Cryptococcus gattii molecular type VGII as agent of meningitis in a healthy child in Rio de Janeiro, Brazil: report of an autochthonous case

ABSTRACT

Cryptococcus gattii causes meningoencephalitis in immunocompetent hosts, occurring endemically in some tropical and subtropical regions. Recently, this fungus was involved in an outbreak in Vancouver Island and British Columbia (Canada). In this temperate region, the VGII type is predominant. The present report highlights the need for clinical vigilance for primary cryptococcal meningitis in nonendemic areas.

Key-words: Meningoencephalitis. Immunocompetent. Cryptococcus gattii.

INTRODUCTION

Cryptococcus gattii is an agent of life-threatening disseminated infections in healthy, immunocompetent hosts. The most common clinical manifestations are meningoencephalitis and pulmonary disease, occurring mainly as endemic mycosis in tropical and subtropical regions. This primary emerging pathogen has attracted special attention during an outbreak of pulmonary and disseminated infection in Vancouver Island since 19991.

CASE REPORT

A five-years-old boy, born and resident in the Metropolitan area of Rio de Janeiro, was admitted to a medical facility near his residence on January 3rd 2005 complaining of an abrupt onset of fever, malaise, frontal headache, abdominal pain and post alimentary vomiting for two days. These unspecific manifestations were treated with oral amoxicillin and symptomatic medication. After four days, with improvement of his symptoms, he was discharged to continue treatment at home.

During the following two weeks, the patient remained well, but in the fourth week of January, recurrence of fever, malaise and headache occurred. He was readmitted in a municipal hospital presenting hepatomegaly and a right convergent strabismus without...
consciousness disturbance or meningeal signs during clinical examination. Computerized tomography (CT) scans of the brain revealed hypodense areas in the right basal ganglia and subcortical region, with ring enhancement after iodine contrast infusion, strongly suggestive of neurotoxoplasmosis (Figure 1). Sulfadiazine and pyrimethamine administration were initiated. After a short stay, the patient was transferred to the Fernandes Figueira Institute (IFF).

Upon admission to IFF, laboratorial tests were negative for HIV (ELISA) and IgG and IgM serology for *Toxoplasma gondii*. A spinal tap was performed and showed 62 leukocytes/mm³, with 92% of mononuclear cells, protein levels of 70mg/dl and glucose levels of 63mg/dl. All bacteriological tests were negative, including tuberculosis investigation (direct bacterioscopy and culture). Antimicrobial drugs for neurotoxoplasmosis were discontinued and vancomycin, ceftriaxone and metronidazole were initiated to treat a possible cerebral abscess. Dexamethasone was also added to ameliorate the cerebral edema. Improvement in the patient's clinical condition was observed.

On day 10 of admission to IFF, the patient presented worsening of intracranial hypertension (ICH) along with meningeal irritation and tonic-clonic seizures. CSF culture was positive for *Cryptococcus sp* and following this result, a latex agglutination test also proved positive. As a consequence, all antibiotics were interrupted and 1mg/kg/d of amphotericin B deoxycholate was initiated. A new CT scan of the brain presented dilatations of the ventricular system (Figure 1) and another spinal tap was performed. The CSF revealed 19 leukocytes, 97% mononuclear cells, protein of 45mg/dl and glucose of 46mg/dl. The patient evolved with fluctuation of mental status. After failure of ICH control with serial lumbar punctures, a peritoneal shunt was implanted.

On day 18 of admission the patient presented with bilateral blindness and severe motor deficits, mainly limbs. Negative results of CSF cultures for fungus and *Cryptococcus sp* occurred on day 22 following the onset of treatment. Other complications observed during inpatient stay were arterial hypertension, salt waste syndrome and low potassium levels as a consequence of amphotericin B administration.

The patient was discharged after 95 days with accumulated amphotericin B dosage of 400mg, over a six week period. The remainder of treatment was achieved with fluconazole at a daily dose of 12mg/kg for four weeks.

Outpatient follow-up continues, showing the persistence of neurological sequelae, mainly hypotonus of the leg muscles, two seizure episodes (controlled with anticonvulsant drugs) and bilateral blindness, during the initial visits. At present, the patient presents expressive improvement of motor disability and attends a school for the visually handicapped.

**DISCUSSION**

Cryptococcosis meningoencephalitis affecting an immunocompetent child represents a diagnostic puzzle, mainly because *C. gattii* is not a typical etiological agent of meningitis, but also because of its nonspecific clinical manifestations. Consequently, delay in the diagnosis and in the onset of specific treatment is frequently observed.

Studies involving infantile cryptococcosis in Brazil demonstrated that the most common manifestations are fever, headache, neck stiffness and vomiting; in this case, these suggestive manifestations occurred after the second week of onset.

Cranial CT scans can also cause confusion, since the aspect of the lesion is very similar to other diseases, such as neurotoxoplasmosis and cerebral abscess. In a study of tomographic alterations in 11 children with meningitis by *C. gattii* in the State of Pará, Brazil, all cases presented hypodense nodules, most of them located in the basal ganglia. The same study also described hydrocephalus and diffuse cortical atrophy.

In the present case, the cryptococcal isolate from CSF was only identified at a species level by a reference laboratory. The fact that the commercially available kits for yeast identification do not discriminate *C. neoformans* from *C. Gattii*, must be taken into account. This fact, together with the absence of case surveillance, limit current knowledge regarding *C. gattii* epidemiology in Brazil.

In the north and northeast regions of Brazil, encompassing the Brazilian Amazon forest and the semiaram savanna areas, the high proportion of HIV-negative children with cryptococcal meningitis configure an unique epidemiological picture in the world. In the State of Pará, *C. gattii* cases are an infantile cryptococcal meningitis frequency of 18.6% was verified for 43 cases diagnosed from 2003 to 2007 and 24.3% in 78 cases diagnosed from 1992 to 1998 in the same state. A frequency of 33% of cases in children was observed in the State of Amazonas and 21% in the State of Piauí. Epidemiological studies in these regions show that the molecular type VGII is the main agent for cryptococcal meningitis in young adults and children. The previous few VGII cases identified in the State of Rio de Janeiro were from patients who came from the northeast of the country. The epidemiological data of the present case were reassessed and a domiciliary visit was conducted. The family reported no travel history and the child was born and has always lived in a poor community within the metropolitan area of Rio de Janeiro in an area of ongoing deforestation. Future environmental studies are necessary in this region to identify potential sources of human infection. Besides colonization of hollow trees and wood decay substrata, deforestation may also be related to *C. gattii* infections in Brazil. Subtyping and genetic studies comparing *C. gattii* isolates from Rio de Janeiro to
those from other regions are also necessary to verify possible variants in the molecular type VGII.

An autochthonous case in Rio de Janeiro caused by \textit{C. gattii} VGII type demands attention. The same molecular type is endemic in the north and northeast regions and seems to be spreading to Southeastern Brazil. The adaptive potential and expansive behavior of VGII has been observed in North America, where this agent is responsible for the ongoing outbreak of meningoencephalitis in Vancouver and is spreading into Pacific Northwest Region of the United States\textsuperscript{1}.

It is necessary to include this agent as a potential etiological agent of meningitis in clinical practice in all regions of Brazil, to increment laboratorial conditions for storage and identification of cryptococcal isolates and to establish surveillance concerning cryptococcal infection in our country.

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**REFERENCES**


