

## Clinical Case Report

### Cryptococcoma of the brain in an immunocompetent man

Y. UGALDE HERNANDEZ, J.F. MONZÓN, R. DELGADO-HERNÁNDEZ, J.L. SOTO-HERNÁNDEZ, G. CÁRDENAS

#### ABSTRACT

Cryptococcosis is a common opportunistic systemic disease in immunocompromised patients. Pulmonary or brain cryptococcosis is the most common clinical presentation. Immunocompetent patients can also be affected, especially in tropical and subtropical zones where the life cycle of the causal agent, *Cryptococcus gattii*, is completed.

We present a previously healthy man with progressive intracranial hypertension and a right paraventricular mass on CT scan and MRI. *Cryptococcus gattii* yeasts were isolated from the cerebrospinal fluid. A ventriculoperitoneal shunt was placed and the patient was treated with amphotericin B, fluconazole and dexamethasone. The patient died due to severe intracranial hypertension.

Natl Med J India 2013;26:216–17

#### INTRODUCTION

*Cryptococcus gattii* and *Cryptococcus neoformans* are causal agents of cryptococcosis, which frequently manifest as pneumonia and meningitis. Immunocompromised patients such as those with HIV infection and recipients of solid organ transplants are frequently affected. Recently, *C. gattii* has re-emerged as an important pathogen in immunocompetent patients.<sup>1,2</sup>

Although infections due to *C. gattii* have been regarded as geographically restricted to tropical and subtropical climates, an unprecedented emergence of this infection in humans and animals has been recognized in non-tropical climates such as the Pacific Northwest region.<sup>2</sup>

#### THE CASE

A previously healthy 34-year-old man presented to the emergency room with a 3-month history of headache, vomiting and blurred vision. His pulse rate was 80 per minute, blood pressure 110/80 mmHg and respiratory rate 18/minute. No rales, ronchi or abnormal sounds were heard on pulmonary examination. There was no hepatosplenomegaly. Examination of the central nervous system (CNS) revealed papilloedema, bilateral abducens nerve palsy and signs of meningeal irritation. Enzyme-linked immunosorbent assay (ELISA) for HIV and venereal disease research laboratory (VDRL) test were negative. The leukocyte count was 7500 cells/

cmm and the haemoglobin level was 15 g/dl. Liver enzymes and C-reactive protein levels were normal as was a chest X-ray. CT and MRI scans of the brain showed asymmetrical hydrocephalus and a right paraventricular mass (Fig. 1). Due to severe intracranial hypertension a ventriculoperitoneal shunt was placed. The ventricular cerebrospinal fluid (CSF) analysis revealed a glucose level of 60 mg/dl, proteins 63 mg/dl and 16 cells/cmm. Yeast grew on CSF culture and was later identified as *C. gattii* by growth on canavanine–glycine–bromothymol-blue selective media. Amphotericin B, fluconazole and dexamethasone were started. Despite treatment, the patient died after 5 days.

#### DISCUSSION

Cryptococcal infections of the brain usually present as meningitis and rarely as cryptococcomas. The disease may affect people of any age, most commonly between 30 and 40 years. Men are affected more often than women. Geographical and climatic differences play a role in the observed variability in disease occurrence.<sup>3</sup>

*C. gattii* is an emerging fungal pathogen that may produce focal lung or brain cryptococcomas associated with hydrocephalus, cranial nerve palsies and seizures.<sup>4,5</sup> Earlier, cases were reported mainly from the tropical and subtropical regions. More recently, outbreaks have been reported from Vancouver island, British Columbia, mainland Canada and Northwest USA.<sup>6</sup> Isolation of *C. gattii* from Europe (Spain), Australia, South Africa and Southeast Asia has shown that infections can also occur in temperate and subtropical climates.<sup>7</sup> *C. gattii* shares all the major virulence factors of *C. neoformans*.

Once phagocytosed by alveolar macrophages, fungal cells are killed by a concerted mechanism, involving the host cellular response. If the cellular response is impaired, phagocytosis of fungi may be detrimental to the host, since the pathogen can grow within macrophages.

