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MUCORMYCOSIS WITH FUNGAL BALL OF MAXILLARY SINUS – A RARE STUDY

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Case Report

ABSTRACT

Background and Aim: Mucormycosis is an infection caused by a group of filamentous molds within the order Mucorales. In developing countries, most cases occur in persons with poorly controlled diabetes mellitus or following trauma. Mortality associated with invasive mucormycosis is high (> 30–50%). Noninvasive fungal ball, a matted collection of fungal hyphae, previously known as 'Aspergillomas', has been rarely reported with Mucoraceaespecies.

Case presentation: A 52-year-old man, known case of diabetes mellitus presented with a discharging sinus in left maxillary region and a blackish ulcer in Left molar region. Computed tomography scan revealed extensive cortical erosion of left hemi-maxilla. Mucormycosis infection with a maxillary sinus fungal ball was confirmed on histopathological examination. The patient was treated with intravenous AmphotericinB.

Discussion: The incidence of fungal rhinosinusitis (FRS), once thought to be a rare condition, has dramatically increased recently. Acute invasive fungal rhinosinusitis is relatively rare that is frequently observed in immunocompromised people specifically uncontrolled diabetics or people on immunosuppressive medications, typically associated with Aspergillus and Mucoraceae species. On the other hand, a fungal ball of the paranasal sinus is noninvasive and typically found in immunocompetent, non-atopic hosts. Aspergillus species are the most commonly isolated fungi, however, fungal ball formation is rarely seen with mucormycosis.

Conclusion: An anomalous presentation of a Fungal Ball associated with mucormycosis is the primary focus of this report.

Keywords: Mucormycosis; immunocompromised; fungal rhinosinusitis; uncontrolled diabetes mellitus; aspergilloma (fungal ball).

1. INTRODUCTION

Mucormycosis is a rare opportunistic fungal infection which was first described by Paultauf in year 1885 [1]. After candidiasis and aspergillosis, mucormycosis accounts for being the most common angioinvasive fungal infection [2]. Maxillary sinus is predominantly affected in paranasal sinus fungus ball [3]. These non-invasive lesions typically appear in immunocompetent people without any risk factors. Mucormycosis species fungal ball have rarely been reported, as *Aspergillus* species are primarily associated to fungus balls. When a patient is immunosuppressed, a fungus ball may start to develop into an invasive mycosis. It is important to distinguish fungus balls from other conditions like common sinusitis, neoplasia, haemorrhage, as it affects the treatment and prognosis. Cone beam CT remains the method of

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choice though MRI is more sensitive. Histopathologically, presence of aseptate hyphae is characteristic. We present a case of a Mucormycosis in an uncontrolled diabetic patient with a coexisting noninvasive fungal ball occupying the maxillary sinus.

2. CASE PRESENTATION

A 52-year-old man came for evaluation of headache and heaviness of head persistent since 1 month. Patient also complained of left sided facial pain present since 2 weeks and history of recurrent upper respiratory tract infection. Patient was a known case of diabetes mellitus, not on regular medication.

On physical examination, a discharging sinus of size 1x2 cm was seen in Left maxillary region. In addition, a facial asymmetry caused by a left-sided facial swelling with tenderness was noted, with a deviated nasal septum towards right side. Intraoral examination revealed a poor oral hygiene. Blackish discoloration with a small sized 0.5 x 0.5cm ulcer was noted in Left 2^{nd} and 3^{rd} molar region.

A computed tomography scan was done which showed extensive cortical erosion with irregularity noted in the left hemi-maxilla, hard palate and all the walls of left maxillary sinus (Image A). Similar changes were noted in the Left pterygoid plate. Mottled calcific loci were indicative of infective fungal etiology.

HbA1c revealed an uncontrolled diabetic status with an average 3 month of 13.8%.

In view of CT findings, patient left nasal tissue was sent for KOH mount which showed no fungal elements. Pus culture and sensitivity showed *Escherichia coli* growth after 72 hours.

