

Cryptococcus meningitis in an immunocompetent teenage boy presented early with diplopia

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Received:2010-01-14 Accepted:2010-03-02

DOI:10.3969/j.issn.1672-5123.2010.03.005

Muslikhan Y,Hitam WHW,Ishak SR,Mohtar I,Takaran J. *Cryptococcus* meningitis in an immunocompetent teenage boy presented early with diplopia. *Int J Ophthalmol (Guji Yanke Zazhi)* 2010; 10 (3): 421-423

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 300mmH₂O. 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 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

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 > 300mmH₂O. 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

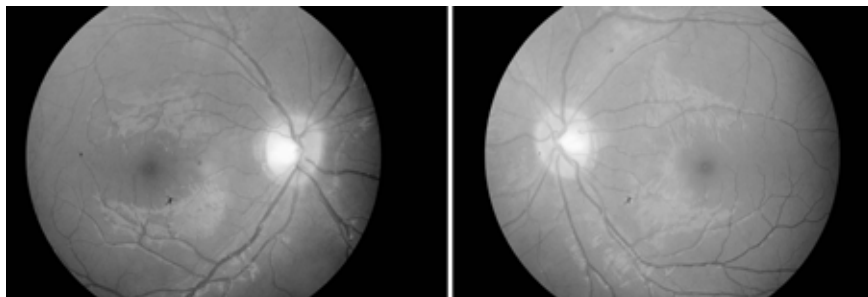


Figure 1 Optic discs appearance at presentation shows hyperaemia and blurring of disc margin in both eyes especially in the nasal area

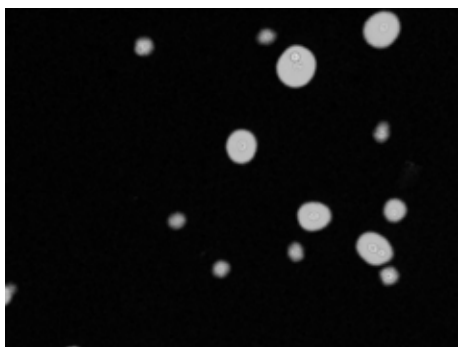


Figure 2 *Cryptococcus* Indian ink preparation

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

Cryptococcus neoformans 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 200mmH₂O 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 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.

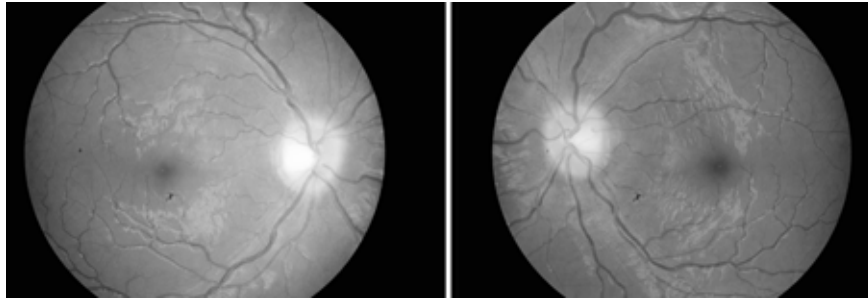


Figure 3 Pictures show progression of the papilloedema

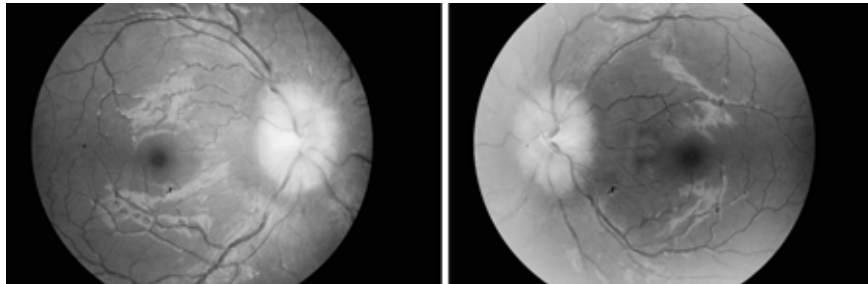


Figure 4 Pictures show bilateral chronic papilloedema at latest follow-up

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. Acknowledgements: The authors thank Nik Zahir, our Lab technician in Microbiology Department, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia for the photo of cryptococcus.

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免疫功能正常少年患早期表现为复视的隐球菌脑膜炎 1 例

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摘要

目的:报告免疫力正常少年的隐球菌脑膜炎 1 例,早期表现为复视和双眼视力低下。

方法:病例报告。

结果:男,17 岁,两眼视物模糊并复视 3wk,伴随严重的搏动性头痛、恶心、呕吐及低热。经体格检查无发热及假性脑膜炎迹象。双眼视力为 6/15 并视野缩窄。双眼前段正常。眼外肌运动表明双侧第六神经麻痹。眼底检查显示双侧视盘充血和轻度隆起。CT 扫描大脑正常,无颅内肿块或脑室异常。腰椎穿刺发现高开放压 >300mmH₂O。脑脊液显微镜下及培养均存在新型隐球菌。本例由神经医疗组联合处理。患者开始静脉注射两性霉素 B 和氟康唑,神经症状 1wk 后恢复,双眼视力提高到 6/6,同时周边视野恢复。随着第六神经麻痹的康复双眼复视得到好转。**结论:**本例强调了隐球菌脑膜炎进展缓慢的性质。即使免疫功能正常,也不会存在明显的假性脑膜炎特征,复视可能是脑膜炎患者的早期表现之一。

关键词:隐球菌脑膜炎;视乳头水肿;双侧第六神经麻痹