

# Rhinomaxillary mucormycosis presenting as palatal ulcer: A case report with comprehensive pathophysiology

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## Abstract

Mucormycosis is an emerging fungal infection which has exceptionally high mortality rates in immunocompromised patients and remains a life-threatening infection in uncontrolled diabetics. The reported cases in literature may be less in number due to its frequent misdiagnosis. Imaging techniques in the early stages are usually nondiagnostic and cytological smears are not very reliable, thus, the gold standard for definitive diagnosis remains with the histopathological examination. A thorough understanding of the pathogenesis and host fungus interaction aids in the histopathological evaluation and clinical management. Despite of surgical and medical management, the overall mortality rate remains high in persistently immunocompromised individuals. We present a case report of a 58-year-old female patient with rhinomaxillary mucormycosis with a history of uncontrolled diabetes.

**Keywords:** Angioinvasion, diabetes mellitus, diabetic ketoacidosis, mucormycosis, palatal necrosis

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## INTRODUCTION

Mucormycosis also known as zygomycosis or phycomycosis is an increasingly common, rapidly spreading, fulminant opportunistic fungal infection caused by saprophytic fungi mainly belonging to rhizopus, mucor and lichtheimia species. This was first described by Paltauf in 1885 and accounts for the third-most common form of fungal infection after candidiasis and aspergillosis. The major predisposing factors include uncontrolled diabetes mellitus and other immunocompromised conditions.<sup>[1]</sup> Diabetes mellitus is a multifactorial systemic disorder which is considered as an important predisposing factor for numerous opportunistic infections because of structural changes in tissue, low serum PH and impaired or altered immune cell response.<sup>[2]</sup> Among

the various clinical forms of mucormycosis, rhinocerebral is the most common, accounting for one third to half of the reported cases. This form is further subdivided into a rhino-orbital-cerebral (ROC) (Type 1) affecting ophthalmic and internal carotid arteries (more fatal) and rhino-maxillary form affecting sphenopalatine and greater palatine arteries (Type 2) (less fatal).<sup>[3]</sup> The ROC remains a common entity among the diabetics which is easily diagnosed. Low isolation rates of mucormycosis can be due to the susceptibility of the delicate hyphae to get damaged during the tissue processing leading to underreporting of cases.<sup>[4]</sup> Here, we present a case of the localized form of rhinomaxillary mucormycosis in diabetic, affecting palate without any involvement of nasal or paranasal sinuses.

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Prompt diagnosis and aggressive treatment approach led to the prevention of its massive spread.

## CASE REPORT

A 58-year-old female patient reported to our institute with the chief complaint of pain and swelling on the left side of the face for 10 days and painful ulcer on the left side of the palate for 2 months accompanied by fever and chills. History revealed the patient to be apparently asymptomatic 2 months back with gradual onset of left-sided facial swelling with painful intraoral ulceration in the palatal region accompanied by purulent discharge with foul taste and halitosis. Past medical history revealed that the patient was known as diabetic (recently diagnosed) and was under medication for the same. Extraoral examination revealed a diffuse soft, tender and febrile swelling on the left side of the face obliterating nasolabial fold, extending anteriorly from the corner of the mouth to the ramus area posteriorly, superiorly extending from infraorbital region to the submandibular region inferiorly [Figure 1] Intraoral examination revealed an infiltrating tender ulcer in the palatal region, crossing midline, measuring around 6 cm × 3 cm in size, with slopping edges, irregular and indurated margins [Figure 2]. A provisional diagnosis of deep fungal infection in relation to the maxilla and a differential diagnosis of the palatal abscess, osteomyelitis and benign inflammatory salivary gland lesion was given. Orthopantomogram, plain and postcontrast computed tomography scan (CT) [Figure 3] were normal. Complete hemogram showed all parameters to be in normal range except for a raised ESR (30 mm/1<sup>st</sup> h) and increased white blood cell count. Current blood glucose levels (fasting and postprandial) were in normal range, however, glycated hemoglobin level was 14, indicating poor glycemic control over the past 3 months, her previous biochemical reports showed the presence of glucose, and ketone bodies in urine. Other biochemical parameters were in normal range.

