Rhino-Maxillary Mucormycosis with Cerebral Extension: A Case Report and a Comprehensive Review of Literature

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Abstract

Mucormycosis is a rare opportunistic infection caused by fungus which belongs to the order Mucorales. A case of a male controlled diabetic patient with rhinocerebral mucormycosis is described. The patient had hemifacial swelling, nasal twang, febrile, sluggish, ocular signs and gross tissue destruction.
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.

INTRODUCTION

Mucormycosis also called as Zygomycosis & Phycomycosis was first described by Paultauf in 1885 [1] is an opportunistic frequently fulminating fungal infection that is caused by normal saprobic organisms of the class Zygomycetes including such genera as Mucor, Absidia, Rhizopus & Cunninghamella [2] .Numerous spores may be liberated into the air & inhaled by human hosts, from where it can spread to brain [3] . Only rarely has Zygomycetes been reported in apparently healthy individuals [2] . Infection commonly occurs in individuals with neutropenia, ketoacidotic diabetics [4] , malnutritioned, severe burns [5] , and hematological malignancies, patients under cancer chemotherapy or immunosuppressive drug therapy [3] .

Initial signs being a nonspecific necrotic ulcer which turns later into a characteristic black necrotic eschar [6] .

The purpose of this article is to report a case of Rhinocerebral Mucormycosis in an elderly diabetic male. A review of literature pertaining to mucormycosis of the maxillofacial region is also performed.

CASE REPORT

A 60yr old patient presented to MMCDSR (Mullana) with a 3 month history of increasing midfacial pain, swelling around the right eye & 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 is significant only for diabetes & asthma since 20 yrs. His social history was significant for smoking tobacco, approximately 30-40 bidis/day since last 25yrs but discontinued the habit from past 1 year.

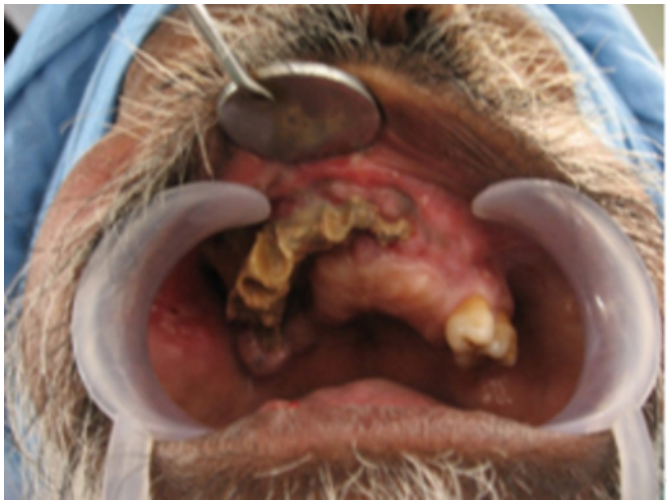
On physical examination the patient is meekly responsive, sluggish in movements and febrile. The right eye was proptotic with chemosis, limitation of movement & decreased visual acuity. He had facial asymmetry with mild to moderate midfacial erythema & swelling over right side of midface, obliterating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

In the oral cavity there was denudation of the right maxillary oral mucosa with a swelling on the palate which pushed the whole mucosa towards the left side leaving denuded & naked bony sockets (Fig 1). The bare bone was visible from 18-22 and the lesion crossed midline. Buccal vestibular mucosa pertaining to right maxillary region was ulcerated & erythematous. Tenderness is also present.

