CASE REPORT

Rhinomaxillary mucormycosis with cerebral extension

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ABSTRACT
Mucormycosis is a rare opportunistic infection caused by fungus belonging to the order Mucorales. A case of a controlled diabetic male with rhino maxillary mucormycosis, with cerebral extension, is described. The patient presented with hemifacial swelling, a nasal twang in his voice, fever, ocular signs, gross tissue destruction, and was sluggish. 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.
Key words: Mucormycosis, phycomycosis, zygomycosis, rhinocerebral, rhinomaxillary

INTRODUCTION

Mucormycosis also called as Zygomycosis and Phycomycosis was first described by Paultauf in 1885.[1] It is an opportunistic fungal infection that is caused by normal saprobic organisms of the class Zygomycetes including such genera as Mucor, Absidia, Rhizopus and Cunninghamella.[2] Numerous spores may be liberated into the air and inhaled by human hosts, from where it can spread to the brain.[3] Only rarely has Zygomycetes been reported in apparently healthy individuals.[2] Infection commonly occurs in individuals with neutropenia, ketoacidotic diabetes,[4] malnutrition, severe burns,[5] hematological malignancies, patients under cancer chemotherapy or immunosuppressive drug therapy.[3] Initial signs are a nonspecific necrotic ulcer, which later turns into a characteristic black necrotic eschar.[6]

The purpose of this article is to report a case of rhinomaxillary mucormycosis with cerebral extension in an elderly diabetic male. A review of literature pertaining to mucormycosis of the maxillofacial region is also reported.

CASE REPORT

A 60-year-old patient presented to MM College of Dental Sciences and Research, Mullana with a three-month history of increasing midfacial pain, swelling around the right eye, and pus discharge from the upper right back region of the jaw. He also encountered headaches and decreased vision in his right eye. His past medical history was significant only for diabetes and asthma since 20 years. His social history was significant for smoking tobacco, approximately 30–40 bidis/day since the last 25 years, but discontinued the habit from the past one year.

On physical examination the patient was meekly responsive, sluggish in movements, and febrile. The right eye was proptotic, with chemosis, limitation of movement, and decreased visual acuity. He had facial asymmetry with mild-to-moderate midfacial erythema and swelling, with tenderness over the right side of the midface, obliterating the nasolabial fold. There was hoarseness and nasal twang in his voice. Bilaterally the submandibular lymph nodes and right upper deep cervical group were palpable, but nontender.

Intraorally denudation of the right maxillary oral mucosa with a swelling on the palate, pushing the whole mucosa toward the left side, was noted. Denuded and naked bony sockets of teeth were seen [Figure 1]. The bare bone was visible from 18 through 22 and the lesion crossed the midline. Buccal vestibular mucosa pertaining to the right maxillary region was ulcerated, tender, and erythematous.

Laboratory findings were significant for a raised ESR of 74 mm/hr, with random serum glucose, urea, and creatinine, under normal range.

The paranasal sinus view showed haziness of the right maxillary sinus, whereas, empty sockets with normal bony trabecular pattern were presented in the maxillary occlusal view. Orthopantomograph showed empty sockets with a normal outline of maxillary sinuses, along with periapical radiolucency with relation to 25, 26, suggestive of periapical abscess. A computed tomography scan of the maxillofacial region revealed the erosion, destruction, and moth-eaten appearance of the zygomatic arch, squamous temporal bone, maxilla involving the hard palate, all walls of maxillary sinus, floor, and posterolateral walls of the orbit, lesser and greater wings of the sphenoid, along with the floor of the middle cranial

fossa, and walls of the sphenoid air sinuses, all of the right side [Figure 2].

