

MUCORMYCOSIS OF THE LEFT MAXILLA: A CASE REPORT AND REVIEW

Dr. Daya K. Jangam^{1*}, Dr. Surabhi S. Ausare², Dr. Pranjali S. Bende² and Dr. Kedarnath K. Kalyanpur³

¹Professor and Head, Department of Oral Medicine and Radiology, Sinhgad Dental College and Hospital, Pune, Maharashtra, India.

²Post Graduate Student, Department of Oral Medicine and Radiology, Sinhgad Dental College and Hospital, Pune, Maharashtra, India.

³Senior Lecturer, Department of Oral Medicine and Radiology, Sinhgad Dental College and Hospital.

***Corresponding Author: Dr. Daya K. Jangam**

Professor and Head, Department of Oral Medicine and Radiology, Sinhgad Dental College and Hospital, Pune, Maharashtra, India.

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ABSTRACT

Mucormycosis, also known as zygomycosis and phycomycosis was first described by Paultauf in 1885. Mucormycosis is an emerging angioinvasive infection caused by the ubiquitous filamentous fungi of the Mucorales order of the class of Zygomycetes. Mucormycosis is a fungal infection commonly affecting structures in the head and neck, such as the air sinuses, orbits, and the brain. The most common genera isolated are Rhizopus, Rhizomucor, Absidia and Apophysomyces. Rhizopus is the predominant pathogen, accounting for 90% of the cases of rhinocerebral mucormycosis. The incidence of this disease is 0.4- 1.7 cases /1,000,000. There are at least six clinical entities of mucormycosis: rhinocerebral, pulmonary, cutaneous, gastrointestinal, central nervous system (CNS), disseminated and miscellaneous like bone or kidney. The term rhinocerebral mucormycosis (RCM) should only be used if the facial, palatal, orbital, paranasal sinus or cerebral regions are involved and the patients generally present with signs and symptoms that may be primarily located in these regions. Common predisposing factors include diabetes mellitus and immunosuppression. Early diagnosis and prompt treatment can significantly reduce the mortality and morbidity of this lethal fungal infection. Here we report a case of mucormycosis of the left maxilla, affecting a male patient aged 42 years, with extensive soft tissue necrosis and bone destruction.

KEYWORDS: Mucormycosis, Angioinvasive, Rhinocerebral, Palate, Paranasal Sinuses.

INTRODUCTION

Mucormycosis, also known as zygomycosis and phycomycosis was first described by Paultauf in 1885, is caused by a ubiquitous filamentous fungi of the Mucorales order of the class of Zygomycetes. Rhizopus accounts for 90% of the cases of rhinocerebral mucormycosis commonly affecting the head and neck.^[1] The incidence of this disease is 0.4- 1.7 cases per million and is the third most common invasive fungal infection after aspergillosis and candidiasis.^[2,3] Common predisposing factors include diabetes mellitus and immunosuppression.^[4,5,6] The most common route of infection is by inhalation usually through the nose or from direct wound contamination with dissemination to other viscera as a common complication.^[1,6] The clinical presentation of mucormycosis depends on the patient's underlying medical condition. There are at least six clinical entities of mucormycosis: rhinocerebral, pulmonary, cutaneous, gastrointestinal, central nervous system (CNS), disseminated and miscellaneous like bone or kidney. The term rhinocerebral mucormycosis (RCM) should only be used if the facial, palatal, orbital, paranasal sinus or cerebral regions are involved and the

patients generally present with signs and symptoms that may be primarily located in these regions.^[1]

CASE REPORT

A 42 year old male patient reported to dental OPD with a chief complaint of pain and mobile teeth in upper left back region since 6 months and inability to chew food. Patient also complains of bad breath. The patient was alright one year ago when he was hospitalised for nasal puffiness, a diagnosis of chronic sinusitis was made and was treated with left maxillary sinus antrostomy. Biopsy report revealed "Angioinvasive Mucormycosis." Two months later, he noticed a swelling on the left side of the face along with foul discharge from nose and severe headache for which he reported to the medical college and was evaluated at the ENT ward. Direct nasal endoscopy and conchoplasty was performed. The biopsy was suggestive of Mucormycosis. Two months after the operative procedure the patient complains of pain and mobility of teeth in the upper left maxillary region. Pain was moderate to severe in intensity, gradual in onset, throbbing type and continuous in nature. It aggravated on palpation of left side of face and cheek region. The

patient also complains of general body ache, malaise, headache. He was a known case of uncontrolled diabetes mellitus and had a paternal history of Diabetes mellitus and hypertension. Patient's past dental history revealed uneventful extractions which were performed in upper and lower back region of the jaw 10-12 years ago. The patient is a Tobacco chewer and has habit since 8 years, 3-4 times a day and placed the quid in lower buccal vestibule for 5-10 minutes and then eventually spat it off. The patient was conscious and was well-oriented with time, space and person.

