Cryptococcus gattii meningitis in a young adult in South India: A case report

Alagiri Sivaranjini, Sekar Uma, Kindo Anupma Jyoti, V. Shankar

ABSTRACT

Introduction: *Cryptococcus* species is one of the leading causes of invasive fungal infections in the world today. The clinical differences between the two *Cryptococcus* species, namely, *Cryptococcus neoformans* and *Cryptococcus gattii* depends on the ecology, epidemiology, virulence of the strain and immune status of the host. *Cryptococcus gattii* is an environmental fungus of the tropics and subtropics but is now known to cause sporadic infections in non-endemic regions as well.

Case Report: This paper reports a case of cryptococcal meningoencephalitis in a young, immunocompetent male, in South India, which is deemed a non-endemic region for *Cryptococcus gattii* infections. The patient presented with sub acute symptoms of headache and visual disturbances of two months duration. Cerebrospinal fluid was sent for investigation. Diagnosis was done by demonstration of capsule by microscopy, culture, detection of capsular antigen by latex agglutination and further confirmed by gene sequencing. In spite of intensive therapy, the disease progressed rapidly and the patient succumbed to the infection.

Conclusion: *Cryptococcus gattii*, which was reported as a fungal pathogen of the endemics, is no longer considered as an accidental pathogen. Prompt detection and timely intervention is of utmost importance in treating this serious infection.

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CASE REPORT

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Keywords: *Cryptococcus gattii*, *Cryptococcus neoformans*, Invasive fungal infections, Meningitis

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INTRODUCTION

Invasive fungal infections are a significant threat to immunocompromised patients. Recently, reports of systemic mycosis in previously healthy individuals are on the rise [1]. This may be attributed to the evolution of the fungal pathogens with increased virulence. This necessitates a high index of suspicion for fungal infections with atypical presentations.

Cryptococcus neoformans species complex belongs to the phylum Basidiomycota. These group of yeasts can cause fatal infections of the central nervous system, lung and skin not only in humans but also in animals.

C. neoformans var. *grubii* (serotype A) and *C. neoformans* var. *neoformans* (serotype D) have been isolated worldwide, causing disease in immunocompromised hosts. *C. neoformans* var. *gattii* (serotype B and C), has been recently elevated to species level as *Cryptococcus gattii*, due to its phenotypic and molecular differences [2, 3]. Moreover, *C. gattii* infects mainly immunocompetent hosts. It is an environmental fungus, first isolated in Vancouver Islands, British Columbia in 1970. By two decades, it has been associated with 176 cases and 8 deaths worldwide [3, 5]. This fungi is generally restricted geographically to the tropical and subtropical climates [6]. It spreads through the inhalation of spores. It is known to produce large space occupying lesions. The sequencing of the genomes of the two species reveals distinct functional differences in similar genes. The microevolution in the genome of *C. gattii* has lead to a change in its ecological niche and its virulence factors, which explains reports of sporadic cases of *C. gattii* infections in non-endemic regions [6]. *C. gattii* meningitis requires a more aggressive and longer duration of therapy when compared to *Cryptococcus neoformans*. Though reported rarely, prevalence of *C. gattii* infections is now on the rise [7].

This paper describes a case of primary central nervous system (CNS) cryptococcosis caused by *C. gattii*. The infection was diagnosed by detection of Cryptococcal capsular antigen and demonstration of capsulated yeast cells in negative staining microscopy and further confirmed by culture and gene sequencing.

CASE REPORT

A 24-year-old unmarried male presented to our hospital with chief complaints of headache, bilateral visual disturbance (diplopia), photosensitivity and intermittent fever. He was an engineering graduate by profession, with no history of travel in the previous 5 years. He gave no history of association with animals. His residence was not in proximity to any vegetation which might serve as a source of *Cryptococcus* infection. He was seronegative for retroviral infection and had no overt immunodeficiency state. It was later found that his CD4 count was below normal (292 cells/mm³). On admission, his systemic examination revealed no abnormalities. Ocular examination showed bilateral lateral rectus palsy and papilledema. Computed tomography (CT) scan and magnetic resonance imaging (MRI) scan of brain were normal. As the patient developed increasing drowsiness and restlessness, he was admitted in the ICU with a provisional diagnosis of meningoencephalitis.

