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Case Report

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A Rare Case Report of Mucormycosis Presenting with Left External Ophthalmoplegia

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Abstract

Mucormycosis is one of the most severe and quickly spreading types of fungal illness which typically starts in the nose and paranasal sinuses after inhaling fungal spores. The subphylum Mucormycotina, which includes the genera *Absidia*, *Mucor*, *Rhizomucor*, and *Rhizopus* is responsible for its majority of cases of mucormycosis. There are roughly 1.7 incidences of mucormycosis per 1,000,000 people annually. Most common risk factors identified in patients with mucormycosis are immunocompromised patients, acidosis, increased serum free iron levels. Diabetic patients (immunosuppressed) with diabetic keto acidosis (DKA) are more prone for mucormycosis. Rhinocerebral mucormycosis which is the most frequently documented form of the condition, is characterized by a gradual fungal invasion of the hard palate, paranasal sinuses, orbit, and brain. Early disease detection and strong medical and surgical interventions are necessary for the successful management of this fulminant infection to reduce the significant morbidity and mortality linked to the disease course. Therefore, early detection of potentially fatal mucormycosis and timely treatment are crucial for lowering the fatality rate. Recently, there have been more reports of people with mucormycosis linked to COVID-19, particularly from India. We discuss a 52-year-old male patient with diabetes who developed rhinocerebral mucormycosis after a tooth extraction.

Keywords

Rhinocerebral mucormycosis, Diabetic keto acidosis, Surgical interventions

Introduction

A rare opportunistic fungal infection, mucormycosis (phycomycosis, zygomycosis) is brought on by fungus from the Mucorales order and Mucoraceae family. Paultauf gave the first account of it in 1885. Mucormycosis ranks behind candidiasis and aspergillosis as the third most prevalent Angio invasive fungal infection in humans [1]. Its occurrence is rare in people who appear to be healthy and mostly affects people who have impaired immune systems [2]. Mucormycosis infection in the immunocompromised host occurs from impaired immunity, which leads to the fast proliferation and invasion of fungal organisms in deeper tissues [3]. Uncontrolled diabetes (especially in patients with keto acidosis), cancers like lymphomas and leukaemia's, renal failure, organ transplant, long-term corticosteroid and immunosuppressive therapy, cirrhosis, burns, protein-energy malnutrition, and acquired immune deficiency syndrome are some of the various risk factors for mucormycosis. Spores can be inhaled through the mouth, nose, or even with direct penetration through a skin wound. People who have weaker cellular and humoral defence mechanisms may not respond adequately leading to

severe infection with the fungus. The fungus may then directly extend to the orbit, meninges, and brain through the paranasal sinuses. However, some individuals with mucormycosis infection have no observable risk factors [4]. Early illness detection, vigorous, and rapid medical and surgical therapies are necessary for the successful management of this lethal infection to reduce the significant morbidity and mortality linked to this disease process [5]. In this case report we describe how the lesion progresses rapidly leading to extensive tissue necrosis and involvement of adjacent structures.

Case Report

A 52-year-old male diabetic patient came to casualty with chief complaints of left sided tooth pain for one week, associated with fever for one week. Patient developed swelling over left side of face. Patient was known case of diabetes since past 7 years not on regular medication and a known case of hypertension since past 5 years not on regular medication. Patient underwent tooth extraction one week prior to admission. His past medical history was evident with poor sugar control (HBA1c – 11.2). The patient later developed poor vision in left eye which progressively worsened until he had only light perception associated with complete external ophthalmoplegia in left eye. Patient had high blood pressure recordings (170/110) at admission which was controlled with oral medications.

Magnetic resonance imaging (MRI) of orbit was done showing TI hypo. T2 stir hyperintense single lesion with restricted diffusion and low ADC values with air fluid levels in entire left maxillary sinus suggesting left maxillary sinusitis/ infected collection. Focal area of defect in the anterior wall of the left maxillary sinus with small collections in soft tissue of left maxillary region - infected collection.

Patient sugars were brought under control by Human Actrapid Insulin, using intravenous infusion and subcutaneous injections in coordinated manner.

