CASE REPORT

Mucormycosis in a Typhoid Treated Patient: A Case Report with Review of Literature.

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Abstract

Introduction: Mucormycosis is an opportunistic fungal infection which is a rapidly progressing disease, and often fatal. Various predisposing factors including uncontrolled diabetes mellitus, immunosuppression, and prolonged use of steroids influence the disease pathology.

Case Presentation: In this article, we present a case of mucormycosis of the palate in a patient treated with prolonged dose of steroids for typhoid fever which led to the appearance of exposed maxillary bone, and subsequent histopathological examination showed mucor hyphae. The treatment included antifungal therapy of Amphoterecine B.

Management: Treatment of typhoid fever with corticosteroids, leading to immunosuppression, may result in patients harbouring opportunistic infections. An insight into the changes of oral cavity caused by corticosteroids is necessary for better diagnosis of the disease and improved patient care. In addition, early diagnosis is critical in the treatment of patients with mucormycosis

Keywords: Mucormycosis, corticosteroids, typhoid fever, hyperglycaemia.

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Introduction

Mucormycosis is an invasive, aggressive fungal infection caused by filamentous fungi. It commonly develops in immunocompromised patients with impaired host defence. It is vital to note that the incidence of mucormycosis is rising globally, particularly in India among patients with uncontrolled diabetes mellitus[1]. In 2019, a multicentre, prospective study was conducted in four tertiary centres in India (two in South India and two in North India) to analyse the epidemiology, underlying pathology, diagnosis and treatment. They identified that uncontrolled diabetes and trauma were the most common risk factors.[2]

Mucormycosis is a rapidly progressing, opportunistic infection and often fatal. According to various studies, several predisposing factors may lead to this disease including poorly controlled diabetes mellitus, prolonged use of corticosteroids, illegal intravenous drug use, malignant haematological diseases like leukaemia and lymphoma, severe and prolonged neutropenia, deficient T cell immunity, immaturity and low birth weight. This case report highlights mucormycosis of the palate in a patient treated with prolonged dose of steroids for typhoid fever.[3,4]

Case Presentation

A 60-year-old female patient reported to the Department of Oral and Maxillofacial Surgery with a chief complaint of pain in her upper jaw with a duration of 3 months. The patient's medical history was significant for typhoid fever, and diabetes. About 10 months prior to the evaluation of the patient, she had experienced fever and cough which was later identified as typhoid fever for which she was admitted to the hospital and was treated with 40mg of methylprednisolone twice daily for one month after which she developed hyperglycaemia (150mg/dL) and was given insulin injections. Later, she developed a vague pain in her left maxillary region

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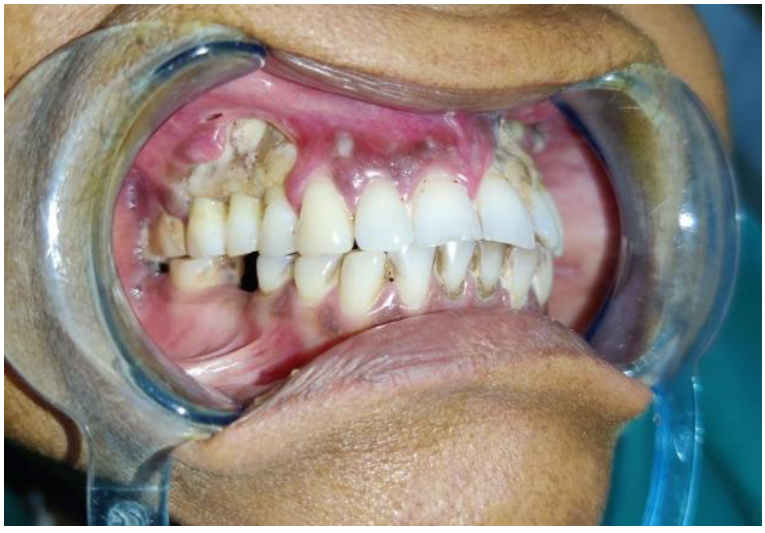
for which the doctors prescribed Ketoral DT (unknown dosage) at a private clinic and later referred to our institution.

Intra oral examination revealed an exposed alveolar bone of the left maxilla (Figure 1A and 1B). A swab was collected from both the left and right alveolar bone of the maxilla during incisional biopsy. The smears were stained with hematoxylin and eosin (H&E) and Periodic-acid Schiff stain (PAS) which were positive for mucormycetes (Figure 2A and 2B). The biopsied sections showed necrosed and degenerated connective tissue stroma with numerous pale eosinophilic, refractile, broad, aseptate fungal hyphae resembling mucormycetes. The hyphae showed branching in different patterns, majority of which were y-shaped forming an acute angle. A diagnosis of mucormycosis was made. The patient was prescribed antifungal therapy of Amphotericine B.