Lumbar puncture was done in which cerebrospinal fluid pressure was high. The CSF parameters showed: sugar-3 mgs/dl, protein 73mg/dl, white blood cells 63 cells/cm³, red blood cells 26 cells/cm³. Gram staining of CSF revealed occasional pus cells and plenty of yeast cells with a clear halo, suggestive of capsule (Figure 1). Negative staining with India ink showed plenty of capsulated

yeasts, compatible with *Cryptococcus* species (Figure 2). Fungal culture of the CSF sample on Sabouraud's dextrose agar yielded cream colored, mucoid colonies, which were identified as *Cryptococcus gattii* by VITEK 2 (BioMerieux, Inc, Durham NC, USA, panel YST 21 343) (Figure 3). The identification was further confirmed by gene sequencing. The sequence has been submitted to the databank. The accession number is BankIt1828989 *Cryptococcus* KTO27381.

The patient was started on Injection amphotericin B for treatment of meningitis, but since he developed anaphylactic reaction to it, the medication was discontinued. Fluconazole 400 mg per day plus flucytosine 100 mg/kg/d in 4 divided doses was given since this patient was unable to tolerate amphotericin B. He was put on mechanical ventilation. A therapeutic lumbar puncture was done to decrease the raised intracranial pressure. A repeat CT brain, done at this point of time, revealed diffuse cerebral edema (Figure 4). A repeat MRI could not be performed. The patient's condition deteriorated through a period of 16 days. Cardiopulmonary decompensation and superadded bacterial infections worsened his condition.

Figure 1: Gram stain of the cerebrospinal fluid showing round to oval budding yeast cells ranging from 5–20 μm in size, with clearing around them suggestive of capsule (Magnification x100).

Figure 2: Direct microscopy of cerebrospinal fluid with 10% Nigrosin showing round to oval yeast cells ranging from 5–20 μm in size with a distinct halo, suggestive of capsule (Magnification, x100).

Figure 3: 48 hr old culture of *Cryptococcus gattii* on Sabouraud Dextrose agar without actidione showing mucoid, cream colored colonies.

Figure 4: Computed tomography scan of brain (plain study) showing diffuse cerebral edema.

After three weeks of intensive therapy, he succumbed to the infection.

DISCUSSION

Being an environmental fungus of the tropics and subtropics, *Cryptococcus gattii* has been reported as an accidental infection in apparently immunocompetent individuals, with history of residing in or recent travel to an endemic area like British Columbian Islands and North West Pacific Coast of America. It has a specialized ecological niche in eucalyptus and almond trees [4, 7]. *C. gattii* more frequently causes pulmonary infections while *C. neoformans* has increased cerebral tropism [8]. *C. gattii* meningitis is characterized by larger space occupying lesions than *C. neoformans*, and associated with more neurological complications increased incidence of neurosurgical intervention and delayed

response to therapy [1, 9]. Radiographic imaging is used to identify mass lesions, which may be the primary finding in this indolent infection. Phenotypically, *C. gattii* is differentiated from *C. neoformans* by L-Canavanine-glycine-bromothymol blue agar. Serotypic determination can be by slide agglutination tests. Molecular methods like PCR and gene sequencing aid in the confirmation of the isolate to species level. Cryptococcal meningitis is treated in 3 phases: Induction (AmpB plus Flucytosine for 2 weeks), Consolidation (Fluconazole for 8 weeks) and Maintenance (Fluconazole for 6 months to 1 year).

The first report of *C. gattii* as a pathogen was in 1896 by pathologist, Ferdinand Curtis. First case of human meningitis by *C. gattii* was reported in 1999 in Vancouver Islands, British Columbia, Canada [5]. Nearly 60 cases of *C. gattii* infection have been reported in United States during the outbreak in 2006–2010. Between 2004 and 2011, 96 cases of *C. gattii* infections were reported from Pacific Northwest. In India, the first case of *C. gattii* infection in an AIDS patient was documented by Abraham et al. [8]. Chakrabarti et al. reported five isolates of *C. gattii* from eucalyptus trees in Northern India, and traced the origin of these trees to Australia, thus validating spread of *C. gattii* infection in nonendemic areas [10]. Marriott et al. recorded five cases of *C. gattii* meningitis among seven HIV patients with cryptococcal infection [11]. Few reports of *C. gattii* meningitis among immunocompetent population of India and other countries are tabulated (Table 1) [12]. It is inferred that though there have been sporadic cases of *C. gattii* infections in immunocompetent individuals, isolated primary cerebral cryptococcosis is found to be rare.

Table 1: Few Reports of cerebral *Cryptococcus gattii* infections in immunocompetent patients globally.

