Isolated palate ulcer due to mucormycosis

S. S. Bist · Saurabh Varshney · Manisha Bisht · Nitin Gupta · Rajat Bhatia

Abstract Mucormycosis is a rare but serious fungal infection that rapidly attacks and kills its untreated victims, who are often immunocompromised. It is one of the most fulminant and often fatal mycotic infections known to human beings. Rhinocerebral mucormycosis is the commonest presentation and its extension to the orbit and brain is quite usual but the palatal involvement is a rare and late occurrence. Isolated location of mucormycosis on the palate in an immunocompetent host is an unusual clinical entity. Here we report a case of deep hard palate ulcer due to mucormycosis in a 56-year-old man without any predisposing factor. He was successfully treated with a combination of surgical debridement and systemic liposomal amphotericin B administration for six weeks. By presenting this case report we would like to emphasize that mucormycosis should be included in the differential diagnosis of the hard palate ulcers even in immunocompetent patient.

Keywords Palate · Ulcer · Mucormycosis

Introduction

Most mouth ulcers are caused by trauma and aphthae [1]. Three form of ulcers have been recognized; minor, major and herpetiform. Only rarely do these lesions occur on attached gingivae and the hard palate [1]. More over, trauma of the hard palate is rare. Mucormycosis is a generic term that includes fungal infections caused by the genera *Mucor*, *Rhizopus*, *Absidia* and others [2]. This fungus is ordinarily saprophytic, but can become an aggressive pathogen under the appropriate conditions, usually a serious predisposition in the host. It has been reported in about 4% of patients without any underlying disease, but generally occurs in patients with debilitating disease. These fungi are found almost ubiquitously in soil, decaying vegetables, seeds, fruits, composite piles, animal excreta and old bread. The distribution of the various clinical forms is based on predisposing factors rather than age, sex, race or geography. More than half of patients have rhinocerebral disease, approximately 10% have pulmonary, cutaneous, or disseminated disease and 2% have kidney or gastrointestinal involvement [3]. In the rhinocerebral type the disease process begins in the nose, paranasal sinuses, or the palate. The nasal or oral mucosa is colonized with the airborne *mucor* spores. In the normal host there is a phagocytic response that prevents any infection. But in diabetics and those with impaired immune systems, this response is suboptimal. Microscopy of these fungi is characteristic- the hyphae are broad, branch at ninety degrees, and are non-septate. Pathologically, mucormycosis is characterized by vascular invasion with hyphae, infarction and necrosis of tissue. Ulceration and perforation of the palate due to tissue necrosis are a rare and late occurrence [4]. Although mucormycosis should be included in the differential diagnosis of the palate ulcers, in the ENT literature this has not been made clear. Here we report a case of a large deep palate ulcer due mucormycosis in an immunocompetent patient.

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Case report

A 56-year-old male presented to our outpatient department with complaints of right-sided facial pain and numbness for past 20 days and a patch on the palate for past 7 days. He gave a history of tobacco chewing for last 20 years. Oral examination revealed poor oral hygiene and a deep, partially black patch mainly on hard palate mucosa without any oroantral or oronasal fistula (Fig. 1). Diagnostic nasal endoscopy and rest of the ENT examination was normal. The ophthalmological examination was normal. Hematological investigations revealed normal and X-rays chest reported normal. CT scan of nose and paranasal sinuses was normal. The biochemical investigation serum glucose, creatinine and urea levels were within normal limit. Clinically it was thought to be a neoplastic condition of palate and deep biopsy was taken. Histopathological examination of the palate tissue revealed large broad non-septate hyphae, which was invading blood vessels without any evidence of any malignant cell. To confirm the diagnosis repeat biopsies were taken from different sites of lesion and were sent for mycology and histology. KOH mount revealed presence of broad aseptate hyphae. Fungal culture was done on Sabouraud's dextrose agar media. The isolate was identified as *Rhizopus microsporum*. A diagnosis of mucormycosis was established. The patient was treated by endoscopic surgical debridement of the palate twice under GA and liposomal amphotericin B 1 mg/kg dose per day for six weeks with regular monitoring of kidney function. Four months after the initial diagnosis the patient had adequate healing of the palate perforation and had no recurrence of disease (Fig. 2). He was subsequently fitted with palatal Obturator with satisfactory closure of perforation with normal swallowing and acceptable speech.