On examination all the vital signs were within normal limits. Extra-oral examination was performed and inspeitory findings revealed a diffuse swelling measuring about 3x3 cm, extending anterioposteriorly from ala of nose to the zygomatic bone region and superio- inferiorly from the Frankfort's horizontal plane to the corner of lip. The color of overlying of skin was normal and surface was smooth. (Figure 1) The inspection findings were confirmed on palpation. The swelling is soft, non-compressible, non-fluctuant and tender on palpation. Intra- oral examination revealed, palatal displacement with 24, 25, 26. There was loss of marginal, interdental and attached gingiva upto the buccal vestibule with 23 to 27. Ulcerative lesion seen in relation to 23 at the attached gingival, with the surface being brown black, having raised edges, floor covered with necrotic debris. Exposed and necrotic bone seen with 23 to 27.(Figure 3) All inspeitory findings confirmed on palpation. Pain on percussion was positive with 23 to 27. Grade II mobility was elicited with 23,24,25,26 and Grade I mobility was elicited with 27.Other findings include : Missing 14,16,36, 37. Early occlusal caries was seen with 47, 38. Moderate distal caries was seen with 44, 34. Advanced mesio-occlusal caries was seen with 26. (Figure 2) A provisional diagnosis of Recurrent Mucormycosis of the left maxilla was given.



Figure. 1: Showing presence of extra-oral swelling over the left side of the face.



Figure. 2: showing maxillary and mandibular arches with Missing 14,16,36,37 and Palatal displacement: 24, 25, 26.



Figure. 3: showing loss of attached, interdental and marginal gingiva with exposed necrosed bone in 23 to 27 region.

The patient was advised haematological investigations and radiographic investigations. The haematological investigations included haemogram, complete blood count, bleeding time, clotting time and blood sugar levels, the values being Fasting : 142 mg/dl Postprandial: 220 mg/dl. Radiographic investigations included intra-oral periapical radiographs, orthopantomogram, cone-beam computed tomography.

Intra- oral periapical radiographs showing rarefaction of alveolar bone seen at the apex of the root w.r.t 11, 21,22 , loss of interdental alveolar bone can be appreciated w.r.t 23,24 (figure 4) root resorption seen at the apex of 25,

26 and loss of interdental bone can be seen (figure 4). The orthopantomogram shows an irregular ill-defined diffuse radiolucency seen with the left alveolar bone, extending, mesiodistally from distal aspect of 12 to the left maxillary tuberosity region and superiorinferiorly from the alveolar ridge involving the left maxillary sinus. Resorption at apex of the root with 12 to 24. Hanging tooth appearance can be seen with 21 to 27 (Figure 5). A cone beam computed tomography (CBCT) scan was done for the patient. The scan was visualised in axial, sagittal and coronal section. As viewed on Axial section, a single, diffuse, irregular, ill-defined radiolucency extending from the alveolar crest to the middle of the hard palate (AP) and (MD), suggestive of bone loss. There was perforation of the buccal cortical plate (Figure 6). The Sagittal section exhibited the discontinuity with floor and lateral wall of maxillary sinus. Hanging tooth appearance which could be appreciated from 21 to 26 region. (Figure 7). The coronal section showed widened Osteomeatal complex on the left side and mucosal thickening of maxillary sinus. (Figure 8). On the basis of radiographic investigation, a radiographic impression of interdental bone loss extending from distal aspect of 12 to 27 region and discontinuity with the floor and lateral wall of maxillary sinus, suggestive of bone loss was made.



Figure. 4: intra-oral periapical radiograph showing root resorption and loss of interdental bone.



Figure. 5. A panoramic radiograph showing an irregular ill-defined diffuse radiolucency seen with the left maxillary alveolar bone, extending into the left maxillary sinus.