An incisional biopsy of the hard palate region was performed and histopathological investigations were conducted. H and E stained slides showed bony trabeculae surrounded by few hematoxiphilic thin-walled, aseptate, rarely branching hyphae of nonuniform diameter [Figure 3]. Periodic acid-Schiff (PAS) stained slides showed broad aseptate fungal profiles, 10–15 µm wide, thin-walled hyphae showing frequent bulbous dilatations and irregular obtuse angle branching were noted, confirming the morphology of Zygomycetes group of fungi. Gomori's methenamine silver (GMS) stain for fungi showed fragments of dead bone and necrosis, with fungal hyphae of mucormycosis, positive for GMS [Figure 4].

The patient was in a severely debilitated state, but consented for aggressive surgical debridement, systemic amphotericin B in the dose of 1 mg/kg/day over 4–6 h IV for 2 weeks. After 2 weeks the condition improved and oral amphotericin B was advised, after which the patient was lost to treatment.

DISCUSSION

The three primary sites of Mucor invasion are the nasal sinuses, lungs, and gastrointestinal tract, depending on whether the spores are inhaled or ingested. In diabetics the fungus may spread from nasal sinuses to the orbit and brain, giving rise to rhinocerebral mucormycosis, a subdivision of which is the rhinomaxillary form.

Mucormycosis is the most acutely fatal fungal infection in humans, with a mortality ranging from 50–100%. It is most commonly caused by a species of Rhizopus, Rhizomucor and Cunninghamella, although species of Apophysomyces, Saksenea, Mucor, and Absidia can occasionally be the cause.[1] The term "Zygomycosis" includes Mucormycosis and Emtomopthora-mycosis, the latter being a tropical infection of the subcutaneous tissue or paranasal sinuses caused by a species of Basidiobolus or Conidiobolus.[1]