During hospitalisation patient underwent FESS with debridement and biopsy was taken and sent for histopathology examination. Patient had elevated white blood cell counts reaching the counts of 13,600. Potassium hydroxide smear was positive for mucor, and patient was started on liposomal amphotericin-b. Patient was started on antifungals. Later patient developed acute kidney injury with amphotericin, which was stopped, and patient was started on intravenous posaconazole. Serum potassium was monitored during the entire hospital stay. Patient was advised MRI brain with contrast to rule out intracerebral involvement and to plan further debridement, but patient wasn't willing for further treatment and went on left against medical advice. Patient was advised follow-up in ENT and ophthalmology OP.

Discussion

Zygomycetes, a group of fungus that develop branching, ribbon-like hyphae and reproduce sexually by producing zygospores, are responsible for a variety of illnesses that are referred to as mucormycosis. *Rhizopus*, *Rhizomucor*, and *Absida* are the most prevalent types. They belong to the phycomycetes subclass, family Mucorales. *Cunninghamella*, *Saksenaea*, *Syncephalastrum*, *Cokeromyces*, and *Mortierella* are further fungal genera linked to the disease [6]. 90% of cases of rhinocerebral mucormycosis are caused by the pathogen *Rhizopus* [7]. In addition to being widely distributed in fruits, soil, and human waste, pathogens can also be cultivated from the throat, nasal passages, and oral cavity of healthy, disease-free people. The fungi are typically non-pathogenic and only become so when the host resistance is extremely low. Most common source of infection in mucormycosis is generally by two routes, i.e., inhalation of asexual spores through nose followed by germination of the asexual spores and growth of hypae, the second route being direct inoculation of the fungus by direct trauma and followed by hematogenous seeding and aggressive local spread. In general healthy population these spores are phagocytosed. In the maxillofacial region, mucormycosis can enter through an extraction wound in the mouth or an ulcer in the mucosa. When it comes through the nose and PNS, the infection may result in palatal ulceration that eventually necroses, and most of the time, the affected area appears black. Clinical manifestations of an infection that has spread due to direct wound contamination can occur anywhere in the oral cavity, including the mandible. Cavernous sinus thrombosis, which is a major consequence of maxillary infections, is a key distinction between infection involving the maxilla and mandible [8]. Malignant haematological disease with or without stem cell transplantation, protracted and severe neutropenia, poorly uncontrolled diabetes mellitus with or without DKA, iron overload, major trauma, prolonged corticosteroid use, illicit intravenous drug usage, neonatal prematurity, and malnutrition are the most significant risk factors for development of mucormycosis [9]. Diabetes mellitus impairs the immune system's ability to fight off mucormycosis by reducing granulocytes' capacity to phagocytose. Additionally, an atmosphere that is acidic and abundant in glucose is ideal for *Rhizopus* species. The atmosphere is more acidic and there are more free iron ions present when a person is in DKA, which encourages fungal development. Neutrophils are recognized to be crucial in the host's defence mechanism against microbial colonization [10]. As a result of malfunctioning neutrophils and myelosuppression brought on by chemotherapy, which in turn causes a deep neutropenia in leukaemia patients, these individuals are more likely to acquire fungal infections, such as mucormycosis. In immunocompromised patients, polymorphonuclear leukocytes are less successful in removing hyphae, therefore the infection becomes established in these circumstances. The condition worsens when the hyphae spread into the walls and lumens of the arteries, where they cause thrombosis, ischemia, and infarction as well as dry gangrene of the affected tissues. Sepsis is caused by hematogenous spread to other organs, such as the lung, brain, and others [11].

The infected nasal mucosa in rhinocerbral mucormycosis may initially appear normal, then progress through an erythematous phase, with or without edema, followed by a violaceous appearance, and finally, the development of a black, necrotic nasal or palatal eschar as blood vessels become thrombosed with ensuing tissue necrosis. On histopathology, the lesion exhibits broad aseptate fungal hyphae with right-

angle branching. An accurate diagnosis of rhinocerebral mucormycosis is typically made through a tissue sample that reveals the distinctive hyphae. The presence of many, large (5 - 30 m), thin-walled fungal hyphae that are non-septate, branching at right angles, and have a ribbon-like appearance are histological features of mucormycosis [12]. Aspergillosis on histopathology presents with septate, narrower, and more acutely angled *Aspergillus* species hyphae and is one of the histopathological differential diagnoses (Figure 1).

