during the COVID-19 pandemic, highlighting the emerging health risks associated with this infection during such crises [7]. This case offers a valuable opportunity to enhance our understanding of a rare condition that has arisen as a new clinical entity associated with COVID-19. Our patient, a renal transplant recipient with a history of uncontrolled type II diabetes mellitus, has been managed through long-term steroid and immunosuppressant therapy due to complications related to COVID-19 pneumonia. By analyzing this case, we can gain insights that may improve future management strategies for similar patients.

Mucormycosis can present in various clinical forms, including rhinocerebral, gastrointestinal, cutaneous, pulmonary, and disseminated sepsis. Among these, rhinocerebral mucormycosis is the most prevalent variant and is characterized by its ability to invade the skull base. This invasion can result in severe complications, such as cerebritis, cerebral abscess formation, intracerebral hemorrhage, and ischemic infarction. These complications are attributed to fungal intravascular thrombosis and associated vasculitis, which weaken the cerebral vasculature. This weakening can lead to the development of aneurysms that may subsequently rupture, resulting in hematoma formation in subdural, subarachnoid, and intracerebral areas [4,9].

Pott's puffy tumor (PPT) is a rare complication from frontal sinus osteomyelitis associated with a subperiosteal abscess which can occur after trauma, untreated or partially treated chronic rhinosinusitis or a complication of reconstruction or obliteration of the frontal sinus. It often originates by polymicrobial infection, including streptococci, anaerobic bacteria, and staphylococci. Our patient's bone biopsy and tissue culture proved the growth of numerous fungal hyphae; morphologically consistent with mucormycosis and no bacterial growth was found.

Clinical presentations of PPT include headache, periorbital or frontal swelling, rhinorrhea, fever can be seen in early stage. Intracranial complications can be noticed in advanced stages of the

disease like meningitis, encephalitis, intracranial abscess, cavernous sinus or venous sinus thrombosis due to direct extension of the infection or venous drainage [8,9].

We believe that clinical examinations using endoscopic findings are crucial for alerting ENT surgeons about this diagnosis. Radiological imaging is also an important tool for the early diagnosis and evaluation of disease progression. CT and MRI are essential for evaluating bony destruction and extra-sinus extension in invasive fungal sinusitis. Similarly a systemic review of reported cases of Potts Puffy tumor in a covid 19 era showed that CT gives an excellent delineation of the bony involvement [10,11]. Extra-sinus spread to the orbital apex and intracranial compartment can also be detected on CT; however, MRI provides better delineation of soft tissues, both intracranial compartment as well as the extracranial compartments [12-14] R(3).

In early infection, imaging may reveal mild nodular thickening of the mucosal lining, which can advance to full opacification of the affected sinus. On a CT scan, this appears as enhancing soft tissue thickening within the sinus, while on MRI, it typically shows low intensity on T1-weighted images and varies from hyperintense to isointense on T2-weighted images. The fungal hyphae may exhibit diffusion restriction. The patterns of enhancement can differ widely, ranging from subtle to heterogeneous or peripheral enhancement. Fungal infections characteristically cause erosion of the underlying bones in ~40% of the cases 13. However, this occurs late in the disease and is best detected on a CT scan. There may also be high-density contents within the sinus, which may show blooming in gradient images. These represent the fungal hyphae contents [13]. [4] As the infection is angioinvasive, it results in ischemia and infarction of the infected tissue, which appears to be non-enhancing areas on CT or MRI. Non-enhancing soft tissue may be appreciated and commonly referred to as the "black turbinate sign" on MRI [14]. The septum can be involved with a high incidence of septal perforation. Imaging also helps identify complications like cavernous sinus and ICA thrombosis.

Extra-sinus extension is common, often without radiological evidence of bony sinus wall destruction. Stranding and soft tissue obliteration of the fat planes are important signs of fungal spread into the deep neck spaces. Involvement of fat planes, including the anterior periantral fat and posterior retro-antral fat is common. Retro-antral fat involvement is considered to be one of the initial imaging signs of deep neck invasion [14].

The anterior cranial fossa is a common site of infection. The dissemination of infection may occur through erosions of the cribriform plate or via perineural pathways associated with the olfactory nerves. Neuroparenchymal infection initially manifests as cerebritis, detectable as areas of hyperintensity on T2/FLAIR imaging, with or without enhancement following contrast administration. This condition may progress to a peripherally enhancing abscess, characterized by contents that exhibit restricted diffusion [14,15].

