A Case Report on Mucormycosis in Non-Diabetic, Non-Covid Recovered Patient with no History of Steroid use

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Rhino cerebral orbital mucormycosis is an aggressively spreading fungal infection caused by filamentous fungi of the Mucoraceae family and is found to be more prone in patients with comorbidities that include: uncontrolled diabetes mellitus, immune-suppressed patients, iron and aluminum overload, chronic steroid therapy, severe trauma, and protein-energy malnutrition. A 51year old male patient was admitted to the hospital with a complaint of headache and intermittent fever. The patient had no history of diabetes or denovo hypertension. Based on the analysis of histopathological and radiological investigations, the patient was diagnosed with mucormycosis. The patient furthermore underwent an endoscopic surgical debridement followed by standard treatment including antifungal antibiotic(ambertericin-B) and azole antifungals

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(posaconazole) along with symptomatic treatment. Though the patient was given all possible therapy available, no improvement was seen in the patient's condition (poor prognosis).

Keywords: Mucormycosis; rhinocerebral; zygomycosis.

1. INTRODUCTION

Rhinocerebral mucormycosis has been a very severe and rapidly developing filament infection in the Mucoraceae family and an opportunistic infection commonly encountered in patients with previously identified risk factors such as diabetes mellitus, immuno-prone people, iron overload, and/or trauma [1]. This fungus is classified into five types. This encompasses rhinocerebral (the most prevalent kind, accounting for 39% of all cases), pulmonary, cutaneous, gastrointestinal, and metastatic cancers, depending on the organ affected. Depending on the affected tissue, these are further classified as rhinonasal, rhinoorbital, or rhinoorbitocerebral [2]. Approximately 1.7 cases per 1,000,000 population annually are associated with mucormitic disease. In most cases, fungal spores are inhaled and move to the nasal mucosa, causing sinusitis, which subsequently spreads to the paranasal sinuses. When the infection spreads from the paranasal sinuses to the orbital wall, it causes involvement. The five species of mucormycosis cause a variety of clinical manifestations, including fulminating lesions of the orbital, nasal, and cerebral tissues, as well as extensive invasion of numerous blood arteries. It consists of three stages of clinical presentation.

**Stage 1:** Infection of the nasal mucosa and sinuses,

**Stage 2:** Orbital involvement,

**Stage 3:** Cerebral involvement.

Pain, chemosis, vision loss, ophthalmoplegia, proptosis, and dark-colored lesions on the nasopharynx and/or hard palate are possible symptoms of this infection, as is ipsilateral peripheral facial paralysis. Ophthalmoplegia occurs when the muscles and orbital space are infected, or when the third, fourth, and sixth cranial nerves are compromised, resulting in inflammation of the skin, nose mucosa, eyes, and brain tissue. Peripheral seventh cranial nerve paresis or paralysis, as well as facial hypoesthesia, are frequently reported [3,4], followed by blood vessel invasion, infarction, and necrosis of host tissue [5]. Some species are responsible for leukemia, sarcomas, and indolent skin ulcers. They have an impact on the quality of life and cause a significant increase in morbidity and mortality. As a result, early detection of this potentially fatal condition and timely treatment are critical in lowering the death rate. Amphotericin B, posaconazole, aggressive surgery, and adjunctive therapeutic modalities such as local amphotericin B irrigation, hyperbaric oxygen, and optimizing the immunosuppressive regimen in transplant patients followed by local treatment with antifungal agents are the standard treatments for mucormycosis. Hyperbaric oxygen was discovered to have a positive influence on prognosis. Simple sinus clearance, radical debridement, and orbital exenteration are all part of the surgery [6]. The infection can be acute or chronic, depending on the stage of development (5.6% of rhinocerebral mucormycosis cases) [7]. There have been very few cases of concomitant mucormycosis and COVID-19 infection recorded [5].

2. CASE PRESENTATION

Here we present the case of a 51 years old male patient with a history of hypertension who was brought to the emergency department with chief complaints of severe continuous occipital headache, a lowgrade fever 99.8ºF for two days (without chills), myalgia, and nausea that were not relieved with the prescribed medication cilnidipine 10mg once a day, naproxen 500mg + domperidone 10mg combination, pantoprazole 40mg once a day, disprin 325mg, cefpodoxime 200mg, paracetamol 650mg along with vitamin supplements for 3 days. He was known to work as a professional teacher in secondary school who was not exposed to dust from construction sites or others.

He was immediately administered with medicines that include: pantoprazole 40mg, ondansetron 4mg, and ceftriaxone 2gm twice a day at the emergency department. His past medical history was noted and it was understood that the patient has denovo hypertension and is not a known diabetic.

The next day he was shifted to the ward, where he developed numbness over the left side of his face with decreased appetite, disturbed sleep,
aphasia, drooping of the left upper eyelid, and loss of left and right eye vision with CF (count fingers vision) > 3 mts including full extraocular movements.

He was administered with ceftriaxone 2 gram twice a day, pantoprazole 40 mg once a day, ondansetron 4 mg, ramipril 5 mg, IV fluids, Inj. optineurin 3 mg and paracetamol 650 mg.