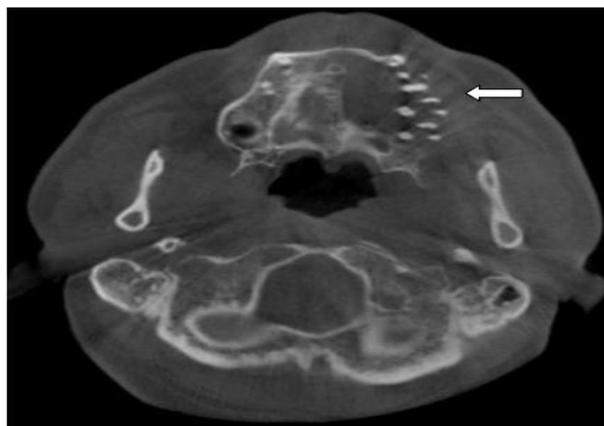


Figure. 6: Axial section showing bone loss and perforation of the buccal cortical plate on the left maxilla.

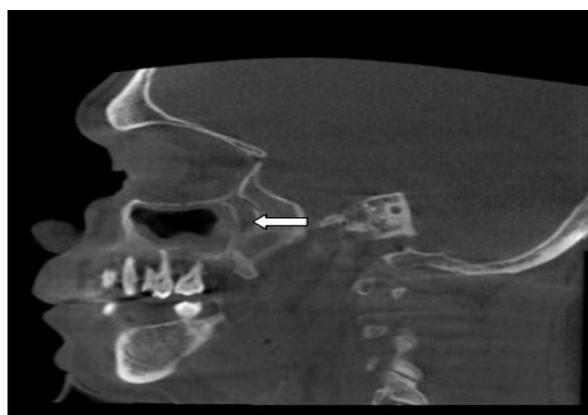


Figure. 7: Sagittal section showing mucosal thickening of the left maxillary sinus.



Figure. 8: Coronal section showing: Widened Osteomeatal complex and mucosal thickening in the left maxillary sinus.

An incisional biopsy was performed and the histopathology revealed many broad aseptate Fungal hyphae of irregular thickness invading the blood vessels and a histopathological diagnosis of Mucormycosis of the left maxilla was given (Figure 9). Taking into account the radiographic impression and the histopathological

diagnosis, a final diagnosis of Recurrent Left rhino-maxillary Mucormycosis was given.

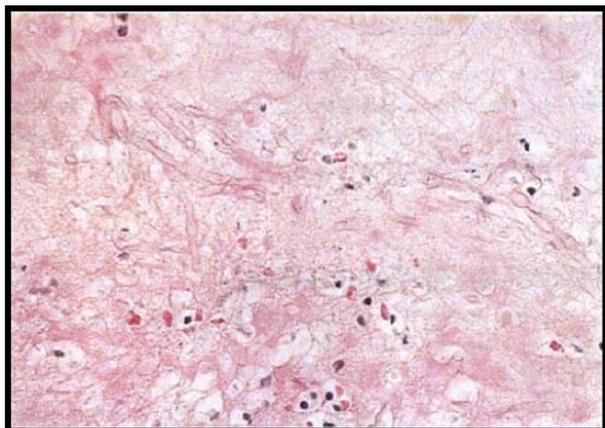


Figure. 9. Many broad aseptate Fungal hyphae of irregular thickness invading the blood vessels.

The patient was administered Amphotericin B 0.8 mg/kg/day infused over 4-6 hours for two weeks along with insulin. The patient was treated surgically by Left Subtotal maxillectomy post-operatively obturator was given. All the required precautions and aseptic measures were taken, keeping in mind the patient's medical history and health status. After complete healing of the lesion Prosthetic rehabilitation was advised.



Figure. 10: showing specimen after Left subtotal maxillectomy.



Figure. 11: Patient's 8 months follow up.