According to the anatomic place of occurrence, mucormycosis is divided into five categories: (1) Rhinocerebral, (2) Pulmonary, (3) Cutaneous, (4) Gastrointestinal, and (5) Disseminated. The brain, orbit, and paranasal sinuses should all be considered when referring to rhinocerebral mucormycosis [14, 15]. Mucormycosis can enter the maxillofacial region through an ulcer or extraction socket in the mouth, especially in patients with impaired immune systems. 4 cases of rhinocerebral mucormycosis were described by Huang et al. during a ten-year period, all of which were discovered after tooth extractions [16]. All four of these patients had uncontrolled diabetes, and two of them were in a DKA stage when they first presented. The maxillary and ethmoid sinuses are the most often affected paranasal sinuses [17]. In individuals with DKA, rhinocerebral mucormycosis predominates, making up 70% of recorded cases [14]. 9 Patients with rhinocerebral mucormycosis typically have low-grade fever, aches and pains, edema, and general malaise. The condition typically starts in the palate or nasal mucosa, then spreads to the paranasal sinuses through the blood vessels nearby. Additionally, mucormycosis can directly extend to the retro-orbital region. When the orbit is involved, the functions of the cranial nerves III, IV, and VI may be compromised or lost, which can cause proptosis, ptosis, pupillary dilation, orbital cellulitis, and vision loss [18]. Local tissue is invaded by the fungus as mucormycosis progresses. The predisposition for thrombosis and tissue necrosis, is explained by direct penetration and growth through the wall of blood arteries. In addition to hematogenous dissemination, perineural invasion is another way that rhinocerebral mucormycosis can spread [18]. There have been numerous reports of deadly cavernous sinus thrombosis and hematogenous dissemination to the cavernous sinus. Cavernous sinus thrombosis, a major consequence of maxillary infections, is a significant prognostic difference between infection involving the maxilla and infection of the mandible.

When a case of mucormycosis is suspected the following differential diagnoses i.e., squamous cell cancer, chronic granulomatous infections such tuberculosis, tertiary syphilis, midline fatal granuloma, and other deep fungal infections, should also be considered. Necrotizing fasciitis is the predominant differential diagnosis, particularly if facial edema is present.

Maxillary mucormycosis commonly manifests radiographically as bone detachment of the sinus walls, thickening of the sinus mucosa, and opacification of the paranasal sinuses without fluid level. McDonogh et al. cautioned that any diabetic patient in a ketoacidotic condition presenting with clinical and radiographic symptoms of rhinosinusitis should be suspected of having mucormycosis unless proven otherwise because some of these radiographic findings may resemble sinusitis [19]. Bone erosion or destruction can be seen on an MRI or computed tomography (CT) scan (Figure 2), which can also assist determine the severity of the condition [20].

When treating patients with mucormycosis, early diagnosis is crucial. For the treatment to be more effective, predisposing issues must be treated and should be brought under control as early as possible. Hyperglycaemia and acidemia in DKA individuals should be treated. Amphotericin B high dose antifungal therapy is part of medical management. Hyperbaric oxygen treatment, intravenous lipid complex, and intravenous liposomal amphotericin have also been employed recently. It is frequently possible to stop the infection from spreading into the eye by performing timely surgical excision of the infected

