

# A Case of Rhino-cerebral Mucormycosis- a Fatal Post Covid Complication

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## A B S T R A C T

**Introduction:** The prevalence of mucormycosis is 80 times higher in India as compared to other countries. While 80% had diabetes, 76% cases were under steroid treatment. Amidst the deadly second wave in India, mucormycosis was declared as an epidemic and a notifiable disease on 20th May 2021, by central government of India.

**Case report:** We report a case of rhino-cerebral mucormycosis of a 40-year diabetic male, an RT-PCR proven COVID-positive patient with history of long ICU stay on ventilator and steroids 2 months ago. CT-brain showed hypodense collection with soft tissue thickening in sphenoid sinuses and an ill-defined hypodense area in right anterior temporal lobe with edema. MRI-brain with contrast revealed heterogenous enhancement in bilateral sphenoid sinuses and adjacent areas with areas of bony erosion at and around right greater wing of sphenoid.

**Conclusion:** Anterior temporal lobe showed an abscess. High index of clinical suspicion by the physicians and awareness of imaging findings by the radiologists plays a vital role in early treatment and reducing the mortality.

**Keywords:** Mucormycosis, Heterogenous Enhancement, CT, MRI, Fungal, Sinusitis, Cerebral, Diabetes, Steroids

## INTRODUCTION

Mucormycosis is a fulminant opportunistic fungal infection affecting various systems of the body. Of the 101 cases of mucormycosis associated with COVID-19 reported in the literature, 82 belong to India<sup>1</sup>, and the count has been adding up since May, since it has been declared an epidemic and a notifiable disease on 20 May 2021, by central government of India. Radiology again proved its vital role in helping to diagnose the deadly epidemic amidst the COVID-19 pandemic.

Factors such as pre-existing diseases like diabetes, respiratory diseases, cancerous conditions, post organ transplant status, immunosuppression therapy superimposed on immune system changes by COVID-19 infection pave the way for secondary infections. Fungal infections, in particular, are due to the characteristic nature of COVID-19 to cause widespread pulmonary disease in severe cases, producing hypoxic conditions in tissues and reduced T cell immunity, thereby increasing the risk for invasive fungal infections.

Recently the widespread use of immunomodulators like steroids, monoclonal antibodies and broad-spectrum antibiotics have led to exacerbation of pre-existing fungal diseases. Secondary infections were also described in influenza, SARS, MERS epidemics and yet to be explored

in COVID-19.<sup>2</sup> Use of contaminated masks and cylinders, elevated ferritin and cytokines as risk factors are also some of the hypotheses yet to be proven regarding the sudden rise in the cases.

## CASE REPORT

A 40-year-old diabetic male, an RT-PCR proven COVID-positive patient with history of long ICU stay on ventilator and steroids 2 months back, presented with headache and tingling sensation over face. There was no other significant past medical history or family history. He was irritable with altered sensorium at the time of study. Vitals were stable.

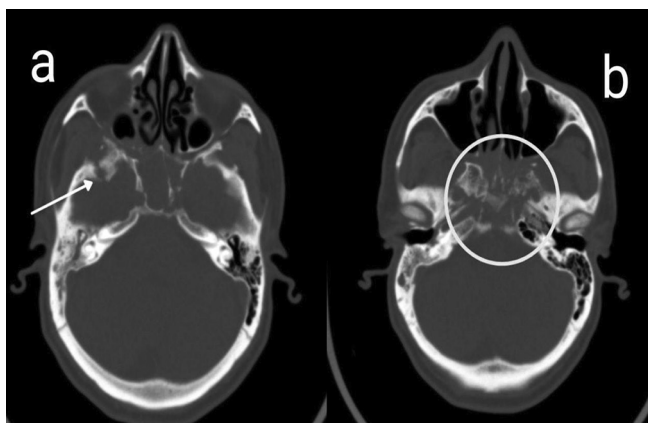
### Imaging findings

CT (Computed Tomography) brain showed a hypodense collection with few air pockets and soft tissue thickening in bilateral sphenoid sinuses (Right >> Left) (figure 1). Bone erosions were evident in the right greater wing of sphenoid, clivus, sella, sphenoid sinuses (figure 2). An ill-defined hypodense area was also seen in right anterior temporal lobe with moderate perilesional edema showing mild mass effect (figure 3). Bilateral orbital bones appeared normal without any erosions at the time of study.

On suspicion of invasive infection in the context of the ongoing epidemic of mucormycosis and to rule out other



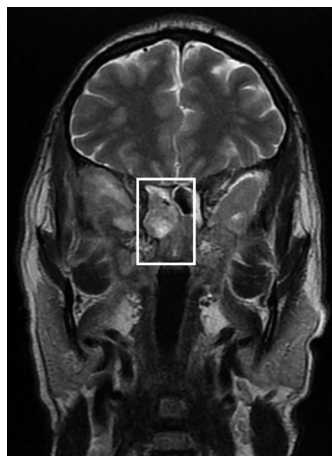
**Figure-1:** Axial non contrast CT image of brain in brain window at the level of sphenoid sinuses showing opacification of bilateral sphenoid sinuses (arrow) with few small air pockets. Orbits and anterior nasal cavity appear normal.



