Intracranial hypertension: An unusual presentation of *mucormycosis* in a kidney transplant recipient

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ABSTRACT

Idiopathic intracranial hypertension (IIH), once called pseudotumor cerebri, presents with nonspecific signs and symptoms of increased intracranial pressure and papilledema, and is associated with high risk of loss of vision. Zygomycosis is a rare but serious fungal infection seen occasionally among renal transplant recipients in the late transplant period with high mortality risk. Early diagnosis coupled with multidisciplinary care can salvage the patient from the risk of death. We present an unusual case of adult renal transplant recipient with IIH followed by rhinocerebral zygomycosis secondary to amplified immunosuppression that was managed successfully.

Key words: Amphotericin-B, idiopathic intracranial hypertension, post-renal transplant, zygomycosis

Introduction

Idiopathic intracranial hypertension (IIH) is a condition characterized by headache, papilledema, and a raised cerebrospinal fluid pressure with normal brain imaging. It commonly occurs in obese women, but is occasionally reported among pediatric chronic renal failure and renal transplant patients. We present a case of adult renal transplant recipient diagnosed with IIH, who manifested rhinocerebral zygomycosis with extraocular involvement due to escalated steroid therapy for IIH.

Case Report

A 20-year-old woman, a case of live-related post-renal transplant (haplomatch), of 5-year duration, with underlying chronic allograft nephropathy (on prednisolone 7.5 mg and azathioprine 50 mg) presented with persistent non-throbbing headache, double vision, and inability to read for 3 weeks. Examination revealed blood pressure of 140/90 mm and bilateral papilledema with restriction of left extraocular muscle movements (lateral rectus paresis). Investigations revealed anemia (Hb 8.8 g/dl), mild azotemia (serum creatinine 2.2 mg/dl and urea 57 mg/dl), normal magnetic resonance imaging (MRI), MR venogram of brain, and normal TSH. A diagnosis of IIH was made and was managed with acetazolamide, oral glycerol, escalated prednisolone dose, and antihypertensive, with continuation of basic immunosuppressive drugs.

One month later, she reported with pain and swelling in the left half of face and inability to open the left eye. Examination revealed redness and swelling of the left half of her face with eyelid edema, partial restriction of extraocular muscles of the left side, resolving papilledema, and left maxillary sinus tenderness. Computer tomography (CT) scan of paranasal sinuses showed left-sided pan-sinusitis with focal calcification [Figure 1], and MRI brain confirmed the same in addition to normal neurological structures and cavernous sinus. She underwent fiber optic endoscopic surgery of maxillary, ethmoid, and frontal sinus of the left side. Histopathologic examination of sinus material and culture confirmed zygomycosis [Figure 2]. She was started on amphotericin-B (liposomal) along with continuation of immunosuppressive drugs for next 2 months. During the course of treatment, she developed nodular swelling at inner canthus of left eye, aspirate of which showed broad branches (aseptate hyphae) of *Mucor* for which

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Access this article online	
Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.109437

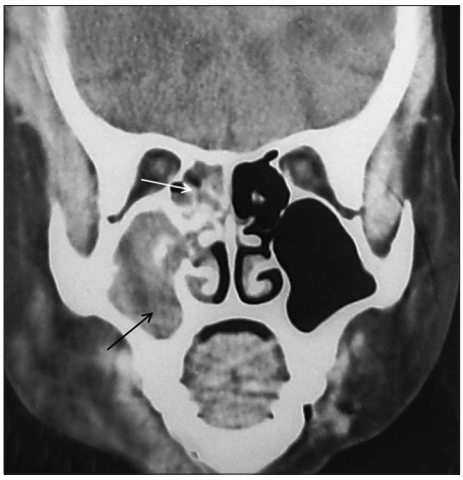

Figure 1: Computer tomography of paranasal sinuses showing involvement of the maxillary and ethmoidal sinuses by *Mucor*

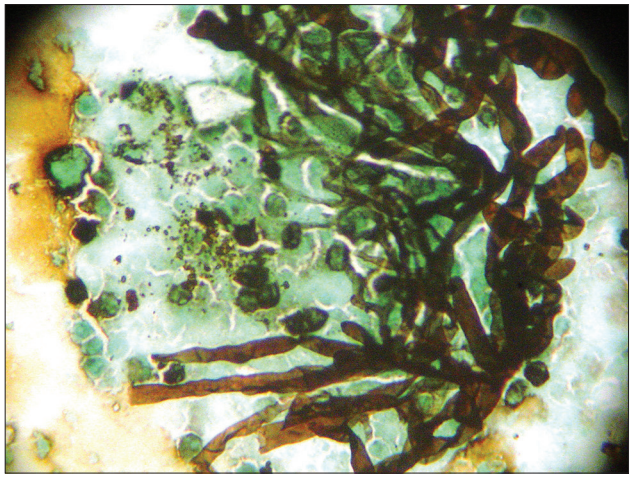

Figure 2: Methenamine silver stain showing mycelia (aseptate hyphae) and spores of *Mucor*

exenteration of the eye was suggested but declined by the patient.