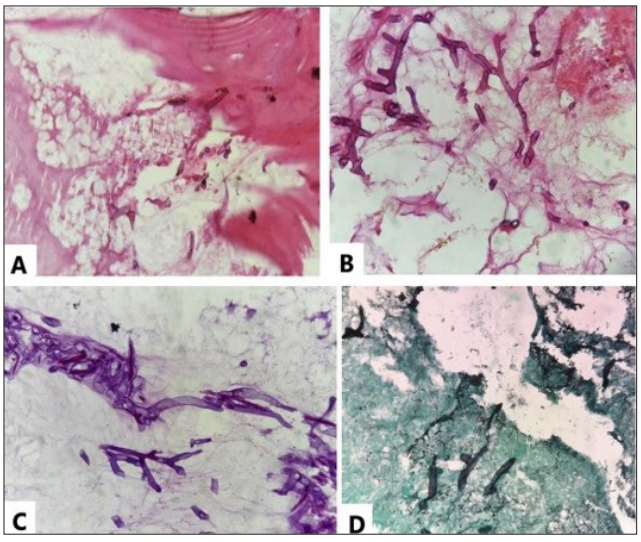

Figure 1: Histopathological images of debrided necrotic bone. Haematoxylin and eosin images **(A)** 200x and **(B)** 400x show fragments of dead bony trabeculae with necrosis and aseptate, wide-angle (≥ 90°) branching hyphae with non-parallel walls. **(C)** Periodic acid Schiff-diastase, 400x and **(D)** Gomori methenamine stain, 400x highlighting hyphal forms of mucor [13].

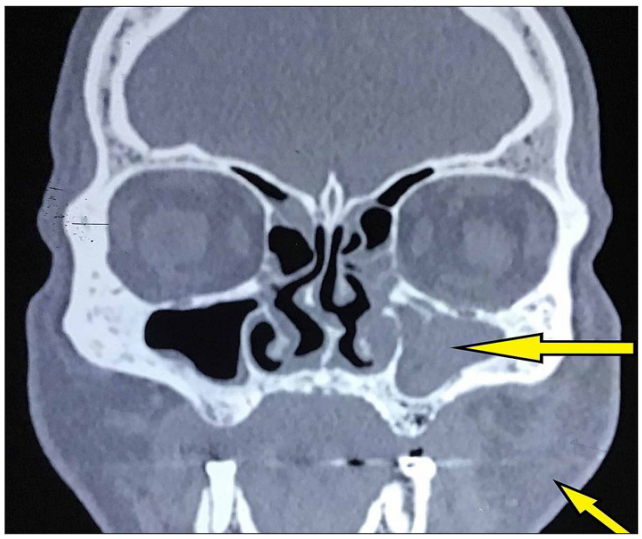

Figure 2: Preoperative facial CT showing facial swelling on the left side of face and obliteration of the left maxillary sinus [21].

sinuses and proper debridement of the retroorbital region. To be sure that all necrotic tissue has been removed and the infection has not advanced, repeated surgical debridement may be required [22]. Posaconazole intravenous or oral can be utilized as a second line agent in mucormycosis if a patient develops complications to or contraindications for intravenous amphotericin-B which include renal failure with increasing serum creatinine, increased potassium levels, drug reaction to amphotericin-B. The early debridement of all diseased and necrotic tissues is an essential part of surgical therapy. Depending on how the condition develops, this could need to be repeated. Radical resection, including partial or complete maxillectomy, mandibulectomy, and orbital exenteration, may be necessary in some circumstances. The patient underwent surgical excision and intravenous antifungal therapy was provided to the patient.

Conclusion

We conclude that early diagnosis is essential for treatment planning, and antifungal therapy facilitates a quick recovery. The most frequent risk factor is diabetes mellitus, and additional risk factors include immunocompromised patients with pre-existing cancers and those who have received bone marrow transplants. The majority of diabetic individuals have rhinocerebral mucormycosis, which affects the sinus and orbit as well as the brain, and affects the paranasal sinuses. Although the likelihood of developing mucormycosis after tooth extraction is quite low, when it does, it can have serious consequences for morbidity and mortality. In order to minimize poor outcomes in clinical practice, dental professionals must be informed of the likelihood of this dangerous and lethal complication. We conclude that early diagnosis and treatment of rhino-orbito-cerebral mucormycosis are crucial for improving survival because the prognosis is quite bad after the patient has cavernous sinus thrombosis and brain infarctions.

Mucormycosis must be identified as soon as possible in order to stop the infection from spreading and causing severe morbidity and mortality. Finally, improving the prognosis of patients with mucormycosis requires a multidisciplinary team approach, early identification, reversal of the underlying medical disease coupled with vigorous surgical surgery, and administration of amphotericin B.

Acknowledgements

None.

Conflicts of Interest

None.

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