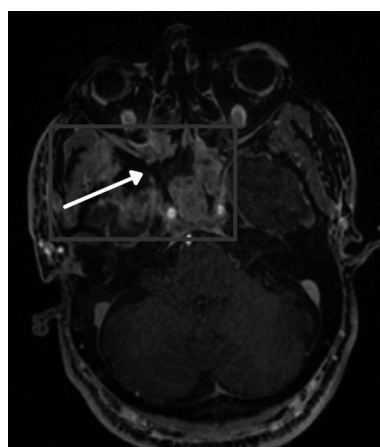
**Figure-2:** Axial non contrast CT image of brain in bone window at the level of base of skull showing bone erosions (a) in greater wing of right sphenoid bone (arrow), (b) clival and sellar regions (circle).



**Figure-3:** Axial non contrast CT image of brain in brain window at the level of orbits showing relatively well-defined hypodense lesion in right anterior temporal lobe (arrow). Orbits and anterior nasal cavity appear normal.



**Figure-4:** Coronal T2 MRI image of brain, showing hypointense lesion in bilateral sphenoid sinuses (Right > Left) (box).



**Figure-5:** Axial contrast enhanced MRI image of brain at the level of orbits showing abnormal right temporal dural enhancement and bone erosions along the regions of right greater wing of sphenoid, bilateral sphenoid sinuses, sella, clivus (box). Arrow points towards the non-enhancing areas.



**Figure-6:** Axial contrast enhanced MRI image of brain at the level of orbits showing relatively well-defined rim enhancing lesion in right anterior temporal lobe (solid arrow). Right sphenoid sinus shows heterogeneously enhancing mucosal wall thickening with internal non-enhancing areas (circle). Cavernous segments of bilateral ICAs appear normal (dotted arrows).

neoplastic etiologies, MRI was suggested.

MRI (Magnetic Resonance Imaging) brain revealed collections in sphenoid sinuses which were hypointense on T2 WI (figure 4). There was heterogenous enhancement with areas of necrosis involving bilateral sphenoid sinuses, sellar and clival regions, posterior part of nasal septum and turbinates and bilateral pterygomaxillary regions. Altered heterogenous enhancement was also noted along greater wing of right sphenoid bone and adjacent temporal dura (figure 5).

Bilateral cavernous sinuses and bilateral cavernous segment of ICAs (Internal Carotid Artery) appeared normal at the time of study (figure 6). Irregular bone erosions were seen at bilateral sphenoid sinuses, sella, clivus and greater wing of right sphenoid bone as evidenced on CT. There was no invasion of extraocular muscles, optic nerves.

Anterior temporal lobe showed a 3x3 cm heterogenous lesion which appeared hypointense on T1W imaging and hyperintense on T2 weighted imaging with peripheral contrast enhancement and an internal non enhancing component showing diffusion restriction, and perilesional edema consistent with abscess (figure 6). Multivoxel spectroscopy showed significantly increased Lipid/Lactate peak.

Based on the above findings a diagnosis of "Bilateral Sinonasal invasive fungal (possibly mucormycosis) sinusitis with skull base and cerebral involvement complicated with abscess in right anterior temporal lobe."

Endoscopic biopsy from sphenoid sinus showed fungal granulomatous inflammation and broad aseptate fungal hyphae on PAS staining suggestive of *Mucor* species.

## DISCUSSION

### Epidemiology

Mucormycosis, which is also called as zygomycosis and phycomycosis, was first described by Paulltauf in 1885. It is an opportunistic fungal infection that is characteristically seen in diabetics and other immune-compromised states.<sup>3</sup> It is a non-pigmented fungus, and it has got a famous misnomer, '*Black fungus*', owing to the black eschars the patients get due to the necrosed infected tissue.

### Etiology

The causative organism is a ubiquitous saprophytic fungus belonging to the *Mucorales* family, which includes *Absidia*, *Mucor*, *Rhizopus*. Mucormycosis can be pulmonary, sinonasal, orbital, cerebral, in disseminated form, of which rhinocerebral form is the most common entity encountered.<sup>4</sup>

### Clinical presentation

The clinical presentation depends on the organ involved. Most of the symptoms are non-specific in the initial stages and hence may be missed. Therefore, in the context of epidemic and awareness of pre-existing risk factors is of utmost importance in such scenarios. In case of rhino-cerebral form, patients clinically present with non-specific symptoms like headache, fever, facial swelling/numbness and blurred vision. *Black eschars*, which are due to necrotic tissues, are seen in late stages of the disease.

