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## Bilateral optic neuropathy in acute cryptococcal meningitis

Qi Zhe Ngoo<sup>1</sup>, Li Min Evelyn Tai<sup>1</sup>, Wan Hazabbah Wan Hitam<sup>1\*</sup>, John Tharakan<sup>2</sup><sup>1</sup>Department of Ophthalmology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia<sup>2</sup>Department of Neurosciences, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia

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### ABSTRACT

We reported a case of cryptococcal meningitis presenting with bilateral optic neuropathy in an immunocompetent patient. A 64-year-old Malay gentleman with no medical comorbidities presented with acute bilateral blurring of vision for a week, which was associated with generalised throbbing headache and low grade fever. He also had somnolence and altered consciousness. Visual acuity in both eyes was no perception of light with poor pupillary reflexes. Extraocular muscle movements were normal. Anterior segments were unremarkable bilaterally. Fundoscopy revealed bilateral optic disc swelling. CT scan of the brain showed multifocal infarct, but no meningeal enhancement or mass. Cerebrospinal fluid opening pressure was normal, while its culture grew *Cryptococcus neoformans*. A diagnosis of cryptococcal meningitis with bilateral optic neuropathy was made. Patient was treated with a six-week course of intravenous fluconazole and started concomitantly on a fortnight's course of intravenous amphotericin B. After that, his general condition improved, but there was still no improvement in his visual acuity. On reviewing at two months post-initiation of treatment, fundi showed bilateral optic atrophy. Bilateral optic neuropathy secondary to cryptococcal meningitis was rare. The prognosis was guarded due to the sequelae of optic atrophy. Anti-fungal medication alone may not be sufficient to manage this condition. However, evidence for other treatment modalities is still lacking and further clinical studies are required.

## 1. Introduction

*Cryptococcus neoformans* (*C. neoformans*) is the most common life-threatening fungal pathogen, especially in those with immunodeficiency<sup>[1]</sup>. Cryptococcal infection typically manifests as meningitis with secondary ocular involvement. Ocular manifestations are found in about 40% of patients with papilloedema being the commonest presentation<sup>[1]</sup>. We reported a case of cryptococcal meningitis presenting with bilateral visual loss in an immunocompetent patient.

## 2. Case report

A 64-year-old Malay gentleman with no previous medical illness presented with acute onset of progressive blurring of vision in both eyes for a week. It was associated with generalised throbbing headache and low grade fever. Patient also had somnolence and altered consciousness.

On examination, visual acuity in both eyes was no perception of light with poor pupillary reflexes. Extraocular muscle movements were normal. Anterior segment examination was unremarkable in both eyes. The fundus showed bilateral optic disc swelling. Neurological examination showed increased muscle tone over all four limbs, but no lateralizing signs.

Urgent CT scan of the brain showed multifocal infarct at left corona radiata, right cerebellum and right basal ganglia but no meningeal enhancement or mass. Magnetic resonance imaging of orbit and brain showed similar findings. Optic nerves appeared to be normal bilaterally. Lumbar puncture revealed a normal opening pressure. Culture of the cerebrospinal fluid grew *C. neoformans*. HIV and other infective screening were otherwise negative. A diagnosis of cryptococcal meningitis with

\*Corresponding author: Wan Hazabbah Wan Hitam, Department of Ophthalmology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia.

Tel: +60 97676362

Fax: +60 97673370

E-mails: [hazabbah@usm.my](mailto:hazabbah@usm.my), [hazabbah@yahoo.com](mailto:hazabbah@yahoo.com)

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bilateral optic neuropathy was made. Patient was started on 200 mg of intravenous fluconazole twice a day and 40 mg (0.7 mg/kg) of intravenous amphotericin B once daily.

At the end of a two-week course of amphotericin B, together with a concomitant six-week course of fluconazole, his general condition improved with resolution of fever and restoration of normal consciousness levels. However, the visual acuity in both eyes was remained poor at no perception of light. Examination of the fundi revealed bilateral optic atrophy.

### 3. Discussion

Cryptococcal meningitis, which is an infection of the brain parenchyma and subarachnoid space by *Cryptococcus* spp., is the most common presentation of cryptococcal disease<sup>[2]</sup>. It is associated with significant morbidity and mortality<sup>[3]</sup>. *C. neoformans* is a fungus, which is commonly found in decayed wood of various trees as well as the air and soil near their tree hosts<sup>[4]</sup>. It has been identified as the main causative organism in both immunocompromised and immunocompetent patients<sup>[3,5,6]</sup>.

The most common presentation of cryptococcal meningitis is subacute headache and confusion<sup>[2]</sup>. Less frequently, patients may also present with meningeal signs and seizures<sup>[7]</sup>. Visual loss in cryptococcal meningitis has been postulated to occur due to direct infiltration of the fungus or secondary to papilloedema associated with intracranial hypertension<sup>[7,8]</sup>. Cerebrospinal fluid outflow obstruction at the arachnoid villi by the organism polysaccharide capsule is the hypothesized mechanism of the intracranial hypertension commonly seen in cryptococcal meningitis<sup>[9,10]</sup>.

Goldman *et al.*<sup>[11]</sup> reported a case of bilateral progressive vision loss with concurrent headache and neck pain in a patient with no co-morbidities. In that case, bilateral optic neuritis was associated with leptomeningeal enhancement seen on magnetic resonance imaging of the brain. Lumbar puncture revealed high opening pressure and culture of the cerebrospinal fluid grew *Cryptococcus gattii*. Seaton *et al.*<sup>[6]</sup> reviewed the ocular complications of 82 immunocompetent patients with *C. neoformans* meningitis and hypothesized that an immune-mediated optic neuropathy may be responsible for the high percentage of visual loss noted in the surviving patients. Our case parallels the findings of that study in that our patient had a poor visual outcome due to the development optic atrophy following the optic disc swelling<sup>[6]</sup>.