She was continued on antifungal therapy and received a total of 1.9 g of amphotericin-B over 2 months along with dual immunosuppression. She continued to remain asymptomatic during the last follow-up at 5 years, with regression of the nodular swelling, improvement in vision, resolved papilledema, and stable renal parameters.

Discussion

The exact incidence of IIH in renal transplant patients is unknown, although a case series has reported it as 4.4%.[1] Several risk factors operational in the general population such as drugs, obesity, and anemia may apply in renal transplant patients as well.[1]

The presentation, as illustrated in our patient, includes persistent diffuse headache (92%), transient visual obscurations (72%), intracranial noises (60%), and diplopia (38%),[2] which in turn is due to unilateral or bilateral sixth nerve palsy. These symptoms demand extensive exploration, especially in transplant patients. Moreover, causes such as drugs in posttransplant (tetracyclines, hypervitaminosis-A, lithium, nitrofurantoin, human growth hormone, thyroxine, cyclosporine, and tacrolimus),[3-5] accelerated hypertension, and anemia[6] are all too frequent in post-renal transplant course incriminated as a causative factor for IIH. Visual impairment can be often mistaken for retinal or optic nerve disorder, hypertensive or diabetic changes, cataracts or calcification of the cornea, or choroidoretinal infections. Also, papilledema, the hallmark of IIH, is difficult to diagnose in a setting of hypertension as hypertensive retinopathy can mimic it (as depicted in our patient). Thus, IIH in renal patients can easily be missed unless looked for, and a high index of suspicion helps to prevent optic atrophy.

Zygomycosis is seldom seen in such a setting of IIH and is usually a fatal, opportunistic fungal infection caused by fungi (commonly by *Rhizopus oryzae*, *Rhizomucor*, *Mycocladus*, and *Mucor*)[7] encountered in patients with diabetes mellitus, malignancy, or those under immunosuppressive therapy. Although there are many case reports of zygomycosis in association with renal transplant,[8] rhinocerebral zygomycosis occurring in a setting of IIH in renal transplant has not been reported thus far.

Many classical diagnostic signs have been proposed such as epistaxis, partial or total ophthalmoplegia, chemosis, and periorbital edema, ptosis, exophthalmos; other signs include grayish black discoloration of the nasal turbinates, palatal ulcers, and frontal lobe signs (all seen in our patient except the latter two). The striking mycopathologic feature of zygomycosis is the vascular invasion by the fungi. Radiologically, CT is superior to MRI in demonstrating orbital involvement, mainly the lateral displacement of a thickened medial rectus muscle, increased density of the orbital apex, and enlargement of the optic nerve.[9] Orbital venography and carotid arteriography are diagnostically useful. As survival is associated with early diagnosis, a high index of suspicion and prompt diagnosis by aggressive investigation such as tissue biopsy significantly affect the treatment outcome. Progression of the disease is usually rapid and it warrants prompt and aggressive combined surgical intervention with antifungal agents.

With the introduction of combined therapy with amphotericin-B and surgery, more than 80% of the patients can be expected to survive.[10] Our patient

underwent early and repeated surgical debridement of all grossly involved tissues as emphasized in the literature on its importance for local control, especially in rhinocerebral, pulmonary, and cutaneous zygomycosis. Administration of liposomal amphotericin-B is associated with adverse effects that are less pronounced, even with administration of larger doses. We administered liposomal amphotericin-B (a total of 1.9 g) and obtained satisfactory resolution of the disease (without resorting to extirpation of the eye). Although universal recommendations on the optimal duration of liposomal amphotericin-B are lacking, factors such as the response of infection to treatment and success in resolving the underlying predisposing condition govern the duration of therapy.

Conclusion

The unusual presentation of IIH in our adult patient mandating escalated immunosuppression which in turn led to the life-threatening complication of rhinocerebral zygomycosis is a wake-up call for clinicians dispensing high-dose immunosuppression. We also highlight the importance of early identification, and aggressive medical and surgical management in tackling zygomycosis which is life-saving despite pessimistic outcomes at times in transplant setting.

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How to cite this article: Jha R, Gude D, Chennamsetty S, Kotari H. Intracranial hypertension: An unusual presentation of *mucormycosis* in a kidney transplant recipient. Indian J Nephrol 2013;23:130-2.

Source of Support: Nil, **Conflict of Interest:** None declared.