



Cryptococcosis due to *Cryptococcus neoformans* var. *gattii* in Brazilian patients with AIDS. Report of three cases

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Summary

Three cases of *Cryptococcus neoformans* var. *gattii* infection in AIDS patients observed in Rio Grande do Sul (Brazil) are related. A brief comment on the epidemiology of cryptococcosis in Brazil is also made.

Key words

AIDS, Cryptococcosis, *Cryptococcus neoformans* var. *gattii*

Criptococosis por *Cryptococcus neoformans* var. *gattii* en pacientes brasileños con sida. Descripción de tres casos

Se presentan tres casos de infección por *Cryptococcus neoformans* var. *gattii* en pacientes con SIDA detectados en Rio Grande do Sul (Brasil). Se hace, también un breve comentario sobre la epidemiología de la criptococosis en Brasil.

Sida, Criptococosis, *Cryptococcus neoformans* var. *gattii*

Mainly as a result of the AIDS epidemic, the incidence of cryptococcosis has increased substantially in the last 15 years [8]. In almost all AIDS patients, regardless their geographic origin, cryptococcal infection has been caused by *Cryptococcus neoformans* var. *neoformans* [8,15]. Exceptionally *C. neoformans* var. *gattii* has been the agent of cryptococcosis in HIV-infected people, even in areas where the infection by this variety occurs endemically [8].

Eighteen cases of the association HIV and variety *gattii* infections could be gathered in the literature [1-6,8-11,16,17]. Two of these cases were observed in Brazil; one was reported [11] and another quoted [4]. In this report three new Brazilian cases will be added and some aspects on the epidemiology of cryptococcosis in Brazil will be commented.

CASE REPORTS

Case 1. This patient was a 31-year-old Caucasian, drug-abuser and HIV infected male. At admission he complained of frontal headache, vomiting, agitation and mental confusion since one week ago. Physical examination revealed fever (38.5°C), stiff neck, and positive Lasegne sign. A brain CT scan did not disclose abnormalities. A lumbar puncture was performed; CSF obtained with increased pressure (600 mm H₂O) and the following values: protein 185 mg/dl; glucose 27 mg/dl; leukocytes 172/mm³, 80% of which neutrophils. Direct microscopic examination and cultures were negative for fungi and bacteria; it was also negative for CVM, IgM, Rubeola IgM, CDRL, FTA-ABS, and cryptococcal polysaccharide antigen tests.

Soon the patient worsened becoming non-responsive to oral stimuli. General measures for intracranial hypertension and treatment for tuberculosis and bacterial meningitis were established. However, 20 days later the patient presented irritability, restless and hallucinations. A second CT scan revealed hypertensive hydrocephalus and cisternal contrast-enhancing. A lumbar tap was performed. Latex agglutination test became positive (1:16) and *C. neoformans* was recovered in culture from CSF. Isolate was identified as *C. neoformans* var. *gattii* serotype B.

Amphotericin B was administered. A slowly neurological improvement was observed, but when the cumulative dose of 870 mg was obtained the patient died suddenly by cardiopulmonary arrest. Death was probably due to hypokalemia related to amphotericin B use.

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Case 2. A 38-year-old Caucasian man was admitted complaining with disorientation and general seizures that appeared suddenly. He had a history of chronic alcoholism and he was HIV-positive. On physical examination neither signs of meningismus or focal encephalic lesions were observed. CD4/CD8 relation was 0.13. Chest roentgenogram showed bilateral infiltrations in the lower lobes with a small effusion in the left side. Cephalic CT scan did not reveal any abnormality. CSF obtained by lumbar spinal tap revealed the following values: protein 160 mg/dl; glucose 60 mg/dl; leukocytes 200/mm³ (62% neutrophils, 35% eosinophils, and 3% lymphocytes). The sediment of the centrifugated CSF, mounted in a drop of India ink or smeared and stained by Gram and Kinyoun techniques did not revealed microorganisms: no growth were seen in cultures for fungi and bacteria. Under the presumption of bacterial meningitis or disseminated cysticercosis, the patient was treated with ceftriaxone and praziquantel, while awaiting for further CSF analysis. In this meantime the patient presented a right sided hemiparesis and sign of meningitis. CSF, obtained in a second lumbar puncture, showed the following values: protein 58 mg/dl; glucose 96 mg/dl; leukocytes 213/mm³ (78% neutrophils and 20% lymphocytes). Negative results were obtained by microbiological examination of the CSF, but serologic test showed a titer of 1:8 by latex agglutination test. A proposed treatment with amphotericin B was refused and the family of the patient asked for his discharge.