CNS cryptococcosis has a poor prognosis and a mortality rate

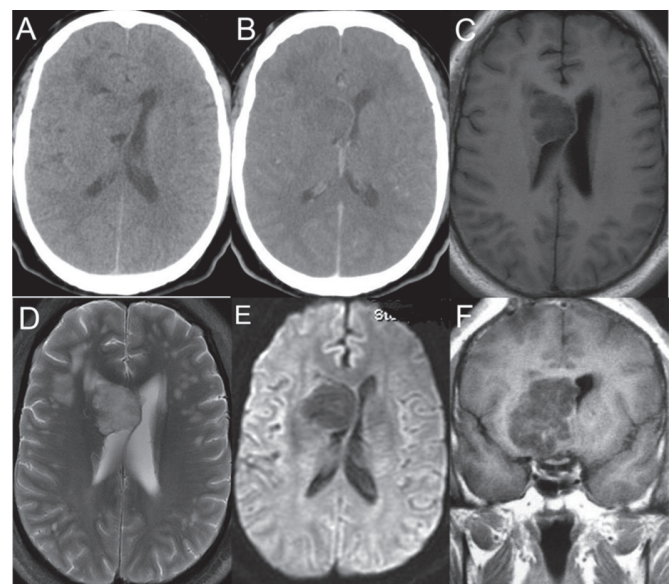


Fig 1. Axial CT scan (A, B) at the time of admission and MRI sequences (C–F) show a defined paraventricular cryptococcoma involving the right basal ganglia

Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Insurgentes Sur 3877, Tlalpan CP. 14269, México, D.F., México

Y. UGALDE HERNÁNDEZ, J.F. MONZÓN, J.L. SOTO-HERNÁNDEZ, G. CÁRDENAS Department of Infectious Diseases

R. DELGADO-HERNÁNDEZ Department of Neuroradiology

Correspondence to G. CÁRDENAS; [grace\\_goker@yahoo.de](mailto:grace_goker@yahoo.de)

© The National Medical Journal of India 2013

as high as disseminated cryptococcosis. The treatment of cryptococcosis is based on the guidelines of the Infectious Diseases Society of America, which depend on the patient's immune profile, the infected organ system, and the species type. Treatment is the same for both *C. neoformans* and *C. gattii*.

Amphotericin B and 5-flucytosine should be administered for 6 weeks intravenously followed by a further 6–18 months of oral treatment with fluconazole. Despite this, some patients may need surgery.<sup>8</sup> Managing increased intracranial pressure is important as well; an opening pressure of 250 mmH<sub>2</sub>O or above is considered as a predictor of poor clinical response. Cryptococcal infections are less frequent in non-HIV patients but constitute a life-threatening condition that requires prolonged hospital stay, lengthy treatment regimens and have long-term sequelae.<sup>4,8,9</sup>

Although several laboratory methods exist for diagnosing cryptococcosis, clinical and radiological diagnosis is a major challenge. The spectrum of MR and CT findings ranges from no apparent abnormalities to meningeal enhancement, hydrocephalus and meningoencephalitis in the form of either a pseudocyst in the basal ganglia or granulomatous lesions. On T<sub>1</sub>-weighted images, avascular pseudocysts are hypointense and on T<sub>2</sub> they are hyperintense without enhancement after administration of contrast medium. Meningeal involvement is often inferred from progressive hydrocephalus, but neither meningeal enhancement nor hydrocephalus is specific for cryptococcosis.<sup>10</sup>

Fungal infections of the CNS are increasingly recognized throughout the world. The infection is usually seen in immunocompromised patients, but some fungi are known to affect apparently immunocompetent hosts. Though involvement of the CNS in most instances is a part of a disseminated infection, a few fungi are predominantly neurotropic. On searching PubMed using 'brain cryptococcoma' and 'non-immunocompromised', we found six reported patients (Table I).<sup>11–14</sup> Clinically, the patients had different syndromes depending on the location of the lesion; the most common was headache associated with intracranial hypertension. Four patients had intracranial hypertension, and the others presented with seizures and headache. CSF findings were available in 3 patients, and 2 of them showed pleocytosis. Patients were treated with amphotericin B and 5-flucytosine; only one patient required surgery along with pharmacological treatment. None of the patients were infected by *C. gattii*.

In addition to fungal cultures and serological tests, MRI findings may provide clues to early clinical diagnosis. Antifungal drug susceptibility testing needs to be improved to guide selection.

### Conclusion

Cryptococcosis is usually seen in immunocompromised hosts. However, it is important to diagnose it when it presents in an immunocompetent patient. Despite antifungal drug therapy, the infection is associated with a high mortality rate. MRI can provide clues to diagnosis, but fungal culture and serology is required. Antifungal drug sensitivity may improve clinical outcome.