Frontal osteomyelitis (Pott's puffy tumor) has been described as a rare complication of fungal sinusitis. The classic triad of frontal sinusitis, osteomyelitis, and subperiosteal abscess formation is characteristic of Pott's puffy tumor. Infection travels from the sinus to the subgaleal space via the diploic veins, resulting in frontal bone osteomyelitis, erosion through the frontal bone, and subperiosteal abscess development. Posterior spread can result in extradural empyema, subdural empyema, an inflammatory reaction in the subarachnoid space, or brain parenchyma involvement [16].

Urgent imaging should be conducted promptly upon suspicion of a Pott puffy tumor, as any delay in swift diagnosis and treatment may adversely affect the patient's outcome and prognosis. The selection between a CT scan with contrast and an MRI remains a topic of professional debate. Contrast-enhanced Head CT is generally agreed as an excellent initial study. It can show frontal sinusitis, bone erosion, subperiosteal collection, and intracranial extension. Contrast-enhanced Brain MRI is the study of choice if possible and available. It characterizes better the intracranial pathology and the extent of the infection, dural sinus thrombosis, and abscess showing restricted diffusion. It has a superior soft-tissue resolution and excellent brain and subdural space evaluation but poorly characterizes bone destruction. MRI is also the study of choice for follow-up during the postoperative period because it eliminates radiation exposure [17].

A comprehensive multidisciplinary approach is critical in the management of mucormycosis and PPT by early recognition of clinical and radiological features which is sometimes challenging. Early treatment by a combination of medical and surgical approaches is the main determinant of survival. Surgical debridement by endoscopic or open approach of the infected tissues with intravenous anti-fungal therapy should be initiated as soon as possible once the diagnosis is confirmed.

The endoscopic approach is preferred for treating early localized infections, while the open approach is reserved for patients with orbital and intracranial involvement or those who have not had success with prior endoscopic surgeries. Open surgery is the primary treatment for frontal sinus osteomyelitis because it provides better visualization, evaluation, and removal of the frontal bone, particularly when both tables are affected. Riedel's procedure, described by Riedel in 1898, involves opening and exenterating the frontal sinus, removing the anterior table and sinus floor, along with performing radical debridement to eliminate the infection [4]. Cosmetic deformity and surgical scars are the main concerns of this procedure. Endoscopic approach become more popular in management of rhinocerebral mucormycosis with advances of equipment and skilled surgeon.

Our patient underwent a combined endoscopic and external frontal bone bifrontal-bicoronal craniotomy done and radical debridement of disease done, and the eroded bone was well removed. Reconstruction done with primary closure using a nasoseptal "Haddad" flap which was sutured to a heathy dural edge and reinforced by an osteoplastic flap cover. The resultant bony defect needed a later repair either by custom mesh or prosthesis or natural cavalinc bone replacement.

Medical therapy is a critical component in the management of rhinocerebral mucormycosis. It is recommended to employ a combination of liposomal amphotericin B (Ambisome) with either posaconazole or isavuconazole. This approach is advised due to Ambisome's tendency to achieve low concentrations in cerebral tissue and its associated risk of nephrotoxicity at elevated doses. Our patient was treated with antifungal therapy incorporating Ambisome and voriconazole, in conjunction with a regimen of intravenous antibiotics, including piperacillin/tazobactam, Levofloxacin, and Ceftazidime, based on the results of culture analyses. A follow-up conducted after three years revealed no signs of recurrent.

## Conclusion

Covid19 associated invasive mucormycosis in Immunocompromised patients complicated by frontal osteomyelitis is a rare but fatal infection which mandate early diagnosis and selecting the right treatment plan. Maintaining a high level of awareness and initiating timely interventions can significantly reduce both morbidity and mortality rate. It is important to identify patients with underlying comorbidities, those who are immunocompromised, and individuals on corticosteroids, as they are at an increased risk for developing this co-infection. By prioritizing vigilance and swift action, we can enhance care for these vulnerable populations.

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## Author Contributions

Dr. Mohammed Al washahi is the primary surgeon who take care of patient during her treatment and responsible author, Dr. Arif Ali and Dr. Qusi is assistant colleagues and ENT resident respectively who are responsible on pre operative preparation of this patient. Dr. Anwar is our radiology resident who take care about pre and post operative images preparations. Dr. Suad is our pathologist who prepare the pathological slide and help on reaching the diagnosis. Prof. Rashid AlAbri and Dr. Yahya Al Badaai contribute to review the manuscript and Images.

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## Data Availability

Data is provided within the manuscript or supplementary information files.

## Consent

Written informed consent was waived by the IRB due to the retrospective nature of the study and the use of anonymized patient

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