For a definitive diagnosis, nasal endoscopy was done which showed g (Image B) and biopsy was taken from left nasal cavity. Histological examination revealed no organism or definitive pathology because of tiny representative sample. So a repeat biopsy was requested. Repeat endoscopy showed an intact fungus ball in the left maxillary sinus which on removal exhibited a characteristic clay-like texture. Biopsy was sent from left maxillary cavity, left nasal cavity and left cheek ulcerative wound.

Histopathological examination of repeat biopsy from left maxillary and left nasal cavity revealedmatted hyphae characteristic of a fungal ball, occupying the left maxillary sinus (Fig A and B) along with broad, irregular and aseptate ribbon shaped hyphae (Fig C) morphologically resembling *Mucoraceae* species. Repeated sections were studied for vasoinvasive component. Few invading soft tissue fragments were identified but vascular invasion was not apparent in the given sections. In addition, areas of necrotic bone and inflammatory granulation tissue with multinucleated giant cells were seen. Periodic acid Schiff (PAS) stain was done subsequently which revealed magenta coloured broad aseptate hyphae in the biopsy tissue (Fig D). In view of the above findings, a histopathological diagnosis of mucormycosis was established.

Subsequently patient was treated with intravenous high dose Amphotericin B (1.5mg/kg daily) for 1 week, following which oral lesions disappeared but ulcer still persisted over left maxilla. He underwent maxillectomy 3 months thereafter and is currently under observation.

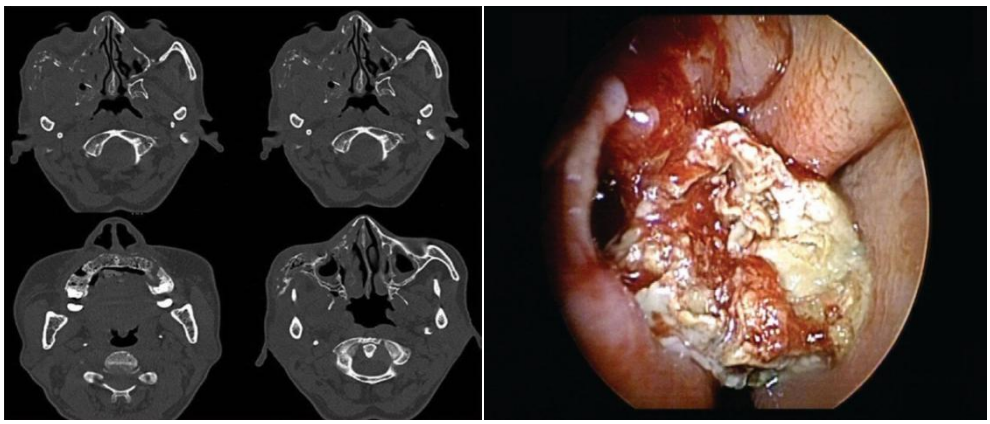

Image A. Computed tomography (CT) scan revealed maxillary antrum hyperdensity, as well as destruction of all sinus boundaries, including the nasal wall and orbital floor. Image B. Nasal endoscopy showing matted fungal ball in left maxillary sinus

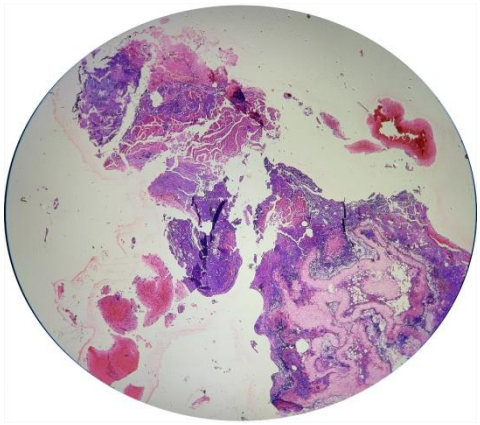

Fig. A. Hematoxylin and Eosin stain demonstrating fungal ball at Magnification X40