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

Figure 1

Figure 1: Intra oral picture showing exposed empty bony sockets



RADIOGRAPHIC FINDINGS

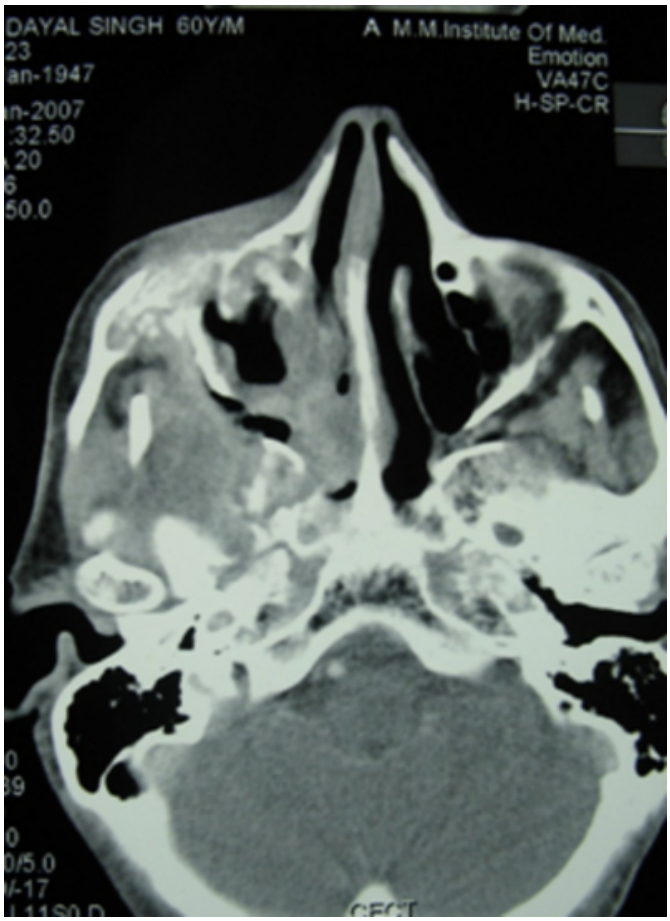
The Paranasal sinus view showed haziness of the right maxillary sinus whereas empty sockets with normal bony trabecular pattern are presented in maxillary occlusal view.

Orthopentomogram showed empty sockets with normal outline of maxillary sinuses along with a periapical radiolucency with relation to 25, 26 suggestive of periapical abscess.

A Computed Tomography (CT) scan of the maxillofacial region revealed erosion, destruction and moth-eaten appearance of zygomatic arch, Squamous temporal bone, maxilla involving the hard palate, all walls of maxillary sinus, floor & postero-lateral walls of the orbit, lesser & greater wings of the sphenoid along with floor of the middle cranial fossa and walls of sphenoid air sinuses, all of the right side (Fig 2).

Figure 2

Figure 2: CT Scan showing extensive soft tissue destruction



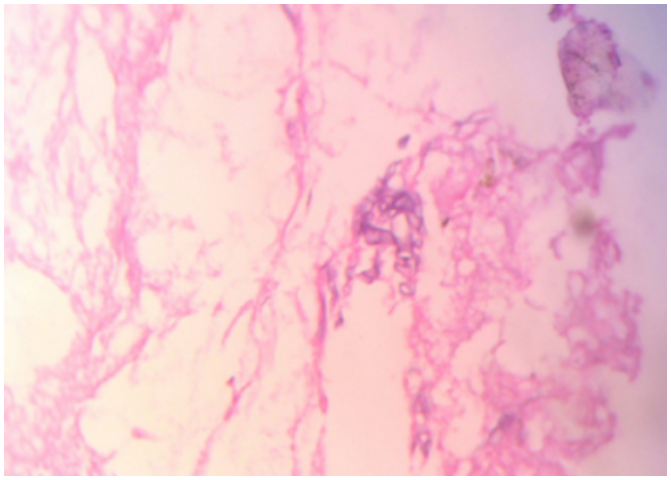
HISTOPATHOLOGICAL PICTURE

An incisional biopsy of the hard palate region was performed and histopathologic investigations were done.

H & E stained slides showed bony trabeculae surrounded by few haematoxiphilic thin walled, aseptate, nonuniform diameter rarely branching hyphae (Fig 3).

