Mucormycosis of nose and paranasal sinuses with orbital complication in young diabetic

R. K. Mundra · Yamini Gupta

Abstract A case report of mucormycosis of nose and paranasal sinuses with sudden loss of vision in a young diabetic with good recovery after endoscopic debridement, systemic and topical amphotericin B and control of Diabetes mellitus.

Keywords Mucormycosis · Nose · Paranasal sinus · Diabetes mellitus · Endoscopic debridement.

Introduction

Sinonasal mucormycosis if unrecognized or inadequately treated is an acutely fatal fungal infection. It can infect CNS, GIT and Skin (in burn patient), but best known for its rhinocerebral presentation, which is initiated with sino-nasal involvement and may progress to involve orbit and brain [1]. Main stays of therapy are reversal of source of immunocompromise, systemic high dose amphotericin B, and surgical debridement of nonviable tissue. Here we report a case of 21 years diabetic (IDDM) male with diabetic Keto-acidosis (DKA) who developed mucormycosis of nose and paranasal sinuses with sudden loss of vision in right eye. He was managed successfully with three dimensional treatment approach with good recovery.

Case report

A 21-years-male patient was referred from department of medicine to ENT department with diagnosis of diabetes mellitus (D.M. type-I) with DKA with pyrexia of unknown origin. He had complaints of fever since 10 days, swelling over right upper eyelid and right cheek since 5 days, occasional purulent nasal discharge since 5 days, sudden loss of vision in right eye since 3 days.

Anterior rhinoscopy showed grayish white, slough covered middle turbinate with mucopureulent secretion in right nasal cavity, left nasal cavity patent. There was diffuse tender swelling over right maxillary antrum region.

Examination of right eye revealed proptosis inferiorly and laterally, upper eye lid edema, drooping of upper eye lid, decreased movement of right eye in upwards and inwards direction. Fundus examination of right eye showed hyperemic disc, full cup, dilated veins, two cotton wool patches and macular edema. Full blood count showed elevated WBC counts, blood glucose level was 400mg per dL, Serum bicarbonate was 10 mEq per L, urinary ketone was 5+. ELISA for HIV was negative. CT scan orbit and

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PNS (Figs. 1, 2) showed irregular infiltrating soft tissue density mass in supero-medial aspect of right orbit with infero-lateral displacement of right globe suggestive of orbital pseudotumor. Inflammatory mucosal thickening in bilateral maxillary, ethmoid and frontal sinuses (more on Rt. side) was also noted.

Nasal Endoscopy (Fig. 3) showed that right sided nasal cavity was filled with grayish white mass, destroying right middle turbinate and right lateral nasal wall, septum was

also involved by lesion on right side and nasal mucosa showed whitish-black discoloration. Left nasal cavity was patent.

Provisional clinical diagnosis of mucormycosis of nose and paranasal sinuses with orbital complication with D.M.type I with DKA (triad of hyperglycemia, ketonemia and acidemia) was made.

The treatment of DKA was started immediately with aim of improving circulatory volume and tissue perfusion, reducing blood glucose and serum osmolality towards normal level, clearing ketones from serum and urine at a steady rate, correcting electrolyte imbalance. Rehydration was done using 0.9% isotonic saline at a rate of 1L/hr with subsequent potassium replacement 30 mEq of potassium in each liter of fluid till potassium level reached 3.3 mEq/L and low-dose insulin therapy 0.1 U/kg/hour as IV infusion until blood glucose level fell by 50–70 mg/dL/hr till it reached 250 mg/dL. Patient was posted for endoscopic debridement under local anaesthesia. Fungal debris [Fig. 4] were removed by wide surgical excision and sent for histopathological Examination (HPE). Thick pureulent secretion was sucked out from right maxillary sinus and sent for culture and sensitivity.

Intravenous administration of amphotericin-B in dose of 1–1.5 mg/kg/day was started in D5% over 1–3 hrs after giving a test dose. Patient was again posted with in 72 hrs. for nasal endoscopy and debridement of residual fungal debris. Patient was continued on systemic amphotericin-B for 4 weeks with monitoring of serum creatinine and BUN levels till patient showed clinical recovery with negative cultures from nose. He was also advised alkaline nasal wash and local amphotericin-B nebulization as 4 ml of 50 mg vial

Fig. 1 CT Scan PNS

Fig. 2 CT Scan PNS and Orbit

Fig. 3 Nasal endoscopy picture (preoperative)

of I/V ampoule and 10 ml of sterile water 2–4 times daily. Patient gradually improved of his nasal complaints, vision and eye movement. Follow up nasal endoscopy was done on day 20 to ensure complete reversal of infection [Fig. 5].

HPE of fungal tissue showed soft tissue mass with extensive necrosis and large number of branched filamentous

structure, at places attempted granuloma formation seen with giant cell reaction suggestive of mucormycosis [Fig. 6]. Culture report also showed mucormycosis.

Discussion

Sinonasal mucormycosis is a relatively uncommon disease which primarily afflict diabetics, but can occur in any immunocompromised individual such as patient with neutropenia, leukemia, Chronic renal failure, long term systemic steroid therapy, protein-calorie malnutrition, solid organ and bone marrow transplantee, leukemia, intravenous drug abusers and having other immunodeficiency states.

The causative organisms are members of the family mucoraceae. *Rhizopus oryzae* is the predominant pathogen and account for 90% of rhinocerebral case of mucormycosis.⁽¹⁾ It can infect the lung, CNS, GIT, Skin (usually in burn patients) but is best known for it's rhinocerebral presentation, which is usually initiated with sinonasal involvement and may progress to involve orbit and brain [1].

