Case Report

Rhinocerebral mucormycosis in a diabetic patient with cranial nerve involvement

Javadzadeh Bolouri A1, Delavarian Z2, Dalirsani Z3, Tonkaboni A4

ABSTRACT

We report a case of 50-year-old diabetic edentulous woman (FBS=396mg/dl) with chief complain of left side facial pain treated by her physician with corticoid and antibiotic for 15 days without any improvement. With pain exacerbation and skin paresthesia she was referred to oral medicine department of Mashhad school of dentistry by a neurologist with diagnosis of dental infection. On examination, she had left side facial palsy, ptosis, and a mass which was anterior to her left ear. Left eye had loss of vision and was fixed. Due to involvement of II, III, IV, V, VI, VII cranial nerves, maxillary sinus, orbit and base of the skull we referred her to neurosurgery department with clinical diagnosis of mucormycosis. Left maxillectomy along with enucleation of left eye was carried out. Histopathology confirmed the diagnosis. Patient was put on amphotericin B under medical care in hospital. Follow up showed the patient is responding and in good health. Early diagnosis and prompt treatment can reduce the mortality and morbidity of this lethal fungal infection.

KEY WORD: Cranial nerve palsy, Diabetes mellitus, Neuropathy, Fungal, sinusitis, Proptosis, Rhinocerebral, mucormycosis.

INTRODUCTION

Mucormycoses are rare and severe diseases affecting immunocompromised hosts, especially diabetic patients during ketoacidosis. The hallmarks of this disease is angioinvasion by organism that is followed by thrombosis and necrosis of the involved tissue. It can be characterized by sinusitis and a painless, necrotic black palatal or nasal septum scar, facial pain, periorbital edema, proptosis, tearing, blindness and ocular or optic nerve involvement and nasal congestion or discharge. The treatment includes surgical debridement and amphotericin B but prognosis remains poor and depend on so many factors.

Fungal pathogens are two groups: those are superficial and infect epithelium and those that invade deep tissues. Mucormycosis is an opportunistic deep fungal infection known as Phycomycetes. It is severe life threatening specially in immunosuppressed patients. Although it can manifest as pulmonary, cutaneous, disseminated and gastrointestinal infections, but rhinocerebral mucormycosis is the
most common presentation. Rhino-orbito-cerebral mucormycosis (ROCM) is a fatal fulminant opportunistic infection leading to death in some cases, which mostly occurs among patients with a weakened immune system.\(^2\)

The most common predisposing factor of this disease is diabetes mellitus, which causes immunologic changes by ketone, low pH, and hyperglycemia. On the other hand high glucose concentrations help fungus growth, besides serum iron excess used by fungus.\(^3\)

The hallmarks of rhino-orbito-cerebral mucormycosis are facial pain and swelling, headache, nasal discharge or obstruction, visual disturbance and rarely symptoms related to cranial nerve involvement.\(^4\)

**CASE REPORT**

A 50 year-old diabetic edentulous woman (FBS=396mg/dl) with chief complain of left side facial pain was seen by physician 15 days ago and treated by parenteral corticosteroid and oral antibiotic therapy. In view of no response, pain aggravation and skin paresthesia, she visited a neurologist who referred her to oral medicine department of Mashhad school of dentistry with diagnosis of dental infection. This patient was a known poor-controlled diabetic on treatment with oral hypoglycemic for the last 10 years. He had been under medical treatment for the first 3 years, and then continued the same medication for the last 7 years without consulting a physician or undergoing any routine blood sugar evaluation.

On clinical examination she showed left side facial nerve palsy, ptosis, pain and anesthesia in distribution of all 3 divisions of trigeminal nerve and a swelling which was anterior to the ear [Fig.1]. By lifting the eyelid she noticed her left eye blindness Light reflex and corneal reflex were negative. Ear examination revealed mastoid and tragus tenderness in the anterior part of the external acoustic canal. Thus with involvement of I,II,III,IV,V,VI,VII cranial nerves, maxillary sinus and orbit we referred her to neurosurgery department with clinical diagnosis of mucormycosis.

Intraoral examination showed a map-like ulcer in size of 3×1 cm on the left side of the palate without any black pus or discharge which was due to irritation of her cracked denture [Fig.2]. CT scan showed erosion in lateral nasal wall, homogen radiopacity and increased sinus density due to thickened sinus mucosa which was perhaps due to infection and inflammation.

In neurosurgery department also periorbital edema, eye redness, conjunctiva ulcer, decreased eye movement, cataract, paleness of optic disc, without artery pulsation, and fading of its contour was reported. The retinal artery was very thin [Fig.3]. With clinical diagnosis of rhinocerebral mucormycosis partial maxillectomy through weber-fergusen approach was performed. The present defective situation corresponded to a Class I situation (resection performed along the palatal midline) according to the Aramany classification of defects. It seemed that there was a need of second debridement so the defect was not obturated with the help of an interim obturator.
Histopathological examination confirmed the clinical diagnosis, and after left eye enucleation intravenous amphotericin B was prescribed and the patient was under medical care in the hospital. She was in good condition and referred to prosthetic department for maxillofacial prosthetics.