After analysis, his report was found to be COVID negative which was done by RT PCR testing. His CT brain findings detected hyper density along the superior sagittal sinus, right transverse sinus, and straight sinus—suspected cerebral sinus venous thrombosis. The MR venogram impression suggests, extensive sinusitis with secondary left orbital cellulitis and fungal etiology. His CT chest impression detected bilateral posterior gravity-dependent ground glass densities. 2D echocardiogram detected normal cardiac function with an ejection fraction of 60%. The patient was informed about the poor prognosis of his condition and the need for an emergency FESS (functional endoscopic sinus surgery) and orbital decompression.

On the following day, the extracted tissue (FESS Left sphenoid sinus) was sent for fungal strain in 10% KOH mount that resulted in occasional broad, hyaline, aseptate hyphae with wide-angle branching (suggestive of an isolate belonging to order Mucorales).

Under examination, his right eye vision had been reduced, suspecting a spread of infection along with a blocked nose and difficulty in swallowing. He was given a conventional amphotericin B 50 mg (5% dextrose to be infused over 16 hours). After the infusion, he was given Inj. amphotericin-B 350 mg, Inj. pheniramine 2 cc, Inj. hydrocortisone 80 mg (in case of reaction) Inj. enoxaparin 40 mg, Inj. ceftazidime 1 gm and Inj. cefoperazone with sulbactam 3 gm.

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**Fig. 1. T2 MRI showing patterns in mucormycosis**
On the 4th day, the patient developed Proptosis, chemosis, and was unable to open his eyes. B/L pupils were dilated and secretions were seen from both oral and nasal cavities. His vital signs monitored were:

BP 150/90mmHg with PR of 136 bpm
Body temperature: 101ºF,
SpO₂:100% on 4liters of oxygen per hour through ventilation.

Inj. clexane was withdrawn after analyzing the MR venogram report as it confirmed that hyper densities noted in the CT scan were fungal strains rather than sinus venous thrombosis and Inj. cefoperazone with sulbactam was replaced with Inj. meropenem 1gm. His MRI report detected an additional involvement of the right orbit with focal signal changes in the left anterior temporal lobe compared to the earlier report.

The patient was completely sedated during the night with Inj. fentanyl 50 µg/50ml.

On the 5th day, the patient was found to be febrile101ºF. Potassium chloride and Mg replacement were added along with his daily medications. The patient was found to have a poor prognosis despite the treatment.

On the 6th day, the patient was supported with mechanical ventilation to undergo an MRI scan. After the MRI scanning, the patient was unable to maintain his SpO₂ levels above 90% without ventilation.

The patient was still undergoing the same treatment with a grave prognosis.

On the 7th day, there was no change in the patient's condition and the same was informed to the patient's attenders.

3. DISCUSSION

A complete investigation was performed from the database of various websites to obtain all available articles related to rhino-orbital cerebral infections caused by fungi of the order Mucorales. We hereby summarize the patient's investigation and his prognosis for the medication.

In 1885 Pautauf first described mucormycosis, also known as Zygomycosis or phycomycosis. It is an acute opportunistic infection caused by wide, nonseptate saprophytic fungal forms found in soil, air, bread molds, and rotten fruits and vegetables. This infection progresses throughout vascular and neural systems and infiltrates blood vessel walls, affecting patients of all ages, from premature infants to the elderly. Rhino ocular cerebral mucormycosis usually affects diabetics and immunocompromised patients and is distinguished by aseptate hyphae, lengthy sporangiospores, and big sporangia with thin walls. The infection erodes the bony walls of the ethmoid sinuses, causing the infusion to expand into the orbital and retro-orbital areas, as well as the brain. (Cerebro-rhino-ocular mucormycosis)

Several predisposing conditions play a role, the most prevalent of which being diabetes with ketoacidosis. Diabetic patients are prone to mucormycosis due to their neutrophils' impaired capacity to phagocytize and attach to endothelium walls. Furthermore, acidosis and hyperglycemia create an ideal environment for fungal growth. Mucormycosis is extremely uncommon in HIV/AIDS patients. The most prevalent presenting sign and symptoms are orbital and nasal abnormalities. Loss of fusion of the 2nd, 3rd, 4th, and 6th cranial nerves with proptosis, ptosis, chemosis, diplopia, orbital discomfort, central retinal artery blockage, diseases pupil, and loss of vision can occur in