Figure 3

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

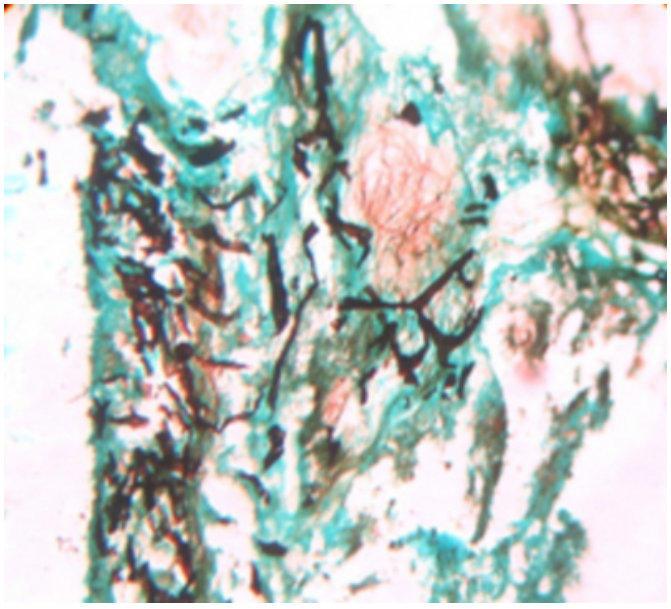


PAS stained slides showed broad aseptate fungal profiles, 10-15µm wide, thin walled hyphae showing frequent bulbous dilatations and irregular obtuse angle branching were noted confirming the morphology of Zygomycetes group of fungi.

GMS (Gomori's Methenamine Silver) stain for fungi showed fragments of dead bone & necrosis with fungal hyphae of Mucormycosis positive for GMS Stain (Figs 4) .

Figure 4

Figure 4: Microscopic picture of bone marrow space showing fungal hyphae. (10X, GMS stain)



DISCUSSION

The three primary sites of Mucor invasion are the nasal sinuses, lungs & 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 Rhino Cerebral Mucormycosis (RCM), a subdivision of which is the Rhinomaxillary form. In our case since nasal mucosa , brain and maxilla collectively were involved it can be labeled as Rhino Maxillo Cerebral Mucormycosis.

Mucormycosis is the most acutely fatal fungal infection in humans, with a mortality ranging from 50%-100%. It is most commonly caused by species of Rhizopus, Rhizomucor and Cunninghamella, although species of Apophysomyces, Saksenea, Mucor, and Absidia can occasionally be the cause [1] .

MORPHOLOGY

The term “Zygomycosis” includes Mucormycosis and emtomopthora-mycosis, the latter being a tropical infection of the subcutaneous tissue or paranasal sinuses caused by species of Basidiobolus or Conidiobolus [1] . Whereas in Mucormycosis the moulds are broad, rarely septate, hyphae of uneven diameters ranging from 6-50µm with long sporangiophores attached.

COLLECTION OF SAMPLES

Zygomycetous fungi have coenocytic hyphae which will often be damaged & become nonviable during biopsy procedures or by chopping up of tissue grinding processes in lab [7] . In our case incisional biopsy of the hard palate region was performed and kept in 10% formalin.

IDENTIFICATION & CULTURE

Scrapings, sputum & exudates can be examined using 10-20% potassium hydroxide (KOH) and parker ink or cauliflour mount. The primary isolation media is Seboraund's Dextrose Agar having antibiotics and maintenance media being Potato Dextrose Agar [7] .

PATHOPHYSIOLOGY

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 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] .

FUNGAL PROLIFERATION

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 immunoiogically 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].

PATIENTS AT RISK

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

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

DISEASE PROGRESSION

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, obtunded, 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, via paranasal sinuses it spread into the orbit leading to visual impairment, into the middle cranial fossa leading to confusion and nonresponsiveness, into the nose leading to nasal twang in voice. Maxillary teeth exfoliated leaving empty bare sockets.

CLINICAL PRESENTATION

RCM is the most distinctive form of mucormycosis [2].The initial symptoms are nonspecific (e.g. headache, malaise & lethargy). However, the characteristic features of RCM are summarized in Table I.

Figure 5

Table 1: Summary of clinical features associated with RCM

Summary of clinical features associated with RCM
• 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

Except for blood tinged nasal discharge, fixed pupils and loss of ocular movements all other signs and symptoms were present in the case reported.

DIAGNOSIS

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].

Management:

Mucormycosis is a medical emergency. Amphotericin B is the anti fungal 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 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 cases [8].

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