Cryptococcal meningitis, when left untreated, is almost always a fatal disease. However, medical treatment with intravenous amphotericin B and oral fluconazole has a guarded prognosis and permanent neurological and ophthalmic sequelae is common<sup>[12,13]</sup>. Alleviation of the increased intracranial pressure may have a role. Some treatments which had variable success in this area have repeated lumbar puncture, cerebrospinal fluid diverting procedures and optic nerve sheath fenestration<sup>[14,15]</sup>. Other researchers have suggested that since the higher rate of visual impairment experienced by immunocompetent patients with cryptococcal meningitis may be related to their underlying cell-mediated immunity and judicious use of immunosuppressive medication may pre-empt a poor visual outcome<sup>[13,16]</sup>. It is obvious that no single formula can be applied to the management of

cryptococcal meningitis, yet the optimal combination of modalities remains to be determined.

Bilateral optic neuropathy secondary to cryptococcal meningitis is rare. The prognosis is guarded due to the sequelae of optic atrophy. Anti-fungal medication alone may not be sufficient to manage this condition. However, evidence for other treatment modalities is still lacking and further clinical studies are required.

### Conflict of interest statement

The authors report no conflict of interest.

### References

- [1] Offiah CE, Naseer A. Spectrum of imaging appearances of intracranial cryptococcal infection in HIV/AIDS patients in the anti-retroviral therapy era. *Clin Radiol* 2016; **71**(1): 9-17.
- [2] Sloan DJ, Parris V. Cryptococcal meningitis: epidemiology and therapeutic options. *Clin Epidemiol* 2014; **6**: 169-82.
- [3] Chau TT, Mai NH, Phu NH, Nghia HD, Chuong LV, Sinh DX, et al. A prospective descriptive study of cryptococcal meningitis in HIV uninfected patients in Vietnam – high prevalence of *Cryptococcus neoformans* var *grubii* in the absence of underlying disease. *BMC Infect Dis* 2010; **10**: 199.
- [4] Chowdhary A, Rhandhawa HS, Prakash A, Meis JF. Environmental prevalence of *Cryptococcus neoformans* and *Cryptococcus gattii* in India: an update. *Crit Rev Microbiol* 2012; **38**(1): 1-16.
- [5] Nyazika TK, Hagen F, Meis JF, Robertson VJ. *Cryptococcus tetragattii* as a major cause of cryptococcal meningitis among HIV-infected individuals in Harare, Zimbabwe. *J Infect* 2016; **72**(6): 745-52.
- [6] Seaton RA, Verma N, Naraqi S, Wembri JP, Warrell DA. Visual loss in immunocompetent patients with *Cryptococcus neoformans* var. *gattii* meningitis. *Trans R Soc Trop Med Hyg* 1997; **91**(1): 44-9.
- [7] Espino Barros Palau A, Morgan ML, Foroosan R, Lee AG. Neuro-ophthalmic presentations and treatment of cryptococcal meningitis-related increased intracranial pressure. *Can J Ophthalmol* 2014; **49**(5): 473-7.
- [8] Corti M, Solari R, Cangelosi D, Domínguez C, Yampolsky C, Negroni R, et al. Sudden blindness due to bilateral optic neuropathy associated with cryptococcal meningitis in an AIDS patient. *Rev Iberoam Micol* 2010; **27**(4): 207-9.
- [9] Baallal H, El Asri AC, Eljebbouri B, Akhaddar A, Gazzaz M, El Mostarchid B, et al. [Cryptococcal meningitis in a patient with a ventriculoperitoneal shunt and monitoring for pulmonary sarcoidosis]. *Neurochirurgie* 2013; **59**(1): 47-9. French.
- [10] Loyse A, Wainwright H, Jarvis JN, Bicanic T, Rebe K, Meintjes G, et al. Histopathology of the arachnoid granulations and brain in HIV-associated cryptococcal meningitis: correlation with cerebrospinal fluid pressure. *AIDS* 2010; **24**(3): 405-10.
- [11] Goldman JD, Vollmer ME, Luks AM. Cryptococcosis in the immunocompetent patient. *Respir Care* 2010; **55**(11): 1499-503.
- [12] Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of America. *Clin Infect Dis* 2010; **50**(3): 291-322.
- [13] De Socio GV, Bernini L, Menduno P, Pitzurra L, Leone F, Baldelli F. Monolateral visual loss due to cryptococcal meningitis. *J Int Assoc Physicians AIDS Care (Chic)* 2011; **10**(2): 76-8.
- [14] Wang H, Ling C, Chen C, He HY, Luo L, Ning XJ. Evaluation of ventriculoperitoneal shunt in the treatment of intracranial

- hypertension in the patients with cryptococcal meningitis: a report of 12 cases. *Clin Neurol Neurosurg* 2014; **124**: 156-60.
- [15] Petrou P, Moscovici S, Leker RR, Itshayek E, Gomori JM, Cohen JE. Ventriculoperitoneal shunt for intracranial hypertension in cryptococcal meningitis without hydrocephalus. *J Clin Neurosci* 2012; **19**(8): 1175-6.
- [16] Nakajima H, Takayama A, Fujiki Y, Ito T, Kitaoka H. Refractory *Cryptococcus neoformans* meningoencephalitis in an immunocompetent patient: paradoxical antifungal therapy-induced clinical deterioration related to an immune response to cryptococcal organisms. *Case Rep Neurol* 2015; **7**(3): 204-8.