### Table 1. Detections of additional parameters by MRI report

| Parameters                  | Day 1  | Day 2  | Day 3  | Day 4  | Day 5  | Day 6  |
|-----------------------------|--------|--------|--------|--------|--------|--------|
| Hb (13-16 gm%)              | 17.3   | 16.7   | 16.1   | 13.1   | 12.1   | 12.1   |
| RBC (4.5 – 5.5 millions/cumm)| 5.81   | 5.67   | 5.52   | 4.49   | 4.5    | 4.24   |
| Haematocrit PCV (40.0 – 50.0 Vol%) | 49.8 | 49.5   | 48.9   | 39.4   | 35.4   | 34.5   |
| WBC (4000 – 11000 cells/cumm) | 22,350 | 26,950 | 25,180 | 15,430 | 17,000 | 13,950 |
| Platelets (1.5 – 4.5 lakhs/cumm) | 1.98  | 2.19   | 1.74   | 0.92   | 0.70   | 1.5    |
| Sr. Urea (17.0 – 43.0 mg/dl)  | 26.0   | 30.0   | 28.0   | 41.0   | 51.0   | 54.0   |
| Sr. Creatinine (0.67 – 1.17 mg/dl) | 0.59  | 0.64   | 0.57   | 1.05   | 0.94   | 0.88   |
| Sr. Sodium (136.0 – 145.0 mmol/ L) | 132.0 | 145.3  | 146.6  | 155.3  | 143.7  | 145.8  |
| Sr. Potassium (3.5 – 5.1 mmol/L) | 3.8   | 3.9    | 3.4    | 2.9    | 3.4    | 3.4    |
| Sr. Chloride (98.0 – 107.0 mmol/L) | 98.8  | 109.5  | 108.9  | 119.1  | 110.6  | 113.7  |
the orbit. Diplopia can occur as a result of motor nerve paralysis, intraorbital exclusion of the infusion, or involvement of the ocular muscles. Due to optic nerve injury or retinal artery obstruction, retrobulbar extension of the process may result in impaired vision or blindness. Cavernous sinus thrombosis, exophthalmos, total ophthalmoplegia, and papilledema can result from the progression of necrosis into the brain [8].

Deepak Venkatesh et al. presented the case study of a 32-year-old male patient who had no history of diabetes and HIV or AIDS and no steroid use and no immunocompromised conditions. Only history of Periodontitis (gum disease). As a result of the observations, it was concluded that a significant proportion of Rhino orbital mucormycosis occurs in patients who have no previously identified risk factors. In the case of Rhino orbital and mucocutaneous involvement, the diagnosis of mucormycosis is relatively simple. However, when deep tissues are invaded, as in cases of pulmonary mucormycosis, a correct diagnosis is more difficult to obtain. The gold standard for determining the presence of mucormycosis is histopathological, cytopathological, or direct microscopic examination of affected organs. The evidence of tissue invasion is used to make the diagnosis. Thus, specimens should be processed for fungal stains, cultures, and any other procedure, such as molecular-based analysis, that is necessary to rule out differential diagnosis. [9].

Mucormycosis was confirmed by the presence of blackish necrotic tissues in the affected area, as well as histopathology. The mucor structures are identified by histological stains. Regular examinations and imaging studies, such as CT and MRI, are critical for detecting the spread of mucormycosis. Mucormycosis is treated with a combination of surgical debridement and antifungal therapy. Surgical debridement of necrotic tissue may involve removing sections of the maxilla, nasal cartilage, palate, mandible, and orbit, depending on the extent of necrosis. The main treatment for the disease is systemic amphotericin-B, and starting treatment early is crucial to lowering mortality. Posaconazole is an oral antifungal agent that has been used as a step-down therapy after Amphotericin-B control of mucormycosis. Patient recovery is dependent on how quickly diagnosed and specific antifungal treatment (amphotericin B) initiated, and in many cases, surgical resection of necrotic tissue is required which may include bone and ocular tissue [10,11,12].

Similar to our case, E.m Gutierrez Delgado et al. described one case report of a mucormycosis patient treated with surgical debridement of involved tissue and systemic Amphotericin-B. Based on their findings, they concluded that patients receiving Dual therapy with surgical debridement and amphotericin-B had a 91 percent chance of survival. [13].

According to several case series, the mortality rate was lower when patients underwent surgical debridement compared to those who did not undergo surgical debridement, revealing that the extent and timing of surgical debridement is necessary to reduce complications and mortality [14].

As a result, reporting under this situation will alert young doctors, perhaps leading to the early discovery and treatment of immunocompromised patients as well as opportunistic mycotic infections. Early diagnosis and successful treatment with surgical debridement, sinus breathing assistance, and antifungal drugs can save a patient's life. After breakthroughs in diagnosis and therapy, the disease still has a high fatality rate of 30 to 70%. If the patient is not treated and the treatment is unsuccessful, death may ensue within two weeks.

In this study, we provide a rare instance of rhino cerebral orbital mucormycosis with clinical presentation and therapeutic outcomes in a non-diabetic patient.

Demographic information, clinical symptoms, underlying systemic diseases, microbiological and radiological findings, medical treatments, and surgical interventions were all documented and analyzed.

4. CONCLUSION

Mucormycosis is an uncommon infection with a high fatality rate that spreads rapidly from the nose to the orbitals and cerebrum. We end our case study by emphasizing the importance of early diagnosis and successful treatment in lowering the mortality rate of this illness.

ETHICAL APPROVAL AND CONSENT

As per international standard or university standard guideline patients consent and ethical
approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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