Discussion

Corticosteroids are used in the treatment of severe cases of typhoid fever and are known to improve clinical response and overall mortality rate.[5] However, a long-standing course of corticosteroids may lead to hyperglycaemia. Combined immunosuppressive effects and hyperglycaemia may significantly increase the risk of opportunistic infections.[6] Although 20% or more may be refractory and others become dependent on corticosteroid use to suppress disease activity. Side effects in the acute situation are relatively minor, although significant side effects (e.g., psychosis).

Mucor is often known as a 'Black fungus' however it is a misnomer as it belongs to a different family. It is called as black fungus due to the presence of tissue necrosis. The pigmented fungi (Dematecious fungi) are referred to as black fungi due



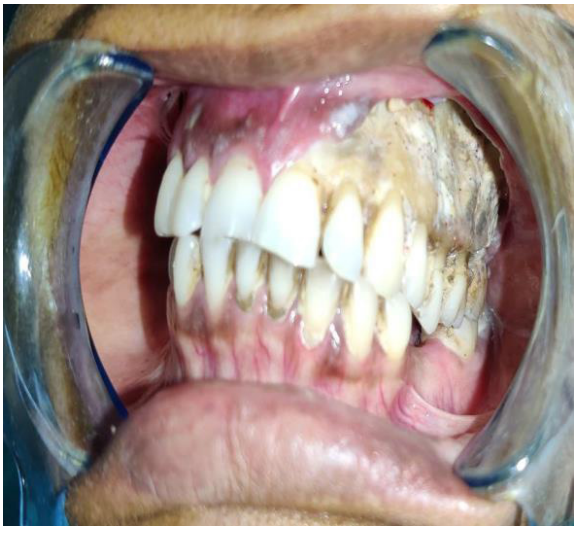


Fig. 1A & 1B: Wide area of exposed denuded maxillary alveolar bone.

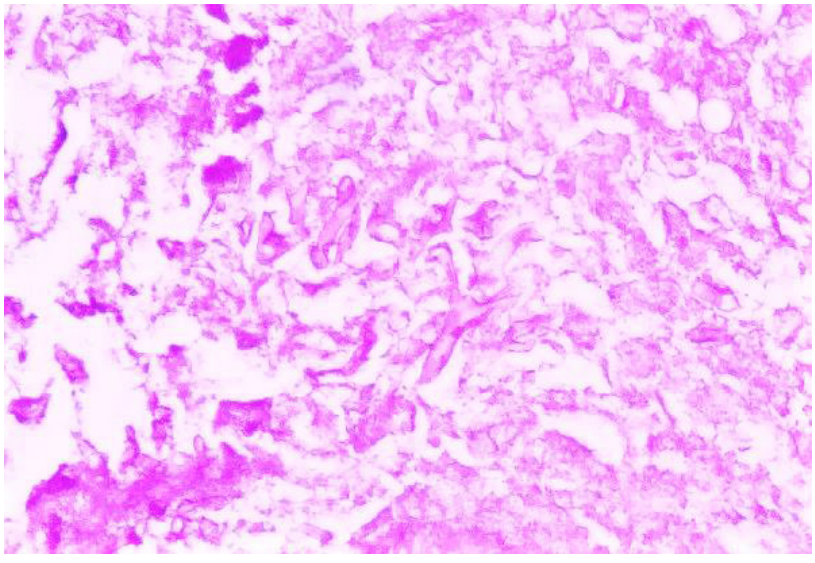


Fig. 2A: H&E-stained image with aseptate, y-shaped acute angled branching hyphae are seen in 10x view

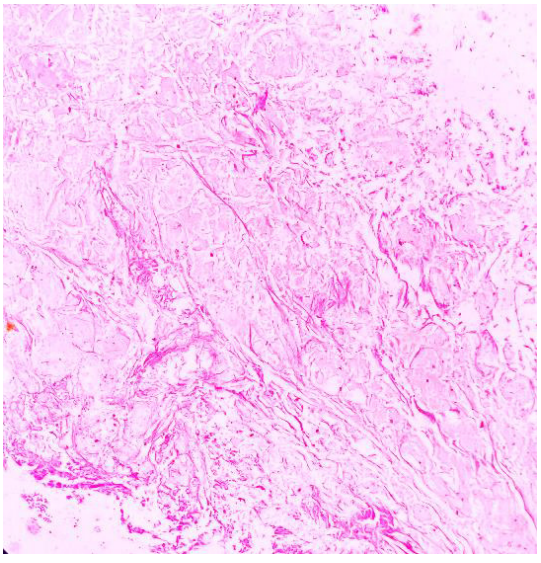


Fig. 2B: Periodic Acid-Schiff (PAS) positive hyphe are seen 10x view

to the presence of melanin pigmentation.[7] Mucormycosis, also called zygomycosis, is caused by a fungus that belongs to the class of phycomycetes. The most common forms of fungus associated with this disease are Rhizopus, Mucor, and Absidia.[8] These fungi are ubiquitous and the spores are found in soil and dust.

