CASE SERIES

Neuro-ophthalmic presentations and treatment of Cryptococcal meningitis-related increased intracranial pressure

Angelina Espino Barros Palau, MD,[*] Michael L. Morgan, MD, PhD,[*] Rod Foroozan, MD,[†] Andrew G. Lee, MD[*,†,‡,§,‖,¶]

ABSTRACT • RÉSUMÉ

Objective: To illustrate three different ophthalmic presentations of cryptococcal meningitis (CM).

Introduction: CM is the most common manifestation of extra-pulmonary cryptococcosis. Intracranial hypertension occurs in up to 75% of patients with CM and is associated with increased mortality. CM can present to the ophthalmologist as vision loss, papilledema, abducens palsy, and/or other cranial neuropathies.

Participants and Methods: We report three cases, two *C. neoformans* and one *C. gattii*, highlighting the various CM presentations. The first was a woman immunosuppressed following kidney transplantation in whom idiopathic intracranial hypertension (IIH) was initially suspected. The second was a man immunocompromised by previously undiagnosed HIV/AIDS who presented with signs and symptoms of increased intracranial pressure. The third case is an immunocompetent man with bilateral disc edema and an incomplete macular star diagnosed with presumed neuroretinitis. Further evaluation revealed positive CSF cryptococcal antigen with culture positive for *C. gattii*.

Conclusions: Ophthalmologists should be aware that cryptococcosis can mimic more benign etiologies including IIH and neuroretinitis. Additionally, *C. gattii*, an emerging organism, can infect immunocompetent patients. In contrast to the typical treatment of increased ICP, serial lumbar punctures are recommended while acetazolamide and surgical CSF shunting may be harmful.

Objet : Illustration de trois différentes présentations ophtalmiques de la méningite cryptococcose (MC).

Introduction : La MC est la manifestation la plus commune de la cryptococcose extra-pulmonaire. L'hypertension intracrânienne affecte jusqu'à 75 % des patients atteints de MC et est associée à un accroissement de la mortalité. La MC peut présenter à l'ophtalmologiste comme pertes de la vision, l'œdème papillaire, la paralysie abductrice et/ou d'autres neuropathies crâniennes.

Participants et Méthodes : Nous faisons état de trois cas, deux *C. néoformans* et un *C. gattii*, soulignant la diversité de présentation de la MC. Le premier concernait une femme immunodéprimée à la suite d'une transplantation rénale, dans laquelle on avait d'abord soupçonné une hypertension intracrânienne idiopathique (HII). Le deuxième concernait un homme immunocompromis par le VIH/SIDA précédemment non-diagnostiqués, qui présentait des signes et symptômes de hausse de pression intracrânienne. Le troisième cas était celui d'un homme immunocompétent qui avait un œdème papillaire bilatéral et une étoile maculaire incomplète, dont le diagnostic présumait une neuro-rétinite. D'autres évaluations ont révélé un antigène cryptococcique positif dans le Liquide Céphalo-Rachidien (LCR) avec culture positive pour le *C. gattii*.

Conclusion : Les ophtalmologistes devraient être informés que la cryptococcose peut imiter les étiologies bénignes, y compris la HII et la neurorétinite. En outre, la *C. gatti*, organisme émergeant, peut infecter les patients immunocompétents. En contraste avec le traitement typique de l'augmentation de la PIC, l'on recommande des séries de ponctions lombaires, alors que l'acétazolamide et la chirurgie du shunt du LCR peut être dangereuse.

Cryptococcus neoformans is a saprophytic yeast that usually affects immunocompromised hosts. We report 3 different presentations of cryptococcal meningitis (CM). In the first, a patient with undiagnosed AIDS presented with signs and symptoms of increased intracranial pressure (ICP). In the second, an immunocompromised post-transplant patient presented with papilledema initially misdiagnosed as idiopathic intracranial hypertension (IIH). In the third, an immunocompetent male presented with bilateral disc edema and macular star formation suspicious for neuroretinitis.

Case Reports

Case 1

A 46-year-old male was referred to the neuro-ophthalmology clinic for evaluation of bilateral optic atrophy. He had been well until 3 months prior when he experienced vision loss, headache, nausea, and fever. He presented to his primary medical doctor and his local hospital emergency department several times and was diagnosed with and treated presumptively for sinusitis. His otolaryngologist questioned that diagnosis and insisted

From the *Department of Ophthalmology, Houston Methodist Hospital; [†]Baylor College of Medicine; [‡]Departments of Ophthalmology, Neurology, and Neurosurgery, Weill Cornell Medical College, Houston; [§]UTMB Galveston, Galveston; [‖]UT M.D. Anderson Cancer Center, Houston, Tex; [¶]The University of Iowa Hospitals and Clinics, Iowa City, Iowa

Originally received May. 2, 2014. Final revision Jun. 25, 2014. Accepted Jul. 15, 2014

Correspondence to Andrew G. Lee, MD, Department of Ophthalmology, Houston Methodist Hospital, 6560 Fannin Street, Scurlock 450, Houston, TX 77030; AGLee@HoustonMethodist.org

Can J Ophthalmol 2014;49:473–477
0008-4182/14/$-see front matter
http://dx.doi.org/10.1016/j.jcjo.2014.06.012

on hospitalization for magnetic resonance imaging (MRI) and lumbar puncture (LP). Contrast-enhanced MRI of the brain was unremarkable. LP showed an elevated opening pressure (OP) of 34 cm H_2O. Cerebrospinal fluid (CSF) had 18 white blood cells (WBC)/μL (75% lymphocytes, 15% monocytes, 10% neutrophils). Cryptococcal CSF antigen was positive at more than 1:128, and culture grew *C. neoformans*. Cytology and flow cytometry were negative for malignancy. HIV-1 testing was positive with a CD4 count of 16 cells/μL and a viral load of 39,000 copies/mL. The patient was started on amphotericin B and flucytosine for CM. Repeat LPs were performed to relieve ICP and monitor antigen titers.