DISCUSSION

Mucormycosis is an angioinvasive fungal infection seen in developing countries following uncontrolled diabetes.^[6] The predisposing factors for mucormycosis are uncontrolled diabetes (particularly in patients having ketoacidosis), malignancies such as lymphomas and leukemia's, renal failure, organ transplant, neutropenia, long term corticosteroid and immunosuppressive therapy, iron overload, cirrhosis, burns, neonatal prematurity, protein energy malnutrition and AIDS.^[4,5,6] Diabetic patients have low immunity to resist mucormycosis due to the inability to inhibit *Rhizopus in vitro* and also reduced phagocytic ability of the granulocytes.^[6, 7] In diabetic patients there is a high incidence of mucormycosis caused by *Rhizopus arrhizus*, because they produce the enzyme ketoreductase, which allows them to utilize the patient's ketone bodies. The increased risk of mucormycosis in patients with ketoacidosis may also be due to the release of iron bound to proteins.^[1,7]

Our patient was a uncontrolled case of diabetes mellitus. Similar case reports were presented by Nupur Hingad et al (2012), R.Madan (2013), Arakkal et al (2017) and Nallapu et al (2017) where the patients had increased or uncontrolled blood sugar levels. Nupur Hingad et al (2012), confirmed that patients with uncontrolled diabetes are at a greater risk of developing mucormycosis, due to low immunity and utilization of ketone bodies in such patients.

In most of the immunologically competent hosts, these spores are contained by a phagocytic response. Germination continues if the phagocytic response fails, leading to the development of hyphae; thereby, infection becomes established. The hyphae invade the arteries and propagate within the vessels, causing thrombosis, ischemia and infarction of the affected tissues. Hematogenous spread to other organs can occur (lung, brain, and so on), as well as overt sepsis.^[1,6]

Mucormycosis of the oral cavity can be of 2 origins. One is from disseminating infection where the portal of entry is by inhalation (usually through the nose); the other is from direct wound contamination with dissemination to other viscera as a common complication. When arising from the nose and paranasal sinuses, the infection may cause palatal ulceration progressing to necrosis. The area appears black in the large majority of the cases. Our patient was a farmer by profession we can suspect the possibility of him acquiring infection through the inhalational route. When the infection spreads from direct wound contamination, the clinical findings may appear anywhere in the oral cavity, including the mandible.^[1] Cavernous Sinus Thrombosis, is a serious complication of maxillary infections.^[1,7] Another difference is the rarity of the mandibular infections as compared to the maxillary.^[1]

Patients with RCM will present with facial pain, headache, and fever. If the infection extends to the nasal turbinates, the orbit can become involved. Infection can lead to proptosis, periorbital oedema, chemosis, ophthalmoplegia, and loss of vision if the orbital apex becomes involved. Infection of the CNS is usually attributed to direct extension of the nose or paranasal sinuses or through vascular channels, the supraorbital fissure, or the cribriform plate. If the disease invades the mouth, a black, necrotic eschar is often found on the palate, and ischemic, necrotic turbinates may be found in the nose. As mucormycosis often invades blood vessels, infarction, necrosis, and thrombosis are the major characteristics.^[1,8,9] Our patient reported with a complaint of facial pain and mobile teeth in the upper left maxillary region. An ulcerative lesion seen in relation to 23 at the attached gingiva, with the surface being brown black, having raised edges, floor covered with necrotic debris. Exposed and necrotic bone seen with 23 to 27. In case reports of Rhinocerebral mucormycosis reported by Nupur Hingad et al (2012), R.Madan (2013), Arakkal et al (2017) and Nallapu et al (2017), patients reported with a chief complaint of facial pain and swelling involving the affected side.

A clinical suspicion of mucormycosis requires confirmation by radiological examination, preferably a CT scan of the maxilla and orbit. Imaging findings may be non-specific and include unilateral or bilateral pan sinus inflammatory changes such as polypoid mucosal thickening. Foci of hyperdensity in the affected sinus on CT scans are highly suggestive of fungal disease.^[1] A cone beam computed tomography (CBCT) scan was done for our patient. There was bone loss and perforation of the buccal cortical plate, discontinuity with floor and lateral wall of maxillary sinus. Hanging tooth appearance which could be appreciated from 21 to 26 region and widened Osteomeatal complex and mucosal thickening of maxillary sinus on the left side. Biopsy of infected tissues yet remains the gold standard for diagnosis of mucormycosis.^[1,4,7]