One week later the patient was readmitted, presenting stiff neck, bilateral Babinski sign and symmetric spastic tetraparesis. CSF from a third lumbar puncture showed: protein 247 mg/dl; glucose 13 mg/dl; leukocytes 37/mm³ (66% lymphocytes and 31% neutrophils). Stained smears were negative for microorganisms but *C. neoformans* grew up in culture, later on identified as var. *gattii* serotype B. Cryptococcal latex agglutination test 1:1024 in the CSF and 1:2048 in the serum. Amphotericin B was administered, producing favorable neurological evolution. Nevertheless the patient presented with septic shock due to *Staphylococcus aureus* pneumonia and died 25 days after the second admission to the hospital.

Case 3. The patient, a 31-year-old man, was HIV-positive for the past five years. He complained of headache, fever and vomiting. On physical examination the

patient was febrile (38°C) and semi-unconscious. Physical exam revealed oropharyngeal candidosis, perianal fistula and multiple skin lesions of Norwegian scabies. Chest X-ray and cephalic CT scan did not reveal abnormalities. Lumbar puncture was performed and initial pressure was 375 mm H₂O. Analysis of CSF showed 272 mg/dl protein; 24mg/dl glucose; leukocytes 184/mm³ (27% neutrophils and 2% eosinophils); antibody test for toxoplasmosis was negative. *C. neoformans* was isolated in culture and, identified as var. *gattii* serotype B. Serum cryptococcal antigen titer was 1:128. The patient was treated with amphotericin B (total dose 3,500 mg) followed by fluconazole (400 mg/day for four weeks). In spite of the treatment the mental status of the patient worsened. Then a CT scan revealed a large contrast ring-enhancing lesion (3 cm in diameter) in the left frontal lobe. The patient acquired a *Staphylococcus aureus* infection (hemoculture positive) which led him to death in spite of therapy.

DISCUSSION

Only three series of cases of cryptococcosis in which the patients' condition were correlated with the variety of the isolated *C. neoformans* have been published in Brazil [4,12,14]. In two of these series [12,14] the isolated variety was also serotyped (Table 1). In spite of these fragmentary data they revealed that variety *neoformans* is prevalent in Rio de Janeiro and Rio Grande do Sul states, respectively of the Southeastern and Southern Brazilian regions, and variety *gattii* prevails in Maranhão and Piauí, neighbouring states of the Northeastern region. They also show that variety *gattii* has been usually isolated from non-immunosuppressed patients and variety *neoformans* is the usual agent of the mycosis in AIDS patient.

A series of seven cases of associated HIV and var. *gattii* infection, occurred in Australia, was presented in an International Conference (patient's history not provided) [7]. The author postulated that the infection was clinically similar to that caused by var. *neoformans*. However, among other differences between the infections caused by each variety, hydrocephalus and cerebral focal lesions are more common in infection due to variety *gattii* [13,15], as it was observed in our patients case 1 and 3.

Table 1. Varieties and serotypes of the *Cryptococcus neoformans* isolated from series of cases of cryptococcosis observed in three Brazilian regions.

Ref.	Region/State	Number of cases	Predisposing condition				
			Total	Variety	Serotype	AIDS	Other
[4]	Northeastern/Piauí & Maranhão	45	13 <i>neoformans</i> 32 <i>gattii</i>	- -	6 1	4 -	3 31
[12]	Southeastern/Rio de Janeiro	83	75 <i>neoformans</i> , 8 <i>gattii</i>	19 A* 8 B	65 1**	5 -	5 7***
[14]	Southern/Rio Grande do Sul	60	51 <i>neoformans</i> 1 <i>neoformans</i> 8 <i>gattii</i>	51 A 1 D 8 B	24 1 -	10 - 1	10 - 7

* the remaining 56 isolates were not serotyped

** previously published (reference 10)

*** this seven patients were natives of the Northeastern Brazilian region

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