·Case Report·

Cryptococcus meningitis in an immunocompetent teenage boy presented early with diplopia

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Abstract

• AIM: To report a case of *cryptococcus* meningitis in an immunocompetent teenager that presented early with diplopia and bilateral poor vision.

• METHODS:A case report

• RESULTS:A 17-year-old boy presented with blurring of vision in both eyes and diplopia for 3 weeks. It was associated with severe throbbing headaches, nausea and vomiting. He was also having low grade fever. On physical examination he was afebrile with no sign of meningism. His vision was 6/15 in both eyes with constricted visual field. Anterior segment was normal in both eyes. Extraocular muscles movement showed bilateral sixth nerve palsies. Fundoscopy revealed bilateral hyperaemic and slightly elevated optic disc. CT scan of the brain was normal with no evidence of intracranial mass or abnormal ventricles. Lumbar puncture revealed high opening pressure >300mmH_2O. Cerebrospinal fluid (CSF) microscopically and culture showed presence of *cryptococcus neoformans*. This case was combinedly managed with neuro-medical team. Patient was started on intravenous Amphotericin B and fluconazole. His neurological symptoms recovered after a week. His vision was improved to 6/6 in both eyes with recovery of peripheral visual field. The diplopia improved with recovery of sixth nerve palsies in both eyes. Unfortunately, patient developed nosocomial lower respiratory tract infection and was treated for the problem.

• CONCLUSION: This case highlights the indolent nature of *cryptococcus* meningitis and the fact that the overt signs of meningism may not be present even in immunocompetent person. Diplopia may be one of the early presentations of meningitis patient.

• KEYWORDS: cryptococcal meningitis; papilloedema; bilateral sixth nerve palsy

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INTRODUCTION

Cryptococcus neoformans meningitis is an important and fatal infection. It is associated with immunocompromised status [1,2]. Major risk factors for this disease are human immunodeficiency virus infection, leukemia, lymphoma, organ transplant and connective tissue disorders [3-5]. We present a case of healthy, immunocompetent teenager with history of subacute onset of blurring of vision and headache without evidence of meningitis.

Case Report

A 17-year-old boy presented with blurring of vision of both eyes and diplopia for three weeks. The poor vision started gradually when he noticed difficulty in mobilising. He also noticed to have diplopia. It was associated with severe throbbing headaches, nausea and vomiting.

On general examination, he was afebrile and his vital signs were stable. The neurological examination was unremarkable. There was no sign of meningism or any focal neurological deficits. On ocular examination, his visual acuity was 6/15 in both eyes. Visual fields examination demonstrated bilateral peripheral field constriction. Anterior segment examination of both eyes showed quiet anterior chambers with no abnormalities noted. Fundoscopy revealed bilateral hyperaemia and slightly elevated discs (Figure 1). There was an impaired abduction of both eyes as well.

CT scan of the brain was normal with no evidence of intracranial mass, dilated ventricles or midline shift. Lumbar puncture demonstrated an opening pressure of more than 300mmH_2O. Cerebrospinal fluid (CSF) chemistry showed significantly elevated protein level of 85mg/dL and slightly raised glucose of 4.5mmol/L. Presence of *cryptococcus neoformans* was noted during the microscopic examination and in Indian ink preparation (Figure 2) . The Cryptococcal antigen titre was elevated of more than 256. Retroviral

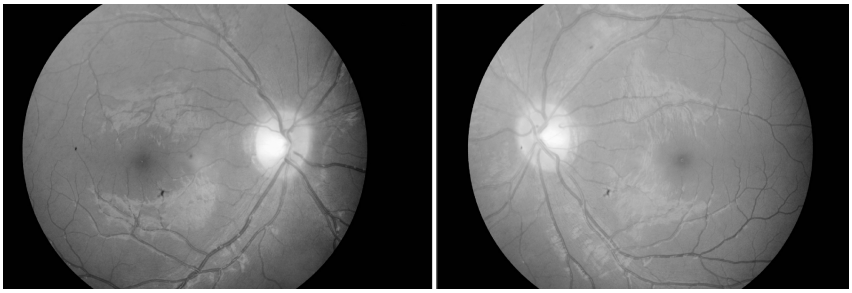

Figure 1 Optic discs appearance at presentation shows hyperaemia and blurring of disc margin in both eyes especially in the nasal area

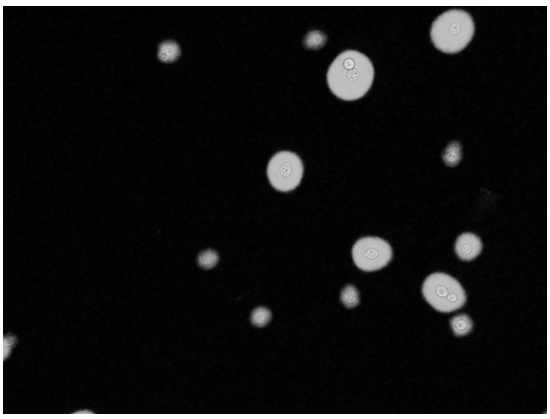

Figure 2 C *ryptococcus* in Indian ink preparation

screening was negative. He was diagnosed to have a cryptococcal meningitis.

Amphotericin B was given intravenously in titration from 0.5 to 1.0mg/ (kg·d). It was administered in combination with oral fluconazole of 200mg twice a day. Symptoms of raised intracranial symptoms were controlled by oral Frusemide 40mg once daily and Acetazolamide 250mg three times a day.

