CASE REPORT

Maxillary Necrosis Following Fungal Infections in Immunocompetent Patients: A Report of Two Cases

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ABSTRACT

Maxillary necrosis can occur due to bacterial infections such as osteomyelitis, viral infections such as herpes zoster or fungal infections such as mucormycosis and aspergillosis. Aspergillosis and mucormycosis are the most common of all the fungal infections involving maxillary sinus manifests as two distinct entities, a non-invasive and an invasive infection. Early diagnosis is essential to avoid high morbidity and mortality associated with the destructive disease and to instigate treatment before irreversible conditions arise. In this paper, we report the two variants of fungus which posed a diagnostic challenge. Early diagnosis and prompt treatment was started thereby reducing the possible mortality and morbidity associated with the two lethal fungal infections. Fungal infections are common in immunocompromised patient; however, both of our patients were immunocompetent at the time of presentation.

Key words: Aspergillosis, fungal infection, maxillary necrosis, mucormycosis, scintigraphy

INTRODUCTION

Opportunistic fungal infections such as mucormycosis usually occur in immunocompromised patients but can infect healthy individuals as well.[1] Since fungal infections occur infrequently, they might pose a diagnostic and therapeutic dilemma for those who are not familiar with its clinical presentation. Early diagnosis is vital in these infections as delay in initiation of treatment can be life-threatening due to propensity of the fungi to invade adjacent blood vessels and connective tissue producing thrombosis and ultimately necrosis of the hard and soft tissues.[2]

We report one case of mucormycoses and one case of aspergillosis where clinical presentations were not obviously indicative of fungal infection but fungal infection was not ruled out as a cause, and various investigations were advised. As soon as fungal infections were found to be the cause prompt treatment was undertaken and the patient recovered satisfactorily with minimal residual deformities.

CASE REPORTS

Case 1

A male patient aged 30 years, businessman by profession reported to the Oral Medicine and Radiology Department with chief complaint of pus discharge in the right posterior region of the upper jaw following extraction of right maxillary 1st molar 2 months ago. The patient was provisionally diagnosed as a case of osteomyelitis and was referred to the Department of Oral and Maxillofacial Surgery.

On further inquiry, patient gave a history of hospitalization 1 year back for dengue. He suffered from multiorgan failure and was on ventilator for 15 days. He was prescribed broad spectrum antibiotics and antifungal therapy as his culture report was positive for fungal growth on the ventilator connections. He later developed multiple periodontal abscesses and was prescribed broad-spectrum antibiotics, to which he responded and further recovery was uneventful. About 2 months ago, patient underwent extraction of his right upper first molar which was mobile. Following extraction, the socket did not heal and pus discharge was present.

On examination, there was unhealed socket, pus discharge, and exposed bone in the region of 1st maxillary molar. The exposed bone was grayish-yellow, mobile and did not cause any pain on manipulation. An oroantral communication was also present. A provisional diagnosis of osteomyelitis secondary to fungal infection was made

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because of the following reasons - History of ventilatory support and intensive care unit for almost 1 month, recent extraction and unhealed socket, osteolysis of maxilla where fungus is one of the more common cause, mobility of dentoalveolar segment, palatal swelling and maxillary occlusal radiograph indicated gross and massive osteolysis. Radiographically (paranasal sinuses [PNS] view and computed tomography [CT] scan) revealed invasion of inferomedial, posterior, and lateral wall of sinus along with destruction of palatal bone and maxillary alveolar process. On routine blood investigations, all parameters were within normal limit. During antral lavage and debridement black granulation tissue was observed which was completely debrided and sent for histopathological and microbiological examination. Antral packing with bismuth iodoform paraffin packing (BIPP) was done.

The histopathological examination of the specimen showed stratified squamous epithelium which was ulcerated with intraepithelial split formation; underlying connective tissue stroma showed large amounts of necrotic tissue with cellular degeneration and debris. Fungal hyphae were seen with neutrophil infiltration and generalized chronic inflammatory cell infiltrate. Hyphae were aseptate, broad, dichotomous branching at 90° angle, suggestive of mucormycoses.

Post-operatively patient was prescribed amphotericin-B 2.4 g in divided doses though parenteral route. After the 3-month follow-up, post-operative scintigraphy suggested no signs of osteomyelitis in the maxilla.