Discussion

Mucormycosis ('synonyms' are zygomycosis or phycomycosis) is the common name given to several different diseases caused by fungi of the order Mucorales [3]. *Rhizopus* species are the most commonly isolated agents of mucormycosis, followed by *Rhizomucor* [3]. These fungi, which are widely distributed in nature and numerous underlying conditions, predispose patients to this infection. Predisposing factors for mucormycosis are poorly controlled diabetes mellitus with ketoacidosis, leukemia, lymphoma, severe burn, renal disease, on desferoxamine therapy, disseminated cancer, severe cachexia, profound dehydration/septicemia due to heroin addiction, immunosuppressed patients, recipients of renal transplants, supraphysiological doses of adrenal corticosteroids, azathioprine, and leukopenics. About 4% of patients have no underlying disease, although a complete immunologic work-up should be undertaken in these patients. Interestingly, there is no mor-

tality difference in those patients without any underlying predisposition. The exact mechanisms responsible for the increased susceptibility to mucormycosis in various patient groups are not clear. Undefined defects of macrophages and neutrophils, present in diabetics and steroid-treated patients, may be important in allowing the replication of the Mucorales [3]. In general, the predilection for type of presentation varies with the underlying or predisposing condition. For example, patients with diabetes most often develop rhinocerebral mucormycosis, leukemic patients who have neutropenia or patients who become neutropenic during bone marrow transplantation for other diseases develop rhinocerebral or pulmonary mucormycosis. The most common risk factor is diabetes mellitus. Diabetics comprise about 60–80% of cases, especially those with poorly controlled disease. *Mucor* occurs in these patients because the acidotic and hypoglycemic environment is ideal for fungal growth, this environment also inhibits the effectiveness and affinity of macrophages. A classic presentation of the rhinocerebral

Fig. 1 Clinical Photograph showing black eschar on hard palate

Fig. 2 Clinical Photograph showing palate perforation with healed margin

disease is the diabetic patient with facial pain, nasal congestion, nasal or eyelid swelling and fever. Extension to the orbit and brain is a common complication [4]. Rhinocerebral mucormycosis starts in the nose and paranasal sinuses and spreads to the eye via the angular vein, lacrimal or ethmoidal vessel as well as direct extension from paranasal sinuses. Intracranial involvement occurs from invasion by way of superior orbital fissure, ophthalmic vessels, cribriform palate and not uncommonly, through carotid artery. Once the fungus begins to grow, the hyphae invade tissue and have a special affinity for blood vessel walls, where invasion may lead to haematogenous spread, thrombosis, bleeding or infarction [5]. Vascular invasion produces a fibrin reaction and the development of a mucor thrombus, which occludes blood vessels. Vascular occlusion results in ischemia and infarction. Infarction produces the characteristic black necrotic eschars on the nasal or palatine mucosa [2] in these patients. Direct penetration and growth through the blood vessel wall explain the propensity for thrombosis and tissue necrosis, two major hallmarks of the histopathology of mucormycosis [3]. Ulceration and perforation of the palate are a rare and late occurrence of rhinocerebral mucormycosis [4]. Our patients present only with palate ulceration without any evidence of rhinocerebral mucormycosis. Based on clinical signs and symptoms alone, palate mucormycosis cannot be differentiated from several other conditions. Inflammatory lesion, such as gummatous necrosis of tertiary syphilis, tuberculosis, midline granuloma and Wegner's granulomatosis should be included in the differential diagnosis. Rarely, oral or nasal and paranasal sinus malignancies, such as lymphoma, squamous cell carcinoma or salivary gland adenocarcinoma may present as ulceration of the palate. Biopsy and culture for bacteria and fungi are required to differentiate these lesions [5], biopsies are performed from areas with absence of frank tissue necrosis and of full thickness mucosa. The specimen should then be divided and one half sent to the microbiology laboratory and the remainder sent for histopathological evaluation. Diagnosis depends on demonstration of the organism in the tissue of a biopsy specimen. Grocott-Gomori methenamine-silver (GMS) stain is the best stain to use, but hematoxylin and eosin and periodic acid-Schiff is also useful [3]. The classical finding is that of necrotic and edematous tissue with neutrophilic infiltrate and presence of broad, nonseptate hyphae with branching at 90° [3]. Growth of this fungus occurs best in brain-heart infusion agar, potato dextrose agar, or Sabouraud dextrose agar [3]. Radiologic studies can be of benefit to document the extent of sinus disease, as well as the presence of orbital infiltrates. CT findings would include a thickened mucosa, or some sinus opacification. MR shows a hyperintense signal and is best used to document intracranial spread of disease and to visualize internal carotid or cavernous sinus thrombosis. MRI can also be helpful to detect early intracranial spread before a patient develops any symptoms of the disease. Making the diagnosis in