**DISCUSSION**

Microangiopathy and atherosclerosis especially in diabetic patients causes ischemia which makes patients prone to infections. Thrombosis of arteries by mucormycosis invade tissues. Such invasion involve the medial wall of the orbit, medial rectal muscle, orbital apex, and ipsilateral cavernous sinus, resulting in many complications like swelling of the optic nerve and ipsilateral brain infarction. These are suggestive feature for mucurmycosis infection. Severe malnutrition, hematologic malignancies, chronic kidney disease, AIDS, immunosuppressive drugs are the most important risk factors. In our patient similar to various studies diabetes mellitus was the most important predisposing factors for zygomycosis. Prolonged use of antibiotics, corticosteroids, and immunosuppressive drugs are predisposing factors. Besides diabetes (FBS=396) our patient was under high dose corticosteroid therapy for two weeks due to diagnostic error before she was examined in our department.

Rhinocerebral mucormycosis can be misdiagnosed with bacterial cellulites, otitis media, or infections of the orbit and this fungal infection can be characterized by sinusitis and a painless, necrotic black palatal or nasal septum scar so it should be considered in all patients with chronic sinusitis, especially in immunocompromised patients. In such condition fever, decreased vision, and facial swelling are the most common complaints in the first 72 hour of the disease. Facial pain and edema, nasal congestion or discharge, headache, multiple cranial nerve palsies, necrotic turbinates, fever, and lethargy are other common complaints. Our patient had orbital edema, headache, nasal congestion facial anesthesia, nasal discharge, lethargy and multiple cranial nerve palsies. Schwartz noted that these nerve abnormalities are often consistent with orbital apex syndrome (unilateral ptosis, proptosis, visual loss, complete ophthalmoplegia, and ophthalmic and maxillary nerve anesthesia and anhidrosis).

However, in contrast to other reports many of these symptoms were absent in this patient. Soft, cool, and non-tender edema can be used in differentiation of facial edema associated with RCM with warm, tender, taut edema of periorbital cellulitis. RCM produces a paralytic ptosis in which the eyelid can be raised easily by the examiner, whereas the edematous ptosis of Cellulitis is resistant to opening. The unilateral involvement is its characteristic. The peripheral 7th nerve weakness with early ecchymosis and necrosis of ocular adenexae distinguish this disease from other causes of orbital Cellulitis and orbital apex syndrome. Central retinal artery occlusion can cause sudden-onset of blindness in rhino-orbito-cerebral mucormycosis.

The most common oral sign of mucormycosis is ulceration of the palate, which results from necrosis due to invasion of a palatal vessel. The most common intra oral site for mucor lesions is gingiva, lip and alveolar ridge which are characteristically large and deep ulcers, causing denudation of the underlying bone with differential diagnosis of tertiary syphilis, leprosy, mechanical trauma, intranasal cocaine abuse, malignancies, especially lymphomas and Wegener’s granulomatosis. Our patient did not have any oral lesion except for a palatal superficial non-specific ulcer which was due to her cracked denture. Nodular thickening of the sinus linings, absence of air-fluid level, and spotty multicentric bone destruction are the most radiographic features. Multicentric bone destruction is an important finding to distinguish mucormycosis from a carcinomatous lesion arising from the mucosa of paranasal sinuses, and the absence of air-fluid level distinguishes it from bacterial sinusitis. CT demonstrates various findings in proportion to the development of mucor invasion. Hyperintense rim along the sinus wall, hyperintense lesion on the T2-weighted images extends from paranasal sinuses to the intracranial cavity via the
orbital apex and narrowing or slow flow occurs in the ipsilateral internal carotid artery are the most specific findings caused by mucor invasion in MRI. The addition of DWI increases the imaging diagnosis of ischemic optic neuropathy, as shown in this patient.3,5,8

Characteristic histopathologic features are broad and ribbon-like hyphae with irregular branching at right angle but tissue invasion and subsequent tissue reaction to the fungi rather than just the presence of the organism confirm the diagnosis.6

Amphotericin B is the first line drug of choice for most cases of zygomycosis, but because of its adverse effects such as nephrotoxicity (30-50%), monitoring serum creatinine, potassium, magnesium levels and blood urea nitrogen (BUN) is very important. Recently, liposomal amphotericin B (where the drug has been inserted into liposomes) is claimed to produce lesser nephrotoxicity, even at higher doses. Hyperbaric oxygen therapy is believed to inhibit the growth of fungal spores and mycelium.1

Surgical treatment is always necessary, with extended resection until bleeding tissue is found. Efforts to save the ocular globe with conservative resections usually lead to a delayed enucleation and worsening of the patient condition.10 Use of other drugs such as the combination of rifampicin and amphotericin, posaconazole in amphotericin resistance or intolerance, has been reported with good results.7

Infection site, quick diagnosis, type and severity of immunosuppression and elimination of predisposing factor like correction of the underlying diabetic ketoacidosis as was done in our patient are most important in prognosis. The mortality rates were nearly 85% in earlier days; however after the introduction of combined therapy, more than 80% of the patients can be expected to survive.1 Hope for cure, however lies in early recognition and aggressive treatment. The patients with chronic form usually have a higher overall survival rate than those with the acute form.6 Clinical diagnosis in most patients was based on oral manifestations especially palatal ulceration and necrosis, but our diagnosis was based on most cranial nerves involvement. There are not many such cases as it is a rare infection. Newer cases had better prognosis and survival which may be due to better medications. On the other hand our patient is perhaps the first case with most cranial nerves involvement.

CONCLUSION

Mucormycosis is a rapidly progressive disease in which morbidity and mortality are directly related to the length of time before diagnosis and treatment. Recognition of the early signs and symptoms of the disease are most important which can be easily achieved by all clinicians.

REFERENCES