Case 2

A 45-year-old male patient, a farmer by profession reported to the Department of Oral and Maxillofacial Surgery in Subharti Dental College with the chief complaint of pain in upper left back tooth region for 10 days. The patient gave a history of intraoral swelling for 2 months and had undergone extraction of left maxillary canine 10 days ago. Following extraction patient had exposed bone and pain in upper left teeth. On examination, patient had exposed bone of grayish-yellow in the left maxillary premolar region, which was slightly mobile on manipulation. Radiographically (PNS view and CT scan) depicted the destruction of inferomedial, posterior, and lateral wall of maxillary sinus. Provisional diagnosis of osteomyelitis was made. On routine blood investigations, all parameters were within normal limit. The patient was otherwise a healthy, immunocompetent individual; however, fungal infection was also considered as the etiological factor owing to his profession as a farmer. The patient was planned for sequestrectomy, debridement, and irrigation of maxillary sinus through oroantral opening. During antral lavage and debridement black granulation, tissue was observed which was completely debrided and sent for histopathological and microbiological examination. Antral packing with BIPP was done.

The histopathology of received specimen showed granulation tissue with intense chronic inflammation with multiple congested blood vessels. Specimen also showed necrotic tissue. Areas of hemorrhage were evident with masses of eosinophilic, entangled hyphae-like structures and spores. The hyphae-like structures were flat, broad, refractile, branching at acute angle and septate, suggestive of aspergillosis.

Post-operatively antifungal drug therapy was started - itraconazole 200 mg thrice daily for 3 weeks. During the follow-up patient's clinical outcome was found to be satisfactory and culture repeated after the fungal therapy was negative for any fungal growth.

DISCUSSION

Opportunistic fungal infections such as mucormycosis usually occur in immune-compromised patients but can infect healthy individuals as well.[1] Over the past decade, the incidence of fungal infections has increased considerably.[2] Although a variety of yeasts and molds can cause invasive fungal infections, *Candida* and *Aspergillus* species account for the majority of the infections, other less common fungal isolates, such as zygomycetes, are recognized as opportunistic pathogens causing infection when the host defenses are breached. Immune response varies with respect to the fungal species and morphotype encountered.[3,4]

Fungal infection of the PNS is an increasingly recognized entity both in normal and immunocompromised individuals. Paranasal mycoses manifest as two distinct entities, a benign or non-invasive infection and the more serious invasive infection, which occurs in immunocompromised individuals and is characterized by its rapid onset, ability to invade tissues. The fungus invades the blood vessels and subsequently spreads through them. Once fungal hyphae enter into the blood stream they can disseminate to other organs such as cerebrum or lungs which can be fatal for the patient. Hyphae form thrombi within the blood vessels that reduce vascularity to the tissues and cause necrosis and tissue destruction.[1]

Mucormycoses are a rare fulminating opportunistic fungal infection caused by a fungus of the order mucorales.[5,6] Although the fungi and spores of mucorales shows minimal intrinsic pathogenicity towards normal persons, they can initiate aggressive and fulminating infection in the patients whose resistance is lowered by immunocompression,[7] diabetes, malignant disease, burns, trauma and rarely by steroids or in solid organ transplant patients.[1-3]

Each form of paranasal aspergillosis has a specific radiologic profile. The presence of radiodense foci in association with homogenous opacity of the sinus is highly

suggestive of a non-invasive mycetoma. Opacity of the sinus with or without destruction may be demonstrated in the invasive form.

Mucormycoses show opacification of the sinus[9] which was seen in our case also. CT is a more sensitive diagnostic tool than plain radiography and is the best way to identify bony destruction. Magnetic resonance image was found to be even more sensitive than CT in diagnosing fungal sinusitis.[8]

Microscopically, *Aspergillus* can be identified as a filamentous structure with a diameter of 3 to 6 μm and with septate hyphae. *Aspergillus* must be distinguished from mucor, which forms broader, non-septate hyphae and can be identified by dichotomous branching at 90° angle,[10] while *Aspergillus* shows branching at acute (45°) angle. In a study done by Ferry and Abedi in 1983[7] and Yohai *et al.* in 1994[9] they reported sinus involvement in 69% and 79% of mucormycoses, respectively. Special histological stains such as Grocott or periodic acid–Schiff should be used to find fungal hyphae. Fungal cultures on Saboraud dextrose agar are needed to confirm the diagnosis.

Among the clinical differential diagnosis, we can consider squamous cell carcinoma of maxillary sinus. Such cases present as chronic ulcers with raised margins causing exposure of underlying bone. A malignant salivary gland tumor arising from the accessory glands of the palate can also be considered in the differential diagnosis. Other features seen in cases of antral carcinoma are local pain, swelling, epistaxis, nasal discharge, epiphora, diplopia or numbness.

Bone necrosis can also occur due to extension of infections such as acute necrotizing ulcerative gingivitis from the gingiva to bone however in the case reported here the gingiva was normal. Recent reports have suggested that jaw necrosis can also occur in patients on bisphosphonate therapy but both cases were not on bisphosphonate therapy.