Mucor prospers in an acid pH and glucose rich medium, so in cases of uncontrolled diabetes associated with ketoacidosis, and hyperglycemia, it is the most common predisposing factor.[4] It is also considered as a fatal complication in patients who have faced combat injuries, burns or suffered in various natural disasters.[9] The portal of entry of the organisms is through inhalation, consumption of contaminated food, through contaminated needles or catheters into the cutaneous tissue, or due to implantation of injured skin by trauma.[10] The host-pathogen interaction plays a crucial role in the development of the disease (Figure 3). The fungal spores enter and invade the host immune system, germinate, leading to angioinvasion and dissemination.

In accordance to the anatomical site of occurrence, it can be described as rhinocerebral, pulmonary, cutaneous, gastrointestinal and disseminated forms. In the oral cavity, the origin can either be through a disseminated infection by inhalation or through direct wound contamination. When the portal of entry is through nose and paranasal sinuses, the infection may cause ulcerations and progressive necrosis in the palate. Clinically, patients may present with nasal obstruction, fever, facial pain or headache, facial swelling or cellulitis, and visual disturbances. With progression into the cranial vault, blindness, lethargy, and seizures may arise, which can also result in death.[11,12,13]

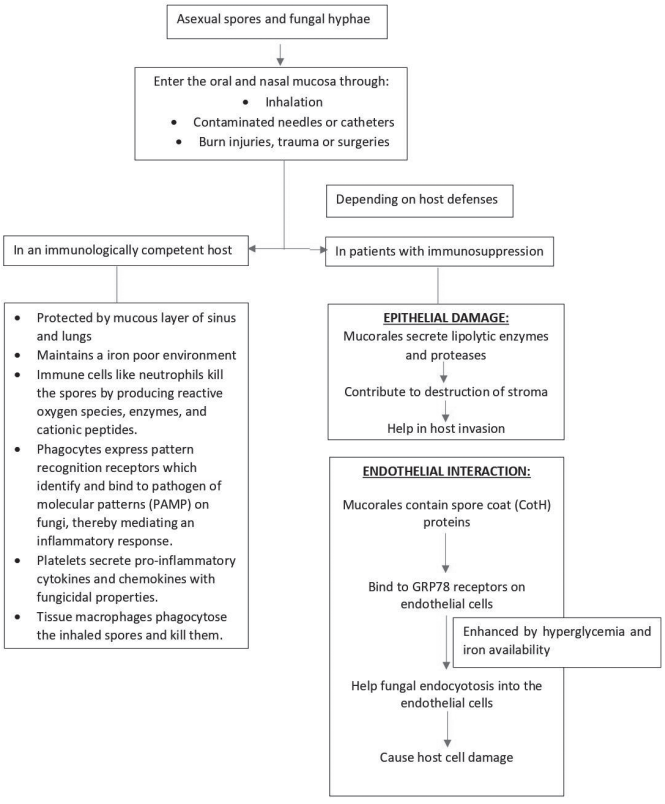


Fig. 3: Pathophysiology of Mucormycosis

Radiographically, the findings are not specific and generally inconclusive. Initially, the CT and MRI appear normal, later develop signs of sinusitis including sinus mucosal thickening or congested sinus. CT with contrast may aid in the demonstration of erosion of bone or sinuses and extent of the lesion.[14]

Cytologic specimen show wide, ribbon like aseptate, hyphal structures in the necrotic debris. Surgical exploration reveals masses of necrotic tissue in which the organisms can be demonstrated histologically. The organisms appear as large, acute angle branching, non-septate hyphae at the periphery.[15] The fungi show an apparent predilection for blood vessels which disrupts the normal blood flow leading to thrombosis and ischemic necrosis.[16] A neutrophilic infiltrate is evident in the viable tissue. The special stains that aid in the identification of these organisms include Gomori methenamine stain (GMS), periodic acid Schiff stain (PAS), and calcofluor white stain. Fungal selective media can be used for culture; however, they are positive only in 15-25% of the cases. The selective media include Sabouraud agar with an antibacterial agent.[17] Immunohistochemical analysis using clone WSSA-RA-1 can be used to differentiate between mucor infection and aspergillosis as the cytoplasm of mucor hyphae showing strong reactivity when compared to Aspergillus.[18]

