

Mucormycosis complicating Interstitial Nephritis - Two cases and brief literature review

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Introduction

Mucormycosis is a dreaded fungal infection caused by fungi of the order mucorales and German Rhizopine, Absidia and Mucor.¹ These fungi are usually found in vegetative and organic matter and have minimal intrinsic pathogenicity. However it can cause serious and fatal infection in immunocompromised conditions especially in patients who have diabetic ketoacidosis, viral hepatitis, chronic renal failure and post transplant patients² on immunosuppressive therapy.^{3,4} Other risk factors include neutropenia, use of systemic steroids, protein-calorie malnutrition, solid organ and bone marrow transplant, immunodeficiency, metabolic acidosis⁵, acute and chronic renal failure⁵, leukemia and intra venous drug abuse. We present two cases with interstitial nephritis who developed mucormycosis of rhino orbital cavity.

Case Report

Case 1

Fifty six year old non-diabetic, hypertensive female presented with recent history of rapidly deteriorating renal function. She was started on dialysis. Ultrasound showed normal renal size with no obstruction. Renal biopsy revealed marked tubulo-interstitial inflammation and extensive tubular atrophy consistent with interstitial nephritis. She was started on oral prednisolone 30mg twice daily with subsequent improvement in renal function. However, fifteen days after the start of her medication, she presented to the emergency room with headache for two days and epistaxis for one day. On physical examination, she was found to be tachycardic and febrile. She was drowsy but oriented to time, place and person with a normal neurological examination. She had a swelling over her right upper eyelid with symmetric and reactive pupils. Examination of the right nostril revealed neutrophilia. Creatinine was 7.8 mg/dl while serum bicarbonate was 9.1 mEq/L. A day later she rapidly developed right ophthalmoplegia,

ptosis and marked decrease in her visual acuity. MRI revealed diffuse infiltration of right retro-orbital fat with hypo/iso-intense material suggesting possibility of some fungal involvement (Figure 1). Nasal endoscopy showed black material in right middle turbinate which was endoscopically debrided. Her right eye and peri-orbital tissue were removed. Histopathology showed necrosis of muscle tissue along with granulomatous inflammation. Multiple broad ribbon-like fungal hyphae (mucor like) were identified. The special stain for fungus was positive (Figure 2). The eyeball itself was not involved by fungus. She was started on intravenous amphotericin for six weeks. She became clinically stable in the next two weeks.

Case 2

Fifty-five year old female diabetic, hypertensive, with mild renal impairment underwent a renal biopsy for deteriorating renal function which revealed interstitial nephritis consistent with end stage kidney disease. She was started on oral prednisolone 30mg twice daily. She presented ten days after initiation of steroids to the emergency room with nausea for four days and drowsiness for one day. On physical examination she was found to be afebrile, severely dehydrated, with a left nasal swelling. She was drowsy but with a normal neurological examination. Complete blood count revealed a WBC of 20,000/mm³. Her blood glucose was 594mg/dl. The following day she developed left sided ptosis, followed by complete ophthalmoplegia, facial weakness and arm drift. Nasal smear

- [(0)]
- [(1)]
- [(2)]

revealed moderate broad coenocytic hyphae consistent with mucormycosis. MRI showed inflammatory exudative material in left paranasal sinuses with minimal infiltration of cavernous sinus (Figure 3). She was started on intravenous amphotericin and advised for debridement and

enucleation of left eye. However, she left against medical advice.

Discussion

Two cases of rhino orbital mucormycosis are presented. Nine fatal cases of systemic mucormycosis in association with renal failure were reported by Gupta et al in 1990. The infection was disseminated in five patients, and isolated pulmonary and rhino cerebral involvement occurred in two patients each.⁶ A case of nasopalatine mucormycosis in a patient with chronic renal failure has also been reported.⁷ Non fatal rhinocerebral mucormycosis in a patient with acute renal failure has been reported by Melnick et al.⁸

The leading symptom in reported cases is fever which occurred in less than half of the individuals, followed by nasal ulceration or necrosis, periorbital or facial swelling and decreased vision. Elevated white blood cell count is an early sign in less than 20% of cases.⁹ In our cases one had fever, the other was afebrile. Both patients had leucocytosis on presentation. Neurological symptoms appeared later in both cases. Anesthesia is an early sign of invasive mucor and precedes mucosal changes. A biopsy with frozen section of the excised tissue in patients with sinusitis and poorly controlled diabetes should be promptly obtained, as nasal swab for fungal culture is inadequate for evaluating presence of mucormycosis involving the sinuses or middle turbinate.

Exposure and inhalation of spores of the mucorales is common but the nasal ciliary clearance system, however, transports these spores out of the nasal cavity effectively. Phagocytes clear spores inhaled into the lungs. In the susceptible individual, the infection usually begins along the middle or inferior turbinate. It may have an acute fulminant course or a slower indolent invasive course. In moderate to severe immunocompromised state, the progression is rapid, whereas in mild immunocompromised state, more indolent picture is seen.

The pathogenicity of the organism is characterized by a ketone reductase system and its ability to invade arterial blood vessels and sometimes veins, causing thrombosis. This contributes to the necrotic ischemic appearance so characteristic of advanced disease. Acidotic environment enhances fungal growth and ischemia limits access to phagocytes. In the largest single series to date of 126 patients with rhino cerebral mucormycosis, 70% were diabetic.¹⁰ Hyperglycemia or acidosis alone does not permit fungal growth in vivo, although acidosis without hyperglycemia has

been reported with invasivemucormycosis. Normal serum inhibits rhizopus growth, whereas serum from patients in diabetic ketoacidosis stimulates growth. Diabetics have increased available serum iron because of impaired transferrin binding, whether this explains their unique susceptibility to mucormycosis remains unknown. While one of our patients had non ketotic hyperosmolar state, the other was on dialysis. The immunosuppressive treatment made them susceptible to mucormycosis.

The standard treatment is directed towards correction of the underlying disorder, surgical debridement, intravenous antifungal agents, and possibly a new adjuvant, hyperbaric oxygen. Recently liposomal preparation of amphotericin B has been found to be less toxic and more effective than the conventional amphotericin B. Delay in diagnosis and late administration of therapy may result in high mortality.

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