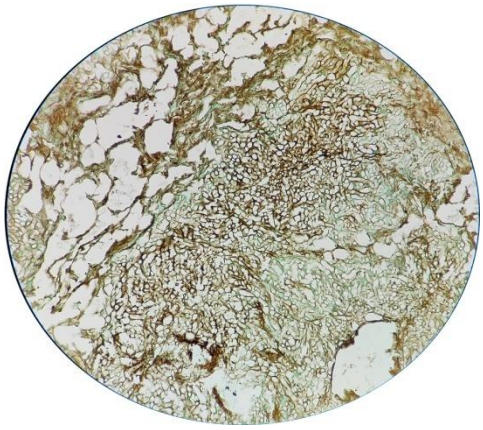

Fig. B. Gomori methanamine stain (GMS) showing matted hyphae (fungal ball) at Magnification X400

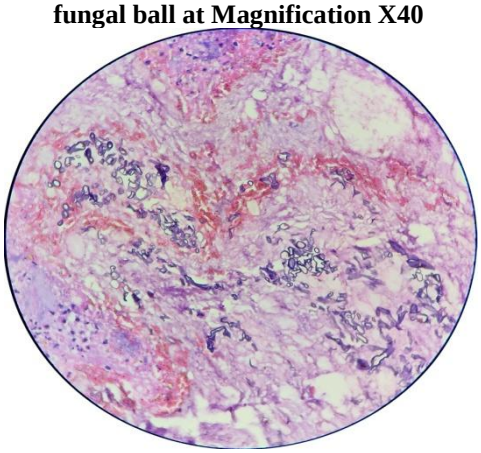

Fig. C. Hematoxylin and Eosin(H&E) stain demonstrating broad aseptate shaped hyphae at magnification X100

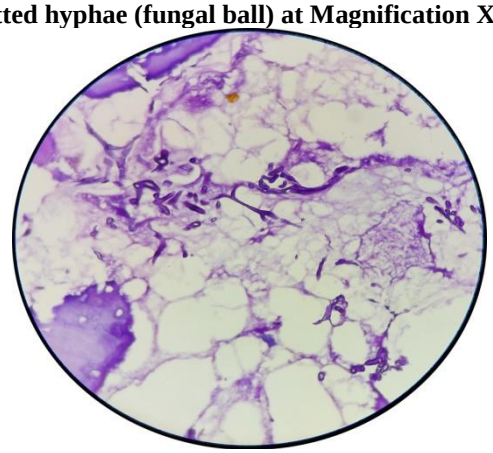

Fig. D. Periodic acid Schiff (PAS) stain showing magenta colored\ ribbon shaped hyphae at magnification X400

Table 1. Broad classification of fungal rhinosinusitis

Types	Subtypes
1. Invasive	A. Acute invasive FRS
	B. Chronic invasive FRS
	C. Granulomatous type.
2. Non-Invasive	A. Localized colonization
	B. Fungal ball (Aspergilloma)
	C. Eosinophil-related FRS

3. DISCUSSION

Many fungal strains cause fungal rhinosinusitis, some of which are normal commensals of nasal cavity [4]. Hora defined two broad categories in 1965: invasive and non-invasive, based on the ability of fungal hyphae to invade tissues through the epithelium (invasive) versus infection confined to the superficial epithelium (non-invasive) (non-invasive). Invasive FRS, as the name implies, can cause dramatic tissue invasion through mucosa, bone, neurovascular structures, and surrounding organs [5], most frequently caused by *Aspergillus family, Mucor, Alternaria, Candida and Sporothrix schenckii* [4].

Lab Diagnosis of fungal rhinosinusitis includes conventional microscopic examinationof biopsy by routine H&E followed by Giemsa stain and microbiological examination by KOH mount. Other tests include - Mannan test for *Candida* species, Antibody & Galactomannan test for *Aspergillus* species, FISH and PCR. Histopathological examination remains the gold standard for diagnosis [6].