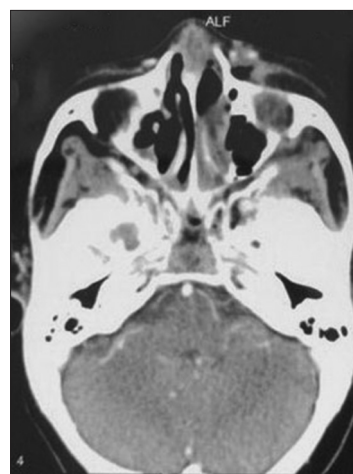
A cytology smear was prepared from the palatal region and stained with periodic acidSchiff (PAS) and GIEMSA stain which revealed the presence of few fungal hyphae interspersed in a background of cellular debris [Figure 4]. An incisional biopsy was taken from lesion site of the palate. Microscopic examination of hematoxylin and eosin stained sections revealed numerous large and small nonseptate, ribbon-like fungal hyphae showing branching at obtuse angle and few knob-like dilatations were seen interspersed throughout the inflamed connective tissue. Fungal hyphae were seen specifically surrounding and occluding the blood vessels suggestive of fungal angioinvasion [Figures 5 and 6]. Numerous round-to-ovoid mature sporangia were also



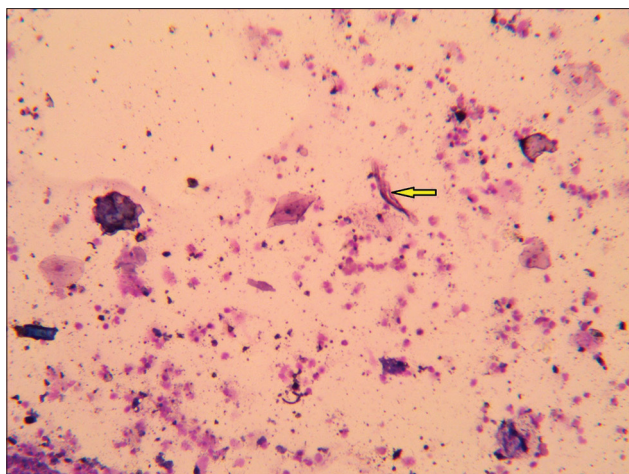
**Figure 1:** Extraoral image of patient showing diffuse swelling on the left side of the face obliterating nasolabial fold



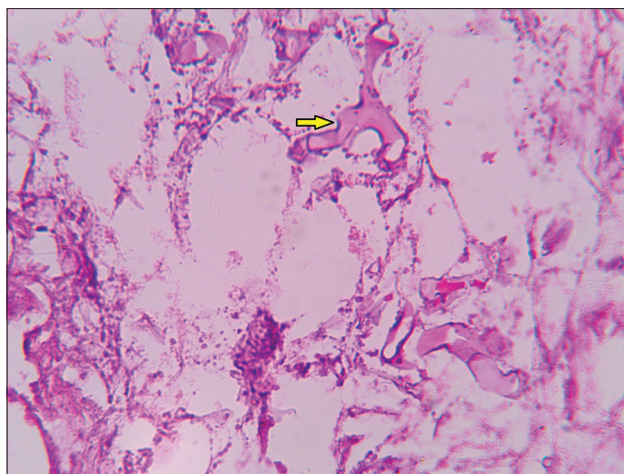
**Figure 2:** Clinical intraoral image shows ulcer in the palatal region, covered by yellowish necrotic scrapable slough extending anteroposteriorly from palatogingival region of 11 and 21-28 and mediolaterally from the crest of alveolar bone of 11, 21 and 22 extending toward the junction of hard and soft palate



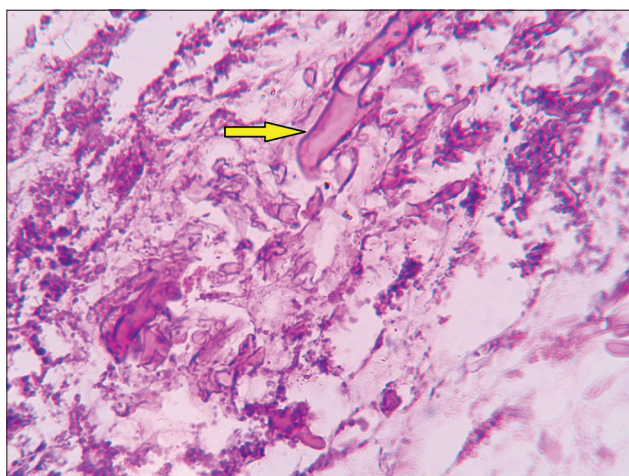
**Figure 3:** A postcontrast computed tomography scan showing no signs of bony erosion or sinus involvement



