

**Case Report**

# Meningitis secondary to *Cryptococcus gattii*, an emerging pathogen affecting immunocompetent hosts

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**BACKGROUND:** Meningitis continues to be one of the most important infections diagnosed and treated by emergency physicians. Despite the advent of anti-infective therapy, meningitis carries a mortality rate of 20%–40%. In this study, we describe the first reported emergency medicine case of meningitis associated with *Cryptococcus gattii* to alert providers of this insidious, emerging global pathogen infecting immunocompetent individuals.

**METHODS:** We provided a case report and accompanying review of the literature. A MEDLINE search for the term *Cryptococcus gattii* was performed to obtain background information on *Cryptococcus gattii*.

**RESULTS:** After two months of hospitalization, the patient was eventually discharged neurologically intact except for a continued mild bilateral hearing deficit.

**CONCLUSION:** *Cryptococcus gattii* is an emerging world pathogen, which affects otherwise healthy, immunocompetent patients and requires timely identification and treatment in order to prevent severe neurological sequelae.

**KEY WORDS:** Meningitis; *Cryptococcus gattii*

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## INTRODUCTION

Meningitis continues to be one of the most important infections diagnosed and treated by emergency physicians.<sup>[1,2]</sup> Despite the advent of anti-infective therapy, meningitis carries a mortality rate of 20%–40%. Neurologic sequelae are common in survivors and include motor deficits, seizure disorders, and visual abnormalities.<sup>[2]</sup> Favorable outcomes depend on timely diagnosis and treatment. Although the emergence of *Cryptococcus gattii* (*C. gattii*) infection has been discussed in recent emergency medicine literature, we describe the first reported emergency department (ED) case of meningitis associated with *C. gattii* to alert providers of this insidious, emerging global pathogen infecting immunocompetent individuals.<sup>[3,4]</sup>

## Case report

A 60-year-old man from southern British Columbia

presented ambulatory, in the spring of 2011, to a Vancouver area ED for further evaluation of intermittent headaches, generalized weakness, fatigue, hyponatremia, weight loss, and a recent hearing deficit. The headache and malaise symptoms had been present for two months and started when the patient and his wife vacationed in southern California. While golfing there, he experienced a thunderclap headache associated with fever, nausea and vomiting. The patient sought care at an urgent care facility and was immediately referred to the ED of a nearby academic hospital where he had a CT scan of the head, was diagnosed with sinusitis, and discharged with a prescription for clarithromycin. When his symptoms failed to improve, he returned home to British Columbia, was evaluated at another ED, and given an oxycodone prescription for symptomatic relief. The patient was then followed up with his primary care clinician who ordered an outpatient CT scan of the head which showed sinusitis. Despite completing a second course

of antibiotics- moxifloxacin, the patient continued to experience headache, malaise and fatigue. A finding of hyponatremia and worsening symptoms prompted a referral to the ED by his family physician.

The patient, a retired communications technician with no significant past medical history and whose only medications included oxycodone and acetaminophen, denied alcohol abuse, illicit drugs use, any known sick contacts, or other recent travel. He gave no history of trauma, change in vision, chest pain, cough, shortness of breath, abdominal pain, night sweats, focal weakness, paresthesias, incontinence, rash, or joint pain but admitted to a recent 10 pound weight loss, debilitating fatigue, intermittent low grade fever and, of most concern to him, gradual hearing loss which he attributed to wax build-up.

His triage vital signs were temperature 37°C (98.6°F), heart rate 127 beats/min, respiratory rate 17 breaths/min, blood pressure 118/57 mmHg, and room air oxygen saturation 98%. The patient was well-developed but appeared fatigued. The external auditory canals were full of cerumen with bilateral decreased hearing which did not improve after wax removal. His neck was supple without lymphadenopathy. The oral cavity and pharynx showed normal mucosa and good dental hygiene. Cardiovascular examination revealed tachycardia without a murmur. Respirations were unlabored and both lungs were clear to auscultation. The abdomen was soft and non-tender with no hepatosplenomegaly. The skin was warm, dry, and without a rash. Aside from subtle hearing loss and lethargy, neurological examination revealed intact cranial nerves, motor function (normal tone coordination and muscle strength against resistance), and symmetrical deep tendon reflexes.

Laboratory examination revealed that the patient had WBC of 13 800/L with a neutrophil predominance and a hemoglobin level of 12.4 gm/dL. A chemistry panel was significant for decreased sodium of 127 mmol/L, potassium 3.3 mmol/L, and chloride 91 mmol/L. Urinalysis, TSH and liver functions tests were normal. HIV antibody was negative. Chest X-ray and head CT angiogram were unremarkable. A lumbar puncture revealed an elevated opening pressure of 27 cmH<sub>2</sub>O with colorless cerebral spinal fluid (CSF) containing 59 WBC (38% neutrophils, 42% lymphocytes, 20% monocytes), 6 RBC, a low glucose of 40 mg/dL, and elevated protein level of 2.9 g/L. A cryptococcal antigen titer was strongly positive (> 1:1 024).

The patient was immediately given amphotericin B and flucytosine in doses for the immunocompetent

host and admitted to the hospital. Several days later, Cryptococcal species were identified as *C. gattii*. Upon further questioning, the patient recalled that he had visited Vancouver Island seven months earlier. After two months of hospitalization, the patient was eventually discharged neurologically intact except for a continued mild bilateral hearing deficit.