### REFERENCES

- 1 Chaturvedi V, Chaturvedi S. *Cryptococcus gattii*: A resurgent fungal pathogen. *Trends Microbiol* 2011;**19**:564–71.
- 2 Bartlett KH, Kidd SE, Kronstad JW. The emergence of *Cryptococcus gattii* in British Columbia and the Pacific Northwest. *Curr Infect Dis Rep* 2008;**10**:58–65.
- 3 Garg M. Update on emerging infections: News from the Centers for Disease Control and Prevention: *Cryptococcus gattii*. *Ann Emerg Med* 2011;**57**:62–3.
- 4 Byrnes EJ 3rd, Bartlett KH, Perfect JR, Heitman J. *Cryptococcus gattii*: An emerging fungal pathogen infecting humans and animals. *Microbes Infect* 2011;**13**:895–907.
- 5 Oliveira Fde M, Severo CB, Guazzelli LS, Severo LC. *Cryptococcus gattii* fungemia: Report of a case with lung and brain lesions mimicking radiological features of malignancy. *Rev Inst Med Trop Sao Paulo* 2007;**49**:263–5.
- 6 Datta K, Bartlett KH, Baer R, Byrnes E, Galanis E, Heitman J, *et al.* *Cryptococcus gattii* Working Group of the Pacific Northwest. Spread of *Cryptococcus gattii* into Pacific Northwest region of the United States. *Emerg Infect Dis* 2009;**15**:1185–91.
- 7 Bovers M, Hagen F, Kuramae EE, Hoogveld HL, Dromer F, St-Germain G, *et al.* AIDS patient death caused by novel *Cryptococcus neoformans* x *C. gattii* hybrid. *Emerg Infect Dis* 2008;**14**:1105–8.
- 8 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**:291–322.
- 9 Ma H, May RC. Virulence in *Cryptococcus* species. *Adv Appl Microbiol* 2009;**67**:131–90.
- 10 Caldemeyer KS, Mathews VP, Edwards-Brown MK, Smith RR. Central nervous system cryptococcosis: Parenchymal calcification and large gelatinous pseudocysts. *AJNR Am J Neuroradiol* 1997;**18**:107–9.
- 11 Díaz-Pérez JA, García-Vera JA, Mantilla-Hernández JC, Pradilla-Ardila G. [Cryptococcoma in the central nervous system of a non-immunocompromised patient.] *Rev Neurol* 2008;**46**:97–101.
- 12 Gologorsky Y, DeLaMora P, Souweidane MM, Greenfield JP. Cerebellar cryptococcoma in an immunocompetent child: Case report. *J Neurosurg* 2007;**107** (4 Suppl):314–17.
- 13 Arayawichanont A, Prayoonwivat N, Churojana A, Sangruchi T, Pongvarin N. Successful medical treatment of multiple cryptococcomas: Report of a case and literature review. *J Med Assoc Thai* 1999;**82**:991–9.
- 14 Hospenthal DR, Bennett JE. Persistence of cryptococcomas on neuroimaging. *Clin Infect Dis* 2000;**31**:1303–6.

TABLE I. Previous reported cases of cryptococcoma of the central nervous system in immunocompetent patients

Author (year)	Age (years)/gender	Onset of symptoms	Neurological syndrome	Topography of lesion	Cerebrospinal fluid			Treatment	Clinical outcome
					Cells/cmm	Proteins (mg/dl)	Glucose (mg/dl)		
Díaz-Pérez <i>et al.</i> <sup>11</sup> (2008)	24/Female	1 day	Epilepsy	Right frontal	0	12	69.4	Surgery and fluconazole	Improvement
Gologorsky <i>et al.</i> <sup>12</sup> (2007)	11/Male	14 days	ICH	Right cerebellar hemisphere	No data	No data	No data	Amphotericin B, 5-flucytosine and fluconazole	Improvement
Arayawichanont <i>et al.</i> <sup>13</sup> (1999)	35/Male	No data	ICH	Frontoparietal	Pleocytosis	—	Low	Antifungals and steroids	No data
Hospenthal and Bennett <sup>14</sup> (2000)	62*/Male	Few days	Headache and blurred vision	Frontal bilateral	90	No data	12	Amphotericin B, 5-flucytosine and fluconazole	Improvement
	26/Male	Few days	ICH	Left caudate nucleus	No data	No data	No data	Amphotericin B and 5-flucytosine	Improvement
	18/Male	2 months	ICH and cranial neuropathy	No data	No data	No data	No data	Amphotericin B and oral 5-flucytosine	Improvement

\*Previous pulmonary cryptococcosis ICH intracranial hypertension