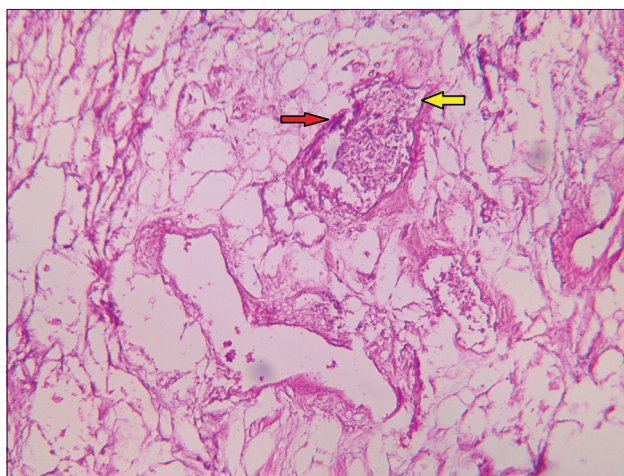
**Figure 4:** Cytology smear from the palatal region showing the presence of few fungal hyphae (yellow arrowhead) in a background of cellular debris (Giemsa stain,  $\times 10$ )



**Figure 5:** Histopathological image shows numerous non-septate, ribbon-like fungal hyphae (yellow arrowhead) branching at obtuse angle (H & E,  $\times 40$ )



**Figure 6:** Histopathological image shows fungal hyphae (yellow arrowhead) showing few knob-like dilatations (H & E,  $\times 40$ )



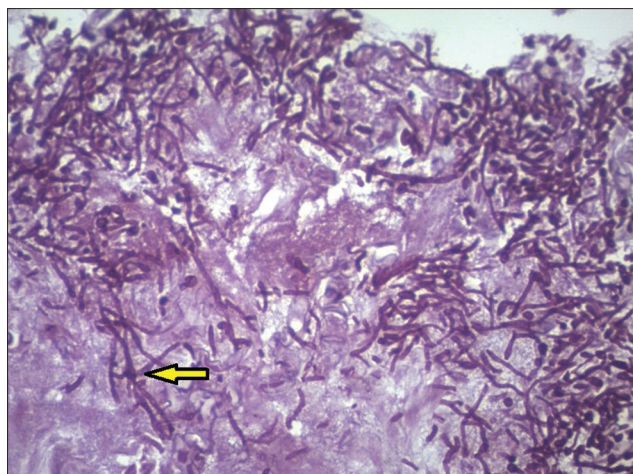
**Figure 7:** Histopathological image shows round to ovoid sporangia (red arrowheads), some were in their late stage of maturation as represented by release of mature spores into the tissue (yellow arrowhead) (H & E,  $\times 10$ )

seen [Figure 7]. PAS and Grocott's Methenamine Silver staining further confirmed and highlighted the presence of many broad, aseptate, irregular and ribbon-like folding mycelial filaments branching at obtuse angle in a fibrous tissue [Figures 8 and 9]. Correlating the histopathological findings with clinical presentation and medical history, a final diagnosis of rhinomaxillary mucormycosis was established.

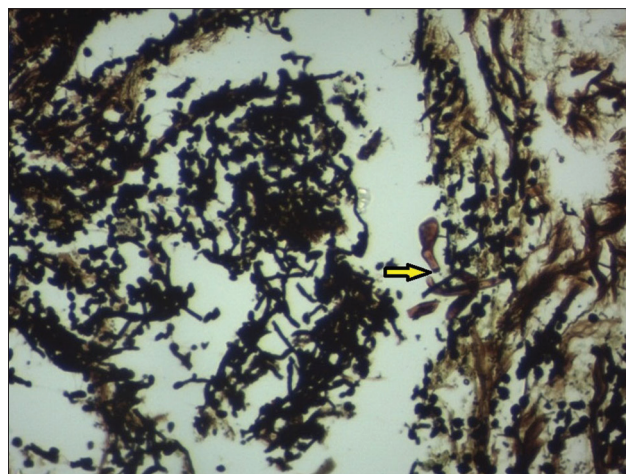
The patient was admitted and was put on amphotericin B; 1 mg/kg body weight intravenously, blood glucose levels were kept under control. Maxillectomy and surgical debridement were planned for the patient, followed by placement of immediate surgical obturator 10 days posttherapy, the patient showed improvement in terms of remission of facial swelling and pain. She was stable and was still under observation at the time of preparation of this document.