Surgical intervention remains the mainstay treatment which includes surgical debridement using external approach or functional endoscopic sinus surgery (FESS), sometimes lifesaving procedures like

Maxillectomy. Medical management includes using systemic antibiotics like 3rd generation Cephalosporins and Antifungal compounds like Voriconazole and Amphotericin B [6].

Mucormycosis is caused by fungi of the order *Mucorales*, belonging to the class *Zygomycetes*. Fungi belonging to the order *Mucorales* are distributed into six families, species belonging to the family *Mucoraceae* are isolated more frequently from patients with mucormycosis than any other family. Among the *Mucoraceae, Rhizopusoryzae* (*Rhizopusarrhizus*) is by far the most common cause of infection. Other less frequently isolated species include *Rhizopus, microsporus*variant, *rhizopodiformis, Absidiacorymbifera, Apophysomyces elegans, Mucor*species, *and Rhizomucorpusillus* [7]. A rough estimate of 1.7 incidences per 1 million people are diagnosed with mucormycosis each year, and is documented as rare disease by NORD (National Organization for Rare Disorders). However, India saw a spike in mucormycosis cases during the second wave of covid-19 disease [8]. It rarely occurs in those who appear to be healthy and mostly affects those who are immunocompromised [9]. Mucormycosis infection in the compromised individual occurs from impaired immunity, which leads to the faster growth and invasion of underlying tissues [10].

In an immunocompromised patient, an extraction wound or mucosal ulcer might also serve as a point of entry for mucormycosis [11]. In immunocompromised patients, polymorphonuclear leukocytes are less successful in removing hyphae, therefore the infection becomes established in these circumstances [12]. Diabetes mellitus has a tendency to impair the immune response to infections in a numerous ways. Besides increased fungal proliferation, hyperglycemia also reduces chemotaxis and phagocytic efficiency, which makes it possible for otherwise harmless organisms to grow in an acidic environment [13]. In our case, the patient had a history of uncontrolled diabetes.

There are two potential causes of oral mucormycosis. One due to inhalation resulting in disseminated infection, and the other due to direct wound contamination. When it occurs due to inhalation, it results in necrosis of palate seen as black coloured lesion, as seen in our case. Direct wound contamination is usually seen affecting mandible [14].

They frequently invade into lymphatics and arteries, forming mucor thrombi that cause ischemia and infarction of the affected organ. The infection may quickly expand into the orbit and surrounding sinuses either directly or indirectly. The cavernous sinus thrombosis can result in either unilateral or bilateral blindness within hours to days and is also a key differentiating factor between infection of mandible and maxilla [15].

Histopathologically, the lesion demonstrates broad aseptate fungal hyphae with wide angle branching [10]. It is differentiated from aspergillosis where there are septate hyphae with acute angle branching.

An extramucosal fungal proliferation which is known as a fungus ball typically manifests as a unilateral infection and completely fills one or more paranasal sinuses, usually maxillary sinus. However, fungal ball formation is rarely seen with mucormycosis and majorly seen with *Aspergillus*. Hang sun cho et al in their study concluded that the presence of a *Mucor* fungal ball is a rare entity and only 5 case reports had been published so far [16].

Since this fungus invades the vessels of the arterial system, a prompt diagnosis by direct examination of KOH mounts of clinical sample can confirm the diagnosis [17] In our case, KOH mount was negative and H&E examination revealed no angioinvasion confirming a diagnosis of non invasive fungal rhinosinusitis and a resultant less aggressive course.

4. CONCLUSION

Various predisposing conditions, such as diabetes mellitus, chronic kidney disease, acquired immunodeficiency syndrome (AIDS), lymphomas or prolonged corticosteroid administration can lead to severe mucormycosis infection which can prove to be lethal. Sinonasal mucormycosis coexisting a with a non invasive fungal ball could indicate a better prognosis for the patient. However an extensive and comprehensive research is required for a better understanding of this unique conjunction.

CONSENT

As per international standard or university standard, patient (s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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