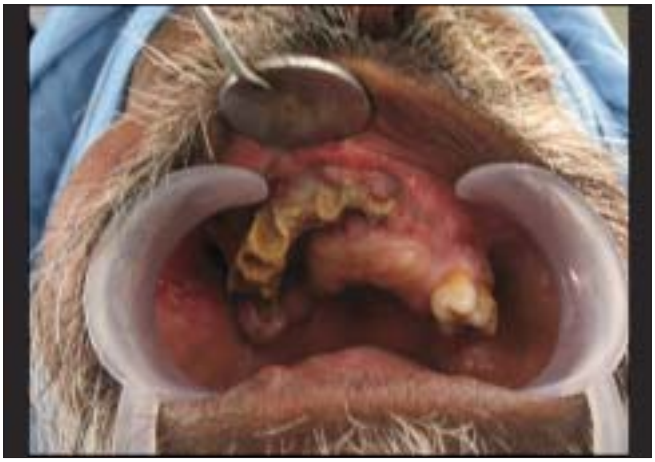

Figure 1: Intra oral picture showing exposed empty bony sockets

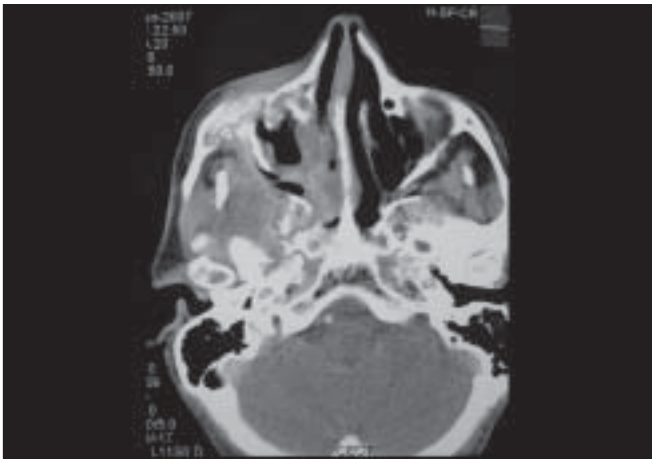

Figure 2: CT scan showing extensive soft tissue destruction

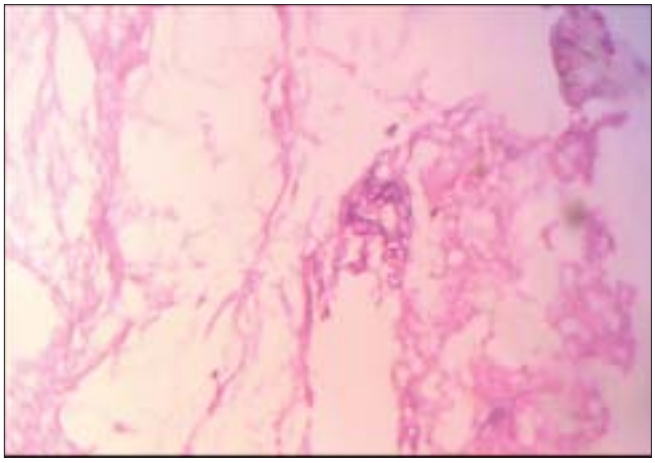

Figure 3: Microscopic picture of bone showing groups of fungi proliferating (H and E, 40×)

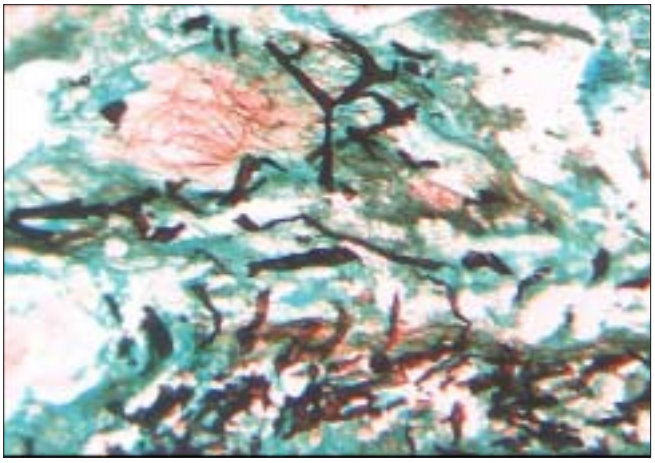

Figure 4: Microscopic picture of bone marrow space showing fungal hyphae (GMS stain, 20×)

Zygomycetous fungi have coenocytic hyphae which will often be damaged and become nonviable during biopsy procedures or during chopping up of tissue grinding processes in the laboratory.[7]

Scrapings, sputum, and exudates can be examined using 10–20% potassium hydroxide (KOH) and parker ink or cauliflower mount. The primary isolation media is Saboraud's dextrose agar having antibiotics and the maintenance media is potato dextrose agar.[7]

Mucormycosis attacks people with compromised immune systems. Reduced ability of the serum to bind iron at low pH may be the basic defect in the body's defense system. Fungal hyphae produce a substance called Rhizoferrin (Siderophores), which binds iron avidly. This Iron-Rhizoferrin complex is then taken up by the fungus and becomes available for vital intracellular processes.[2]

Human infection is said to be caused by asexual spore formation. The tiny spores then become airborne and land on the oral and nasal mucosa of humans. In the vast majority of immunologically competent hosts, these spores will be contained by a phagocytic response. If this fails, germination will ensue and hyphae will develop. It progresses as the hyphae begin to invade arteries, where they propagate within the vessel walls and lumens causing thrombosis, ischemia, and infarction with dry gangrene of the affected tissues.[7]

Rhinocerebral mucormycosis is the most common form of infection and predominantly occurs in patients with poorly controlled diabetes mellitus. In the present case the patient was a controlled diabetic, but with poor oral hygiene. He was a farmer by profession, so was liable to contract the infection from the soil and harbored the fungi due to his immunocompromised state.