Reported By	Year	Site	Geographical Area
Zahra et al.	2003	Cerebral	Malta, Southern Europe
Georgi et al.	2009	Cerebral	Zurich, Switzerland
Shu Hao Chang	2009	Disseminated (Cerebral & Cutaneous)	Taichung, Taiwan
Manoj Kumar Pranigrahi et al.	2010	Disseminated (Pulmonary & Cerebral)	Tamilnadu, India
Suchitha et al.	2012	Disseminated (Cutaneous, Pulmonary & Cerebral)	Mysore, India
Rajesh T Patil et al.	2013	Cerebral	Uttarakhand, India
Olivia Cometti et al.	2014	Cerebral	Cuiaba, Brazil

The present report is a case of *C. gattii* meningitis in a young adult who was seronegative for HIV infection and apparently immunocompetent. He presented with indolent signs of meningitis like intensifying headaches and diplopia of two months duration, which later progressed to acute cryptococcal meningitis. Further, anaphylaxis to amphotericin B posed a hurdle in clearing the cryptococcal infection. Hence, the patient was started on fluconazole combined with flucytosine. However, the combination of fluconazole and flucytosine is clinically inferior to amphotericin B-based therapy. The patient expired after 23 days of stay in the intensive care unit.

CONCLUSION

This case report heralds the need for suspicion of *Cryptococcus gattii* infection even in non-endemic regions. It contradicts the popular belief that invasive cryptococcosis is usually caused by *Cryptococcus neoformans* and not by *Cryptococcus gattii*. Environmental and clinical surveillance of cryptococcosis is important in preventing under reporting of *C. gattii* infections in non-endemic areas.

Author Contributions

Sivaranjini Alagiri – Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

Uma Sekar – Substantial contributions to conception and design, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Anupma Jyoti Kindo – Substantial contributions to conception and design, Analysis of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

V. Shankar – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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REFERENCES

1. Perfect JR. The triple threat of cryptococcosis: it's the body site, the strain, and/or the host. *MBio* 2012 Jul 10;3(4). pii: e00165–12.
2. Smith RM, Mba-Jonas A, Tourdjman M, et al. Treatment and outcomes among patients with *Cryptococcus gattii* infections in the United States Pacific Northwest. *PLoS One* 2014 Feb 19;9(2):e88875.
3. Kwon-Chung KJ, Boekhout T, Fell JW, Diaz M. Proposal to conserve the name *Cryptococcus gattii* against *C. honduricus* and *C. bacillisporus* (Basidiomycota, Hymenomycetes, Tremellomycetidae). *Taxon* 2002;51(4):804–6.
4. McLaughlin J. *Cryptococcus gattii*-An Emerging Infectious Disease in the Pacific Northwest. *State of Alaska Epidemiology-Bulletin* 2010;27.
5. Galanis E, Waters S, Li M, Hoang L, MacDougall L, Phillips P. *Cryptococcus gattii* in BC: Update on an emerging disease. *BCM J* 2007;49(7):7374–5.
6. Kidd SE, Hagen F, Tschärke RL, et al. A rare genotype of *Cryptococcus gattii* caused the cryptococcosis outbreak on Vancouver Island (British Columbia, Canada) *Proc Natl Acad Sci U S A*. 2004 Dec 7;101(49):17258–63.
7. Springer DJ, Chaturvedi V. Projecting global occurrence of *Cryptococcus gattii*. *Emerg Infect Dis* 2010 Jan;16(1):14–20.
8. Heitman J. Clinical perspectives on *Cryptococcus neoformans* and *Cryptococcus gattii*: implications for diagnosis and management. *ASM*; 2012. p. 595–606.
9. Cogliati M. Global Molecular Epidemiology of *Cryptococcus neoformans* and *Cryptococcus gattii*: An Atlas of the Molecular Types. *Scientifica (Cairo)* 2013;2013:675213.
10. Chakrabarti A, Jatana M, Kumar P, Chatha L, Kaushal A, Padhye AA. Isolation of *Cryptococcus neoformans* var. *gattii* from *Eucalyptus camaldulensis* in India. *J Clin Microbiol*. 1997 Dec;35(12):3340–2.
11. Nagarathna S, Kumari HB, Arvind N, Prevalence of *Cryptococcus gattii* causing meningitis in a tertiary neurocare center from south India: a pilot study. *Indian J Pathol Microbiol*. 2010 Oct-Dec;53(4):855–6.
12. da Costa MM, Teixeira FM, Schalcher TR, Mioni Thielli Figueiredo Magalhães de Brito, Valério ES, Monteiro MC. Cryptococcosis, A Risk for Immunocompromised and Immunocompetent Individuals. *The Open Epidemiology Journal* 2013;6:9–17.

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