Recently, the molecular diagnosis of mucormycosis has been identified to improve the management of the disease through better identification of cultured isolates, and by direct identification on clinical tissue samples. PCR-based, non-invasive procedures are being used to detect Mucorales-DNA in plasma or serum within a shorter time frame and a reasonable expense.[19]

Conclusion

Treatment of typhoid fever with corticosteroids, leading to immunosuppression, may result in patients harbouring opportunistic infections. An insight into the changes of oral cavity caused by corticosteroids as reported in this case is necessary for better diagnosis of the disease and improved patient care. In addition, early diagnosis is critical in the treatment of patients with mucormycosis. Correcting or controlling the predisposing factors are also vital in improving the prognosis. Medical management includes antifungal drug administration of amphotericin B. Early appropriate debridement of the retro-orbital space and surgical excision of the infected sinuses may prevent the spread of infection into the eye.

References

1. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi. 2019;5(1):26.
2. Prakash H, Ghosh AK, Rudramurthy SM, Singh P, Xess I, Savio J, et al. A prospective multicenter study on mucormycosis in India: epidemiology, diagnosis, and treatment. Med Mycol. 2018;57(4):395–402.
3. Binder U, Maurer E, Lass-Flörl C. Mucormycosis - from the pathogens to the disease. Clin Microbiol Infect. 2014;20(6):60–6.
4. Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis. 2012;54(SUPPL. 1):23–34.
5. McGee S, Hirschmann J. Use of corticosteroids in treating

infectious diseases. Arch Intern Med. 2008 May 26;168(10):1034–46.
6. Buchman AL. Side effects of corticosteroid therapy. J Clin Gastroenterol. 2001;33(4):289–94.
7. Wong EH, Revankar SG. Dematiaceous Molds. Infect Dis Clin North Am [Internet]. 2016;30(1):165–78. Available from: http://dx.doi.org/10.1016/j.idc.2015.10.007
8. Spellberg B, Edwards J, Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. Clin Microbiol Rev. 2005;18(3):556–69.
9. Walsh T, Hospenthal D, Petraitis V, Kontoyiannis D. Necrotizing mucormycosis of wounds following other trauma. J Fungi. 2019;5(3):1–11.
10. Challa S. Mucormycosis: Pathogenesis and Pathology. Curr Fungal Infect Rep. 2019;13(1):11–20.
11. Bhansali A, Bhadada S, Sharma A, Suresh V, Gupta A, Singh P, et al. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgrad Med J. 2004;80(949):670–4.
12. Compain F, Aït-Ammar N, Botterel F, Gibault L, Le Pimpec Barthes F, Dannaoui E. Fatal Pulmonary Mucormycosis due to Rhizopus homothallicus. Mycopathologia. 2017;182(9–10):907–13.
13. Dioverti MV, Cawcutt KA, Abidi M, Sohail MR, Walker RC, Osmon DR. Gastrointestinal mucormycosis in immunocompromised hosts. Mycoses. 2015;58(12):714–8.
14. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SC, Dannaoui E, Hochhegger B, Hoenigl M, Jensen HE, Lagrou K, Lewis RE, Mellinghoff SC. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. The Lancet infectious diseases. 2019 Dec 1;19(12):e405-21.
15. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. Clin Microbiol Rev. 2000;13(2):236–301.
16. Ibrahim AS, Spellberg B, Avanessian V, Fu Y, Edwards JE. Rhizopus oryzae adheres to, is phagocytosed by, and damages endothelial cells in vitro. Infect Immun. 2005;73(2):778–83.
17. Garg D, Muthu V, Sehgal IS, Ramachandran R, Kaur H, Bhalla A, et al. Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature. Mycopathologia [Internet]. 2021;186(2):289–98. Available from: https://doi.org/10.1007/s11046-021-00528-2
18. Jung J, Park YS, Sung H, Song JS, Lee SO, Choi SH, et al. Using immunohistochemistry to assess the accuracy of histomorphologic diagnosis of aspergillosis and mucormycosis. Clin Infect Dis. 2015;61(11):1664–70.
19. Millon L, Scherer E, Rocchi S, Bellanger AP. Molecular strategies to diagnose mucormycosis. Journal of Fungi. 2019 Mar 20;5(1):24