The effective management of PNS fungal infection requires early diagnosis, histological classification, surgery, and appropriate chemotherapy. The diagnosis is based on history, clinical examination, diagnostic radiography, and biopsy.[10] Debridement of nonviable necrotic tissue has been the mainstay of treatment over the years and remains so even today. With the advent of potent antifungal medications, a combination of surgery and medication has provided better outcomes. Overall aggressive medical support of these critically ill patients also improves chances for survival.[10] Despite the risk of renal toxicity, which can be as high as 80%, high doses (1-1.5 mg/kg/day) of amphotericin-B has remained the gold standard antifungal agent against mucormycosis[11,12] and aspergillosis. Its numerous side effects condition an initial low dose with progressive increase if well tolerated. The most frequent ones include chills, fever, backache, chest pain, dyspnea, bronchospasm, tachycardia, hypotension, rash, nausea and vomiting, abdominal pain, diarrhea, and phlebitis. Some authors recommend premedication with diphenhydramine, pethidine, paracetamol, and cortisone to avoid these side effects.[13-16]

CONCLUSION

Fungal infections in the maxillofacial region usually affect immunocompromised or immunosuppressed individuals. However, it may rarely affect an immunocompetent individual. Careful clinical and radiologic examinations are the key to early diagnosis of early infections, especially in disseminated form. Early histologic confirmation leads to prompt surgical and medical management and can certainly reduce the morbidity and mortality. In conclusion, an immunocompromised or immunosuppressed patient having bone necrosis following tooth extraction should alert a clinician of possible fungal infection, but at the same time if the patient is immunocompetent it should not be ruled out.

REFERENCES

1. Auluck A. Maxillary necrosis by mucormycosis. A case report and literature review. Med Oral Patol Oral Cir Bucal 2007;12:E360-4.
2. Alam A, Chander BN, Sabhikhi GS, Bhatia M. Sinonasal mucormycoses: Diagnosis using computed tomography. Med J Armed Forces India 2003;59:243-5.
3. Shoham S, Levitz SM. The immune response to fungal infections. Br J Haematol 2005;129:569-82.
4. Falorth MS. Aspergillosis of the paranasal sinuses: A case report and radiographic review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;81:255-60.
5. Sivapathasundaram RA. Shafer WG, Hine MK, Levy BM, editors. Shaferedi Textbook of Oral Pathology. 5th ed. New Delhi: Elsevier; 2006. p. 510-1.
6. Parfrey NA. Improved diagnosis and prognosis of mucormycoses: A clinicopathological study of 33 cases. Medicine (Baltimore) 1986;65:113-23.
7. Ferry AP, Abedi S. Diagnosis and management of rhino-orbital cerebral mucormycoses (phycosis): A report of 16 personally observed cases. Opthalmology 1983;90:1096-104.
8. Zinreich SJ, Kennedy DW, Malat J, Curtin HD, Epstein JI, Huff LC, *et al*. Fungal sinusitis: Diagnosis with CT and MR imaging. Radiology 1988;169:439.
9. Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycoses. Surv Opthalmol 1994;39:3-22.
10. Fogarty C, Regenniter F, Viozzi CF. Invasive fungal infection of the maxilla following dental extractions in a patient with chronic obstructive pulmonary disease. J Can Dent Assoc 2006;72:149-52.
11. González-Ramos MM, Bertrán-Pasarell J, Guiot H, Soto R, Santana J, Amador R, *et al*. Clinical experience with

posaconazole in patients with invasive mucormycosis: A case series. P R Health Sci J 2008;27:328-32.
12. Georgala A, Vekemans M, Husson M. Zygomycosis in the immunocompromised patient: A case report. Acta Biomed 2006;77 Suppl 2:5-9.
13. Martpliomed sed Calleja JM, Garcej BM. Rhinoorbitocerebral mucormycosis: A case report and literature review. Med Oral Patol Oral Cir Bucal 2008;13:E792-5.
14. Kadziora K, Stominski JM, Gil K, Porzezinska M, Gorezewska A. Invasive aspergillosis of paranasal sinuses, lung and brain. Pol Pneumonol Allergol 2008;76:400-6.
15. Singh V, Sharma B, Sen R. Rhinocerebral mucormycosis: A diagnostic challenge and therapeutic dilemma in immunocompetent host. J Oral Maxillofac Surg 2012;70:1369-75.
16. Badiee P, Hashemizadeh Z. Opportunistic invasive fungal infections: Diagnosis & clinical management. Indian J Med Res 2014;139:195-204.

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