The exact mechanism of increased susceptibility of diabetics is unknown, probably the affinity of *Rhizopus* for diabetic patient is related to the fact that they have active ketone reductase system so they thrive in environment rich in glucose and in acidotic conditions [2]. Once the spores enter the tissue it becomes angioinvasive and shows predilection for internal elastic lamina of arteries, veins and lymphatics. The invasion causes extensive endothelial damage, thrombosis with secondary ischemic infarction and hemorrhagic necrosis. The organism thrives in necrotic tissue and spread by direct extension along injured blood vessels [3]. Depending on degree of immunocompromise

Fig. 4 Fungal Tissue Removed from Rt. Nasal Cavity

Fig. 5 Endoscopic picture day 20

Fig. 6 Mucormycosis 45x – GMS Stain

mucormycosis may have an acutely fulminant course or a slower indolent invasive course. Infection usually begins along the middle or inferior turbinate. The leading symptom and signs reported within 72 hrs of onset of infection are fever followed by nasal ulceration or necrosis, periorbital and facial swelling or decreased vision. Ultimately 80% of patients develop a necrotic lesion on either the nasal or oral mucosa [1].

Rigid endoscopic nasal examination should be performed on every immunocompromised patient who continues to have fever of unknown origin even after 48 hours of appropriate broad-spectrum intravenous antibiotics, or who has localizing sinonasal symptoms. Nasal endoscopy findings are alteration in the appearance of the nasal mucosa. Discoloration, granulation, and ulceration often replace the normal pale-pink mucosa. Mucosal discoloration is variable and may be gray, green, white, or black. White discoloration of the mucosa indicates tissue ischemia secondary to angiocentric invasion, whereas black discoloration is a late finding signifying tissue necrosis [4]. Disease limited to the nasal cavity represent an earlier stage in the pathogenesis of acute invasive fungal rhinosinusitis, if diagnosed while confined to the nasal cavity, the disease is more amenable to complete endoscopic surgical resection, which may have a positive impact on patient survival.

A presumptive diagnosis of mucormycosis can be made histologically based on the broad ribbon like hyphae, the absence or paucity of hyphal septations with haematoxylin and eosin tissue stains and with special fungal stain like gomori methenamine silver (GMS) [1]. CT PNS is preferred over plain radiographs. In early disease plain radiographs may be normal. Only late in the progression of disease bony erosion can be appreciated [5].

The main stays of treatment for mucormycosis of the paranasal sinuses are reversal of immunocompromise state, systemic and topical amphotericin-B and surgical debridement. The first goal of therapy is control of underlying disease process. Improving circulatory volume and tissue perfusion, correction of diabetic acidosis, hyperglycemia, clearing ketones from serum and urine at a steady rate, correcting electrolyte imbalance will slow aggressive spread of disease.

Once the metabolic status is stabilized immediate surgical debridement of all devitalized tissue should be undertaken. It has important role as fungus thrives in devitalized necrotic tissue and also vascular thrombosis prevents chemotherapeutic agent from reaching the diseased tissue. Surgical techniques have evolved from Caldwell-Luc procedures and ethmoidectomies to endoscopic debridement, which benefits of is associated with better outcome [1]. Benefits of using endoscopic sinus surgery include improved visibility, minimal invasiveness and less operative morbidity especially in acutely ill patients.

Amphotericin B remains the standard drug for life threatening systemic fungal infections [6]. Intravenous ad-

ministration of amphotericin-B in dose of 1–1.5mg/kg/day was started in D5% over 1–3 hrs after giving a test dose. Cumulative dose is 2.5–3 gm, which can be individualized. Weekly monitoring of serum creatinine and BUN is done to avoid renal toxicity (azotemia.) Serum creatinine levels >3 mgm/dL and BUN 50mg/dL requires temporary discontinuation of therapy. Long-term treatment is required as the drug is fungistatic rather than fungicidal. Clinical recovery like no fever, wound healing and negative cultures from nose serves as guide for cessation of treatment. Once patient starts improving amphotericin-B is given on alternate days.

Despite its clinical effectiveness, toxicities associated with amphotericin-B administration, including infusion related reactions, electrolyte wasting and nephrotoxicity have made its use problematic with many patients. Infusion related reactions are acute in onset and extremely common, more than 50% of patients experience these. They are chills, rigors, fever, headache, nausea and malaise. Nephrotoxicity is seen in upto 80% of patients and is manifested by azotemia, electrolyte wasting (hypokalemia) and decrease in urine concentrating ability [6].

Varieties of lipid containing formulations are now available which are not only more potent but allows higher dose to be given in cases of renal toxicity. Only limitation is there high cost.

Topically amphotericin-B is given as nebulization. 4ml of 50mg vial of intravenous amphotericin-B and 10ml of sterile water (Not saline or dextrose) is nebulized 2–6 times daily [1]. Though it is not absorbed orally but still it gives unpleasant taste.

Conclusion

Aggressive evaluation of patients at risk with diagnostic nasal endoscopy, biopsy and frozen section, or immediate fungal stains of aspirated material contribute to prompt recognition and treatment, preventing an otherwise fatal outcome.

Reversal of underlying cause of Immunocompromise, institution of amphotericin B and repeated aggressive endoscopic debridement results in significantly improved prognosis especially in diabetic patients in whom the source of immunocompromise is reversible.

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