these patients requires a high index of suspicion. The finding of nasal or palate necrosis would strongly suggest this diagnosis. Treatment can be broken down into four main concomitant approaches. These involve rapid correction of the underlying host conditions, (such as diabetic ketoacidosis,) antifungal therapy, surgical debridement of devitalized tissue and the use of adjunctive therapies, such as hyperbaric oxygen. The overall treatment should be guided by the severity of the disease. The mainstay of antifungal therapy is systemic amphotericin B. Prior to the development of amphotericin B in the 1950s, mucormycosis was almost universally fatal. The dose should be rapidly advanced to the highest possible tissue levels, approximately 1 mg/kg dose per day. Patients generally receive a cumulative dose of 3 to 5 grams, and the duration of therapy depends on the extent of the infection and the clinical response, averaging around 6 weeks. The liposomal forms of amphotericin B may be more efficacious; it is less toxic, allowing higher dose of medication to be given over the standard form [3]. Aggressive surgical debridement of all necrotic tissue is necessary, the principle of surgical treatment is to debride until one encounters normal bleeding tissue. The infected mucor tissue bleeds very little because of the vaso-occlusive effect of the fungus. Patients may need repetitive debridements. Imaging studies can be helpful here to document the extent of disease after initial surgery. Frozen section-guided debridement has been advocated as a method for operative intervention and as an alternative to the extensive debridement that has traditionally been performed in patients with invasive mucormycosis [6]. Orbital exenteration may be necessary if ocular invasion exists [5]. Attempts to treat the disease have also been made by using adjunctive hyperbaric oxygen therapy [5, 7]. The principle behind this is that lengthy exposure and high pressures of oxygen are fungicidal in vitro. Hyperbaric oxygen should reduce tissue hypoxia and acidosis that occur with vascular invasion of mucormycosis. The use of hyperbaric oxygen may be able to salvage hypoxic marginally viable tissue. It can also augment the fungal effects of amphotericin B against other pathogens. The increased oxygen tension allows the fibroblasts to lay down new collagen providing a framework for new vessel formation and facilitates wound healing. With earlier diagnosis and a combination of amphotericin-B and radical debridement of infected tissues, the fatality rate has dropped [2, 5]. The prognosis of the disease surely depends on how early and aggressively it is managed. Overall the earlier the diagnosis of mucormycosis is made, the better is the outcome.

Conclusion

Mucormycosis is usually encountered as a secondary disease or an opportunistic infection due to numerous predisposing factors, but it has been reported in healthy patients.

By presenting this case report we would like to suggest that mucormycosis should be included in the differential diagnosis of hard palate ulcers, even in the immunocompetent patients. Making the diagnosis in these patients requires a high index of suspicion and the keys to survival are rapid diagnosis and prompt anti-fungal therapy combined with surgical debridement.

References

1. Scully C, Porter S (1989) Recurrent aphthous stomatitis: current concepts of etiology, pathogenesis and management. *J Oral Pathol Med* 18:21–27
2. Raj P, Vella EJ, Bickerton RC (1998) Successful treatment of rhinocerebral mucormycosis by a combination of aggressive surgical debridement and the use of systemic liposomal amphotericin B and local therapy with nebulized amphotericin. A case report. *J Laryngol Otol* 112:367–370
3. Sugar AM (2000) Agents of mucormycosis and Related Species. In: Mandell GL, Bennett JE, Dolin R, editors, *Principles and Practice of Infectious Diseases*, 5th edn. New York: Churchill Livingstone; pp. 2685–2691
4. Regezi JA, Sciubba JJ (1999) Ulcerative conditions. In: Regezi JA, Sciubba JJ, eds. *Oral Pathology Clinical Pathologic Correlations*, 3rd ed. Philadelphia: W.B. Saunders, 30–82
5. Schmidt JM, Poulton RML (1998) Rhinocerebral mycosis in immunocompromised patients. A case report and review of the literature. *Rhinology* 36:90–93
6. Langford JD, McCartney DL, Wang RC (1997) Frozen section-guided surgical debridement for management of rhino-orbital mucormycosis. *Am J Ophthalmol* 124:265–267
7. Ferguson BJ, Mitchell TG, Moon R, Comporesi EM, Farmer J (1988) Adjunctive hyperbaric oxygen therapy for treatment of rhinocerebral mucormycosis. *Rev Infect Dis* 10:551–559