On examination, acuity was 20/25 OD and 20/100 OS. Automated visual fields showed a right dense superior arcuate and inferior altitudinal field defect and a left central scotoma. Ishihara plates were 12/14 on the right and 0/14 on the left. There was a left relative afferent pupillary defect (RAPD). Ophthalmoscopy showed diffuse optic atrophy bilaterally. Antifungal treatment was continued.

Case 2

A 43-year-old female presented with 3 weeks of headache, horizontal diplopia, and bilateral vision loss. Medical history was significant for renal transplantation for congenital kidney disease in 2005 and repeat transplantation for focal glomerulosclerosis requiring immunosuppression for 9 years. Post-transplant kidney function was stable. She had chronic, but stable secondary renovascular hypertension, hyperlipidemia, anemia of chronic disease, and prior deep venous thrombosis events in 2005 treated with warfarin until her most recent transplant 6 months ago.

She was well until 3 weeks prior when she experienced new-onset headache followed 1 week later by horizontal binocular diplopia and blurry vision. Her comprehensive ophthalmologist noted esotropia and mild disc edema. Noncontrast brain MRI was unremarkable. She denied fever, nausea, vomiting, and transient visual obscurations. She had gained 30 pounds while on steroids after the second transplant.

On neuro-ophthalmic examination, visual acuity was 20/25 OU. Her pupils were isocoric and briskly reactive without a RAPD. Automated visual field testing was normal OU. Extraocular motility examination showed a mild abduction deficit bilaterally and a 10 prism diopter esotropia comitant in right and left gazes. Ophthalmoscopy showed Frisén grade 1 disc edema bilaterally. The remainder of the fundus was normal. The neurologic examination was unremarkable, and blood pressure was normal.

The presumptive diagnosis of IIH was made, and outpatient LP was scheduled. She subsequently experienced fever and confusion leading to hospitalization. Contrast-enhanced brain MRI showed mild diffuse leptomeningeal enhancement and punctate areas of enhancement in the pons and basal ganglia (Fig. 1).

LP yielded clear, colourless CSF with OP markedly elevated at 38 cm H_2O. Cell count showed 7 red blood cells/μL and mildly elevated 14 WBC/μL (5% neutrophils, 42% lymphocytes, and 53% monocytes). Protein measured 45 mg/dL with glucose low at 33 mg/dL.

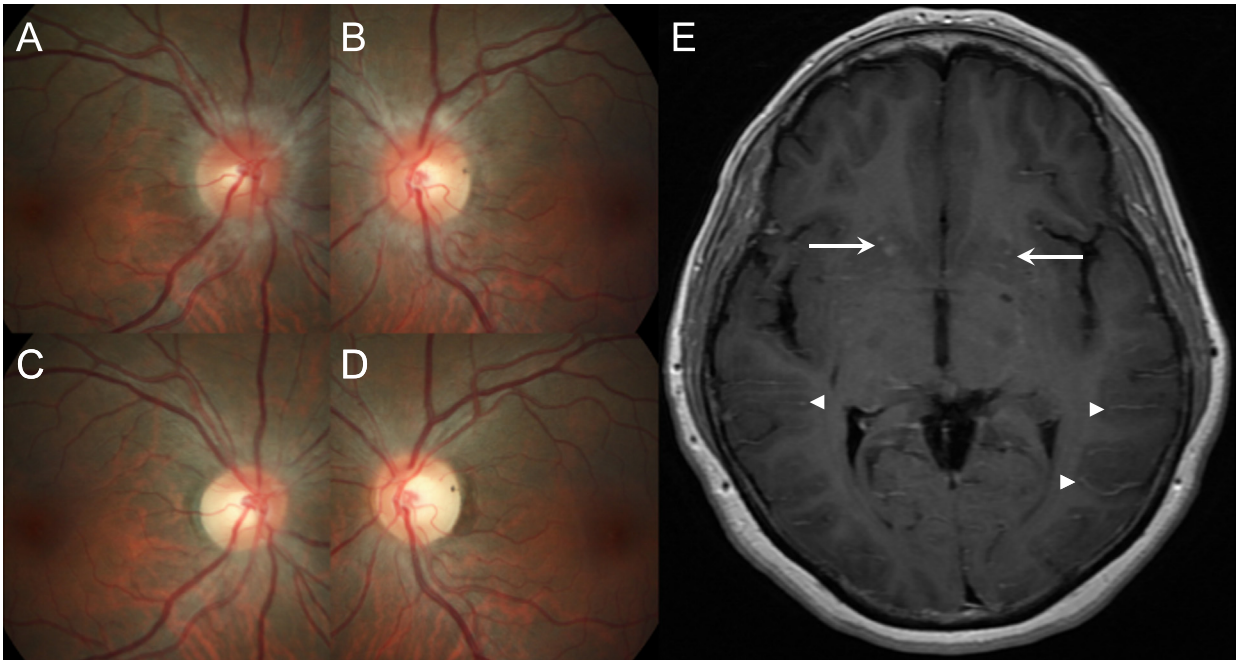

Fig. 1—Patients with *Cryptococcus neoformans*. Mild disc edema is evident (A: OD; B: OS) with resolution 5 weeks later (C: OD; D: OS). Magnetic resonance imaging T1 postcontrast (E) shows leptomeningeal enhancement (*arrowheads*) and multiple enhancing basal ganglia puncta (*arrows*).