## DISCUSSION

*C. gattii* infection, previously only reported in the tropics and subtropics of Australia and South America, is now spreading to temperate zones.<sup>[4-6]</sup> It was first diagnosed in the Pacific Northwest in 1999 in a previously healthy patient from Vancouver Island. Within several years, *C. gattii* was diagnosed in residents of mainland British Columbia with no history of travel to Vancouver Island.<sup>[5-7]</sup> Since 2004, dozens of cases have been reported from Washington, Oregon, Idaho, and California.<sup>[8-10]</sup> It is an encapsulated basidiomycetous yeast, an environmental pathogen that has been isolated from many mature native trees and their detritus. It also infects native and domestic animals.<sup>[4]</sup>

*C. gattii* targets the lungs as the primary site of infection has an incubation period of six months, and can spread hematogenously to the central nervous system (CNS), skin, and eyes.<sup>[5]</sup> It affects both sexes equally and the mean age of patients at diagnosis is 59 years. Pediatric cases are uncommon.<sup>[7]</sup> Pulmonary symptoms are cough and dyspnea. Neurological symptoms include predominantly headache associated with nausea, fever (less common), muscle pain, and loss of appetite. Radiological findings may show a solid tumor – like mass, a cryptococcoma, on head CT or an infiltrate on chest X-ray. The CSF is positive for the cryptococcal antigen and, when cultured, *C. gattii* will grow on agar not routinely available in most laboratories.<sup>[5,9,11]</sup> It is important, during treatment, to monitor opening pressures on lumbar puncture as elevated intracranial pressure progressing to hydrocephalus can occur due to inflammation. Blindness, mass lesions, cranial neuropathies are additional neurological sequelae.<sup>[12]</sup>

Treatment of *C. gattii* infection of the CNS requires the use of antifungal agents for three months or longer with repeated lumbar punctures to ensure CSF sterility and monitor the hydrocephalus. Amphotericin B and flucytosine, sometimes with the concomitant use of fluconazole, are recommended.<sup>[11]</sup> If unrecognized and untreated, *C. gattii* infection of the CNS can leave patients with neurological deficits and is associated with

a fatality rate of 8.7%–20%.<sup>[8,9]</sup>

*C. gattii* infection of the CNS is difficult to recognize because of its indolent course, although, as in viral and other fungal meningitides, it can present with a thunderclap headache. Multiple visits to providers and prolonged clinical deterioration usually occur before the diagnosis and treatment of the infection. Our patient visited five health-care facilities and had two courses of treatment with antibiotics before definitive care occurred. Although he presented with the typical symptoms of *C. gattii* such as fatigue, anorexia, headache, and intermittent fever, these common nonspecific symptoms are easily misdiagnosed.

While acute bacterial meningitis is rapidly diagnosed by emergency physicians, *C. gattii* of the CNS can elude initial and subsequent evaluations because of its indolent course and paradoxical proclivity for immunocompetent individuals. Increased awareness and recognition of this insidious and globally spreading disease may facilitate earlier treatment and mitigate debilitating neurological sequelae.

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## REFERENCES

- Loring KE, Tintinalli JE. Central nervous system and spinal infections. In: Tintinalli JE, Stapczynski JS, eds. Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 7th ed. New York, NY: McGraw-Hill; 2011: 1172–1178.
- Meurer WJ, Lavoie FW. Central nervous system infections. In: Marx JA, Hockberger RS, eds. Rosen's Emergency Medicine: Concepts and Clinical Practice. 7th ed. Philadelphia PA: Elsevier Inc; 2010: 1417–1429.
- Garg M. Update on emerging infections: news from the Centers for Disease Control and Prevention. *Cryptococcus gattii*. *Ann Emerg Med* 2011; 57: 62–63.
- Springer DJ, Chaturvedi V. Projecting Global Occurrence of *Cryptococcus gattii*. *Emerg Infect Dis* 2010; 16: 14–20.
- Dixit A, Carroll SF, Qureshi ST. *Cryptococcus gattii*: An emerging cause of disease in North America. *Interdiscip Perspect Infect Dis* 2009; 2009: 840452. Epub 2009 May 25.
- Fyfe M, MacDougall L, Romney M, Starr M, Pearce M, Mak S, et al. *Cryptococcus gattii* infections on Vancouver Island, British Columbia, Canada: Emergence of a tropical fungus in a temperate environment. *Canada Communicable Disease Report* 2008; 34: 1–12.
- Galanis E, MacDougall L. Epidemiology of *Cryptococcus gattii*, British Columbia, Canada, 1999–2007. *Emerging Infect Dis* 2010; 16: 251–257.
- Upton A, Fraser JA, Kidd SE, Bretz C, Bartlett KH, Heitman J, et al. First contemporary case of human infection with *Cryptococcus gattii* in Puget Sound: Evidence for spread of the Vancouver Island outbreak. *J Clin Microbiol* 2007; 45: 3086–3088.
- Centers for Disease Control and Prevention. Emergence of *Cryptococcus gattii* – Pacific Northwest, 2004–2010. *Morbidity and Mortality Weekly Report* 2010; 59: 865–868.
- Okamoto K, Hatakeyama S, Itoyama S, Nukui Y, Yoshino Y, Kitazawa T, et al. *Cryptococcus gattii* Genotype VGIIa infection in man, Japan, 2007. *Emerg Infect Dis* 2010; 16: 1155–1157.
- Berrie C. Outbreak of *Cryptococcus gattii* infection in humans in British Columbia. Presented at: Joint 17th European Congress of Clinical Microbiology and Infectious Diseases and 25th International Congress of Chemotherapy, April 1, 2007; Munich, Germany.
- Rauchway AC, Husain S, Selhorst JB. Neurological presentations of fungal infections. *Neurological Clinics* 2010; 28: 293–309.

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