## DISCUSSION

Mucormycosis is a rare, opportunistic and fulminant mycotic infection which is infamous for its grave prognosis. Natural habitat of the organism is soil and decaying organic matter from where the asexual spores can become airborne, if get inhaled or ingested by humans these are killed by the host's first line of defence cells; phagocytes by producing defensins, cationic peptides, and oxidative mechanisms. It becomes pathogenic only under deranged host immune responses. Diabetic ketoacidosis deranges the phagocytic potential of leukocytes, thereby giving opportunity to the spores to germinate into the hyphal form which is capable of local tissue invasion and destruction.<sup>[1-3]</sup> The mucorales sporangiospore secretes certain proteases which may cause direct destruction of epithelial and endothelial cells.<sup>[5]</sup> Host's



**Figure 8:** Histopathological image shows numerous ribbon-like filamentous, magenta colored hyphae (yellow arrowhead) seen branching at obtuse angles (Per Iodic AcidSchiff stain, x40)



**Figure 9:** Histopathological image shows nonpigmented (hyaline), pauciseptate ribbon-like hyphae (yellow arrowhead). (Grocott methenamine silver stain, x40)

ketone bodies can be used by fungus for their nutrition by producing an enzyme ketoreductase. Another virulence factor of fungus is its ability to thrive on unbound iron found in host serum due to deranged binding of serum transferrin with iron under the acidic environment of diabetes.<sup>[6,7]</sup> The port of entry for organism is usually nasal mucosa, from where it can invade into paranasal sinuses through angioinvasion. Pterygopalatine fossa acts as a reservoir for fungus from where it can spread into retro-orbital or infratemporal space.<sup>[3]</sup> Involvement of the maxilla is usually secondary via greater palatine and sphenopalatine vessels and generally manifests as a small ulcer.<sup>[5,8]</sup>

A hallmark of progressive mucormycosis is angioinvasion which involves interaction between glucose-regulated protein 78 (GRP78), present on host endothelial cells which selectively and specifically interacts with hyphae of Mucorales. A study has established that elevated glucose and iron levels, upregulated the GRP78 expression on endothelial cells in a receptor-dependent manner leading to extensive angioinvasion and tissue destruction.<sup>[9]</sup>

The common clinical forms include rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and miscellaneous forms. The early symptoms include facial swelling, periorbital edema, maxillary sinusitis, fever and nasal inflammation with foul-smelling discharge. It may spread to the palate, orbit and CNS and can result in fatalities.<sup>[6]</sup>

Radiographically in early stages, mucormycosis may show no changes on CT and magnetic resonance image scan study. Later stages can present as localized opacification or bone erosions. McDonogh hypothesized that any diabetic patient with ketoacidosis showing clinical and

radiographic features of sinusitis should be suspected as a case of mucormycosis until proven otherwise.<sup>[7]</sup> In our case, there was no evidence of bony erosion or involvement of sinuses on contrast CT scan, fungus manifested as a localized lesion of the maxilla, this is similar to some previously documented reports.<sup>[10]</sup>

Histopathologically, a close resemblance between the fungal hyphae of mucormycosis and aspergillosis may be a diagnostic dilemma. Hyphae of mucormycosis are ribbon-like, coenocytic (non septate) with the branching of right to obtuse angles whereas aspergillous hyphae are septate, lesser in width and have acute angle branching.<sup>[11]</sup>

Early diagnosis along with a combined medical and surgical intervention using systemic amphotericin B, extensive surgical debridement along with the healthy tissue margins results in cure of the disease. Supportive measures such as hyperbaric oxygen may play a beneficial role by neovascularization of viable tissue and reducing lactic acidosis.<sup>[7]</sup>

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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