### Pathology

Initially, the infection is limited to any of the paranasal sinuses. Later due to the notorious angio-invasive and perineural spreading nature of the fungus, it induces necrotizing vasculitis and extends into the surrounding face, orbital structures (through the naso-lacrimal duct and medial orbital wall), base of the skull and ultimately reaches the intracranial cavity and brain (through the foramina and neurovascular structures).<sup>5</sup> The survival rate is up to 80% when the infection is limited to paranasal sinuses, but once cerebral involvement is seen, the mortality is >80%.<sup>6</sup>

### Diagnosis & Role of Imaging

It is found that, though the diagnosis is dependent on clinical and pathological aspects, imaging has an indispensable role in evaluating the extent of the involvement and spread of the disease.<sup>7</sup>

While histopathology remains the gold-standard test for confirmation, a high index of clinical suspicion and radiological diagnosis are indispensable in starting the treatment at the earliest and preventing mortality. Nasal endoscopy is also done to view the typical black eschars and necrotic tissue.

Imaging plays a vital role not only in the assessment of the extent of disease, but also in identifying its complications like ICA thrombosis, cranial nerve palsies, cerebral abscess and also for the planning of surgeries.<sup>8</sup>

Radiography in Waters view may show non-specific findings like opacification of sinuses, bony erosions.

On CT, isodense collections, soft tissue thickening, some air pockets are seen in involved paranasal sinuses. Unilateral involvement is more common. Sometimes hyperdense collections can be seen due to inspissated secretions because of secondary obstructive changes, which are more common in allergic and chronic fungal sinusitis rather than acute invasive fungal sinusitis. Bone involvement and erosions are better delineated on CT than MRI.<sup>3</sup>

On MRI, predominant hypointensity on T2WI is characteristic due to the susceptibility effect to iron, manganese, and magnesium in fungal elements. Lesions appear isointense on T1WI. Diffusion-weighted imaging shows restricted diffusion in the involved areas. MRI with contrast is the investigation of choice as it better evaluates Cavernous sinus invasion which appears hypointense on T1WI and T2WI, showing heterogenous enhancement.

Cavernous part of ICA, which is frequently involved, and may be narrowed, leading to ischemic infarcts.<sup>9</sup>

Intracranial spread (by dural/leptomeningeal enhancement) The enhancement pattern is usually heterogenous and mostly non-enhancing due to necrotizing areas. The famous 'Black turbinate sign' is black/hypointense/non-enhancement of turbinate due to infarcted tissue, is seen only in the early stage of disease.<sup>10</sup>

The anatomic involvement also provides a clue to the diagnosis. Simultaneous involvement of paranasal sinuses, orbits, and brain should always raise suspicion of invasive fungal infection in the setting of pre-existing risk factors. Nasal cavity involvement is commonly non-specific in turbinate hypertrophy, presence of fluid. The nasal septum may show perforation changes. Involvement of retro-antral,

facial, premaxillary and orbital fat stranding and soft tissue extension indicate aggressive nature.<sup>11</sup>

Visual abnormalities in the early course of disease favors the diagnosis of rhino-orbital-cerebral mucormycosis over bacterial causes and

cavernous sinus thrombosis as they cause blindness only in a late stage.

### Treatment

The primary protocol is to rectify the underlying cause but unfortunately, this cannot be done in patients for whom withdrawal of steroids in COVID may itself turn out to be fatal. Medical or surgical treatment depends on the stage and extent of involvement of the disease.

Medical treatment comprises of Amphotericin B. The second-line drugs are Posaconazole and Isavuconazole. Hyperbaric oxygen and local Amphotericin B are additional therapies.<sup>2</sup>

Surgical management is the final and best effort. Ethmoidectomy, medial maxillectomy, debridement of nasal vault are done based on the extent of spread. Orbital exenteration is done in case of extensive orbital involvement.

### Prognosis

Early detection and treatment are the essential factors in determining prognosis. Though the debulking and mutilating surgeries are disfiguring and disabling, they can be lifesaving in cases that are out of scope for medical treatment.<sup>2</sup>

### Differential diagnoses

- Other invasive non fungal infections
- Sinonasal squamous cell carcinoma
- Sinonasal lymphoma
- Wegeners granulomatosis.
- Paranasal sinus tumours

## CONCLUSION

Imaging with CT and MRI is invaluable in complementing the clinical diagnosis, severity of the infection, and impending complications.<sup>11</sup> Fungal infections characteristically appear predominantly *hypointense on T2* owing to the susceptibility effects of manganese, magnesium, iron in fungal elements.<sup>11</sup> *Invasion of vascular structures* and contiguous spread of the disease *not respecting the anatomical boundaries* are characteristic of mucormycosis infection.<sup>3</sup> *Rapid interval change* in imaging features within few hours to days and increase in thickness of dural enhancement is suggestive of mucormycosis infection.<sup>3</sup> *Rapid Combined involvement* of paranasal sinuses, orbits, pterygomaxillary fissures, facial soft tissues, intracranial involvement should always raise suspicion of invasive fungal sinusitis.<sup>3</sup> Prognosis is still grave despite the aggressive surgeries and potent antifungals.<sup>3</sup>

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