Other risk populations include immunosuppressed patients with organ transplant, hematologic malignancies, severe burns, treated with chronic corticosteroids, and end-stage renal diseases. No person-to-person spread has been reported.[7]

Once established in the paranasal sinuses, the infection can easily spread to and enter the orbit via the nasolacrimal duct and medial orbit. Spread to the brain may occur via the orbital apex, orbital vessels or via the cribriform plate.[7] As the disease progresses to the orbit and skull, the patient may become confused and comatose. Fungal invasion of the globe or retinal artery leads to blindness.

The male patient presented with a grayish black eschar on the palate, and via paranasal sinuses it spread into the orbit leading to visual impairment, into the middle cranial fossa leading to confusion and nonresponsiveness, and into the nose leading to a nasal twang in the voice. Maxillary teeth exfoliated leaving empty bare sockets.

Rhinocerebral mucormycosis is the most distinctive form of mucormycosis.[2] The initial symptoms are nonspecific (e.g., headache, malaise, and lethargy). However, the characteristic features of rhinocerebral mucormycosis are summarized in [Table 1]. Except for blood tinged nasal discharge, fixed pupils, and loss of ocular movements all other signs and symptoms were present in the case reported.

Because of the rapidity of invasive infection CT or magnetic resonance scans should be obtained at frequent intervals to monitor disease extension and response to therapy.[7] The fungi have a predilection for the internal elastic lamina of the blood vessels; thus arterial thrombosis ensues, and later, invasion of veins and lymphatics leads to further thrombosis, edema, and hemorrhagic necrosis.[7]

Mucormycosis is a medical emergency. The initial medical approach to mucormycosis is to treat aggressively any underlying predisposing disorder. Surgical management also should be initiated early in the course of treatment. This should involve debridement of all infected tissues. In some cases, radical resection may be required, which can include partial or total maxillectomy, mandibulectomy, and orbital exenteration.[8]

Debridement is commonly defined as the process of removing necrotic, devitalized tissue and foreign material from a wound. The presence of necrotic tissue within a wound may impair wound repair processes by stimulating inflammation and delaying granulation and epithelialization. Several methods for debridement exist including surgical, enzymatic, mechanical, autolytic, and biosurgical. Surgical debridement is the removal of necrotic, devitalized tissue by using a sharp instrument, such as, scalpel, scissors, curette or forceps.[9] Wounds with large quantities of necrotic debris are good candidates for surgical debridement and hence form the treatment of choice in the case presented, along with systemic antifungals.

Amphotericin B is the antifungal agent of choice. It is a polyene antifungal agent that acts by binding to sterols (primarily ergosterol) in the fungal cell membrane with a resultant change in membrane permeability. Lipid complex

Table 1: Summary of clinical features associated with rhinocerebral mucormycosis

• Dark blood tinged nasal discharge
• Facial pain and anesthesia of the affected side
• Periorbital or perinasal swelling and edema
• Ptosis of the eyelid
• Fixed dilated pupil
• Loss of extraoccular movements
• Progressive lethargy
• Black necrotic palate, alveolar ridge or turbinate (which may be mistaken for dried blood)
• Decreased visual acuity progressing to blindness and loss of corneal reflex

Amphotericin B is a formulation designated to be less nephrotoxic than conventional Amphotericin B.

Although studies have shown that hyperbaric oxygen exerts a fungistatic effect, the most important effect of hyperbaric oxygen is to aid neovascularization, with subsequent healing in poorly perfused acidotic, and hypoxic, but viable areas of tissue.[1]

Rhinocerebral mucormycosis, as the most frequent form of mucormycosis, accounts for more than 75% of the cases.[10] Prognosis involves high morbidity and mortality; survival depends on reversibility of underlying risk factors and early surgical intervention.[11] No reports document survivors of mucormycosis before 1955 (Amphotericin became available in the 1950s). Survival rates among groups of patients with invasive sinus disease without cerebral involvement may be as high as 50–80%. If infection spreads to the brain, case fatality ratios exceed 80%.[11] Prognosis may improve with rapid diagnosis, early management, and reversible underlying risk factors. The underlying disease is the most important determinant of survival. 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).[8]

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