The patient showed complete resolution of the sixth nerve palsies and the visual acuity by the 8th week of hospital stay. There was slight improvement in his visual field on the day of discharge. But the papilloedema was still present and showed progression (Figure 3). Oral fluconazole 200mg twice a day was continued for six months. The patient was reviewed monthly at neurology and ophthalmology clinic to detect early sign of recurrence of the disease. Eventhough patient was symptoms free but the papilloedema seemed to progress to chronic stage (Figure 4). At the same time, periodic serum level of cryptococcal antigen was taken to monitor the response to medication.

DISCUSSION

Cryptococcal neoformansis an encapsulated, yeast-like fungus that reproduces by multiple budding. The organism is round to oval and about 4-6 micrometer in diameter. The surrounding thick capsule which consists of several polysaccharides measuring about 3-5 micrometer protects the fungus from phagocytosis [6]. It is found almost anywhere in nature but mostly concentrated in pigeon's dropping and their nesting places.

Although exposure to the organism is common, infection is rare because of substantial role of normal host defences. Therefore it is not surprising that the majority of patients who developed the disease are mostly immunocompromised. But there are circumstances where infection occurs in apparently healthy individuals such as in our case. This exception may be demonstrated by abnormalities in cell-mediated immunity [7] in otherwise immunocompetent person. An understanding of the potential defence mechanisms of a host against *cryptococcosis* would provide an insight to better understanding of the pathophysiology of the disease.

The onset of the *cryptococcal* meningitis is variable. In immunocompromised patients, the onset is usually subacute and chronic but in immunocompetent it can be acute. Most patients developed nonspecific neurological and systemic symptoms and signs. For this reason, a high index of suspicion of the disease is mandatory for early identification and treatment.

Our patient presents with neurological and ocular symptoms that related to the raised intracranial pressure. The diplopia is generally caused by bilateral sixth nerve palsy due to false localising sign. However, the optic disc does not show gross papilloedema even though the symptoms of raised intracranial pressure have been present for three weeks. The reduction in visual acuity is most probably from optic neuropathy due to inflammation or vasculitis with secondary ischaemia in any part of the optic nerve. Papilloedema is a common finding in the disease but it occurs in only one third of cases [8].

Cryptococcus meningitis does not produce any abnormalities in baseline haematological testing. However, it almost always shows an abnormal CSF. Opening pressure is often elevated of more than 200mmH_2O and there is usually pleocytosis. Protein concentration is always increased. These abnormal CSF biochemical parameters are present in our patient. But the definitive diagnosis is made through direct identification of the cryptococcal capsules through microscopic examination of the CSF.

Both CT scan and MRI are valuable in showing ventricular size and detecting intraparenchymal lesions which are absent

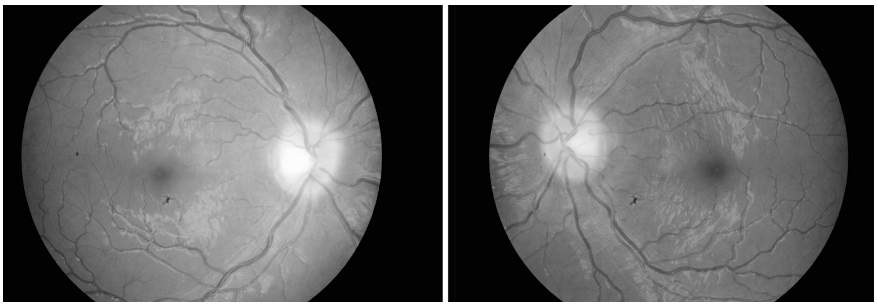

Figure 3 Pictures shows progression of the papilloedema

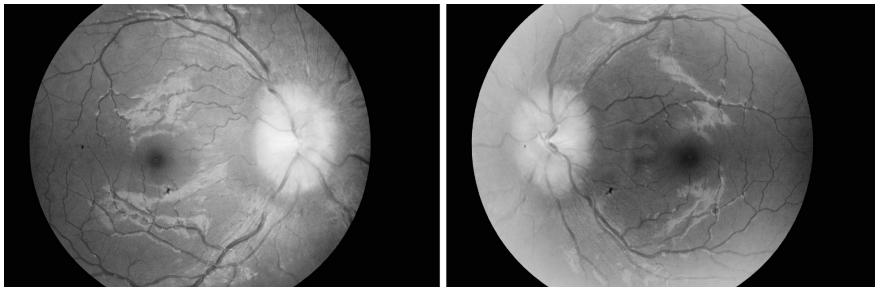

Figure 4 Pictures shows bilateral chronic papilloedema at latest follow up

in our patient. The development of intracranial hypertension without intracranial mass lesion or ventriculomegaly may lead to diagnosis of pseudotumour cerebri until CSF examination shows abnormalities consistent with infection.

Before the introduction of Amphotericin B,the disease is invariably fatal, and most cases with direct ocular involvement were positively diagnosed at necropsy or following enucleation [9]. Pappalardo *et al* [10] show that Amphotericin B exhibits fungicidal activity even though this effect is not demonstrable at higher concentration. Intravenous Amphotericin B in combination with oral fluconazole has been used successfully to treat cryptococcal meningitis. There is no evidence that the organism has developed resistance against the antifungal as yet.

Cryptococcus neoformans infection involves any part of the central nervous system leads to a wide spectrum of neurological clinical presentation. Without prompt detection of the disease, cryptococcal meningitis can cause severe neurological disability and death [11]. The mortality rate of treated cryptococcal meningitis is about 25%-30% in most patients and usually associated with hydrocephalus and its associated complications. The incidence is higher in patients with underlying neoplasm and AIDS. Those who was cured initially has 25% rate of relapse and 40% has significant residual neurological deficits. These include visual loss from optic atrophy, visual field defect from postchiasmal visual sensory system and diplopia from ocular motor nerve paresis.

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