Four factors are critical for eradicating mucormycosis: rapidity of diagnosis, reversal of the underlying predisposing factors (if possible), appropriate antifungal therapy and appropriate surgical debridement of infected tissue.^[1,4,7] The initial medical approach to mucormycosis is to treat aggressively any underlying predisposing disorder. The use of amphotericin B in patients with mucormycosis has been a widely published and accepted treatment, with a survival rate of up to 72%. Although combined treatment of surgery and amphotericin B has a survival rate of 80%, 70% of those who do survive will encounter some type of functional deficit (i.e., blindness or cranial nerve palsy). Surgical management also should be initiated early in the course of treatment. This should involve debridement of all infected tissues.^[1] Our patient was treated by administration of Amphotericin B 0.8 mg/kg/day infused over 4-6 hours for two weeks along with insulin and Left Subtotal maxillectomy followed by

use of a post-operative obturator. Similar approaches were taken up in case reports by Nupur Hingad et al (2012), R.Madan (2013), Arakkal et al (2017) and Nallapu et al (2017). A one year follow up was done for our patient and no signs of active infection were seen.

Though Amphotericin B formulations have remained the mainstay of treatment for mucormycosis, recent studies have demonstrated that posaconazole, an extended-spectrum triazole agent, has in vitro activity against zygomycetes and may represent a therapeutic option for patients with serious invasive fungal infections. Posaconazole can also be an attractive alternative in patients intolerant to Amphotericin B or in whom its use is limited by nephrotoxicity.^[3,10] Hyperbaric oxygen (HBO) has also been used to treat rhinocerebral mucormycosis as it aids neovascularisation.^[1,7,11]

CONCLUSION

Mucormycosis was long regarded as a fatal infection with poor prognosis. However with early medical and surgical management survival rates are now thought to exceed 80%.^[4,5] Early recognition of mucormycosis is necessary to limit the spread of infection, which can lead to high morbidity and mortality. Therefore, health practitioners should be familiar with the signs and symptoms of the disease and should maintain a high level of suspicion in patients with diabetes.^[1] Hence, early diagnosis, use of amphotericin B, aggressive surgical intervention and reversal of the underlying disorder are keys to improved outcome for patients with mucormycosis.

REFERENCES

1. Nupur Hingad, et al. Oral Mucormycosis Causing Necrotizing Lesion in a Diabetic Patient: A Case Report. *International Journal of Oral & Maxillofacial Pathology*, 2012; 3(3): 08-12.
2. Prakash, H., & Chakrabarti, A. Global Epidemiology of Mucormycosis. *Journal of Fungi*, 2019; 5(1): 26. doi:10.3390/jof5010026.
3. Prabhu, R. M., & Patel, R. Mucormycosis and entomophthoromycosis: a review of the clinical manifestations, diagnosis and treatment. *European Society of Clinical Microbiology and Infectious Diseases, CMI*, 2004; 10(Suppl.1): 31-47. doi:10.1111/j.1470-9465.2004.00843.x.
4. Prerna Pratik et al. Mucormycosis of Oral Mucosa: A Rare Case Report. *IJPCBS*, 2014; 4(3): 509-511.
5. Madan R, Barde D, Rawlani S, Chandak R.: Maxillary necrosis by mucormycosis: a case report. *J MGIMS*, 2013; 18No(i): 67-70.
6. Arakkal G, Kasetty HK, Damarla S, Chintagunta S. Mucormycosis: A rare case report. *Int J Oral Health Sci.*, 2014; 4: 46-8.
7. Nallapu V, Vuppalapati HB, Sambhana S, Balasankulu B. Rhinocerebral mucormycosis: A report of two cases. *J Indian Acad Oral Med Radiol*, 2015; 27: 147-51.

8. Mohammadi A, Mehdizadeh A, Ghasemi, Rad M, Habibpour H, Esmali A. Pulmonary mucormycosis in patients with diabetic ketoacidosis: a case report and review of literature. *Tuberk Toraks*, 2012; 60: 66-9.
9. Bhansali A, Bhadada S, Sharma V, 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: 670-4.
10. Spellberg B, Walsh TJ, Kontoyiannis DP, Edwards J Jr, Ibrahim AS. Recent advances in the management of mucormycosis: from bench to bedside. *Clin Infect Dis.*, 2009; 48(12): 1743-1751. doi:10.1086/599105.
11. John, B. V., Chamilos, G., & Kontoyiannis, D. P. Hyperbaric oxygen as an adjunctive treatment for zygomycosis. *Clinical Microbiology and Infection*, 2005; 11(7): 515–517. doi:10.1111/j.1469-0691.2005.01170.x.