Immunocompetent patient with cerebral cryptococcosis: case report

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Abstract

A 14-year-old female, presenting sudden and progressive holocranial headache along with incoercible vomiting arrived to emergency room. Acute confusional state and meningoencephalitis syndrome where identified. Brain computed tomography-scan with normal results was performed. Lumbar puncture with crystal-clear cerebrospinal fluid was obtained: low glucose, elevated proteins and cell-count of 15/mm. China-Ink and Cryptococcus neoformans culture both positive. Viral, lupus-anticogulant, and HIV tests negative. Fluconazole 200 mg/kg/day, amphotericin-B 0.7 mg/kg/day, dexamethasone 1 mg/kg/day were prescribed. 48-h later evolved to cerebral edema, multiple-organ-failure and death. Hereby we present a Cryptococcus spp. infection case report, addressing the public health challenge and vulnerability of immunocompromised patients in Mexico.


Introduction

Cryptococcosis is an opportunistic fungal disease caused by a globally-distributed yeast-like, encapsulated fungus. There are two pathogenic varieties in the human being: Cryptococcus neoformans var. neoformans, which causes the majority of infections in immunocompromised patients, and var. gatti, which affects immunocompetent individuals and exists in both tropical and subtropical areas.

Cryptococcosis diagnosis is based on a detailed patient history, since symptoms depend on the area compromised in the central nervous system (CNS). In case of clinical suspicion after cytological, cytochemical and cerebrospinal fluid (CSF) staining tests, an enzyme-linked immunosorbent assay (ELISA) or a latex agglutination test should be carried out; when both these are negative, the CSF culture results should be awaited. Untreated meningitis by Cryptococcus spp. is fatal, while 60-70% of patients without AIDS who are treated have good prognosis.

The present case exemplifies the importance of Cryptococcus spp. infection in immunocompetent patients in our country, since in spite of medical management and standardized treatment, the patient had organ dysfunction and died.

Case presentation

This is the case of a 14-year-old female patient, resident of an urban area in Morelia, Michoacán, who had a low socioeconomic status and poor hygienic-dietary habits. She had complied with her vaccination schedule. She had no relevant personal, family or...
psychiatric history. Her condition had started in 
December 2014 with holocranial headache of sudden 
and progressive onset, which was oppressive, con-
stant, with no rhythm or irradiation, 8/10 intensity in 
the verbal rating scale for pain (VRSP), and was un-
succesfully treated with acetaminophen, with one-
month evolution.

At her admission to the emergency department on 
January 2014, the patient presented with constant 
holocranial headache of VRSP 9/10 in intensity, ac-
companied by nausea, vomiting and tonic-clonic sei-
zures. Her vital signs were: heart rate, 110 beats per 
minute; respiratory rate, 25 breaths per minute, blood 
pressure, 100/75 mmHg, moderate dehydration, acute 
confusional syndrome with psychomotor agitation 
state and meningoencephalic syndrome. Laboratory 
tests at admission showed blood count with leukocy-
tosis and normal blood chemistry and coagulation 
times; normal plain and contrast cranial computed 
tomography (CT) (Fig. 1). Empirical treatment was 
started with ceftriaxone, 1 g every 12 h by intravenous 
(IV) route, and vancomycin, 15 mg/kg IV every 12 h. 
Lumbar puncture for CSF showed 80 mmH2O opening 
pressure; cytochemistry: xantochromic color; trans-
parent appearance; protein, 78 mg/dL; glucose, 
14 mg/dL; cellularity, 15/mm; lymphocytes, 20%; poly-
morphonuclear cells, 76% and monocytes, 4%. Crypt-
ococcus neoformans was observed with India ink 
(Fig. 2). Therefore, treatment was started at 48 h with 
fluconazole 200 mg/kg/day, amphotericin B 
0.7 mg/kg/day and dexamethasone 2 mg/kg/day. The 
TORCH, VDRL, B19 parvovirus, Epstein-Barr virus, 
anti-dsDNA (256 IU/mL), ANA (1:40) and HIV tests 
were negative. The CSF culture showed development 
of C. neoformans (sensitive to flucytosine ≤ 1 mini-
mum inhibitory concentration [MIC] amphotericin B = 
1 MIC and fluconazole = 2 MIC).

In spite of the treatment, the patient evolved with 
severe cerebral edema and neurological deterioration 
(Fig. 3), she developed multiple organ failure and died 
3 days later. No autopsy was practiced.

**Discussion**

Cerebral cryptococcosis in immunocompetent pa-
tients is rare, and only a few have been reported in 
the world cases8. The variety of Cryptococcus is de-
terminant for infection in immunocompetent patients 
but, unfortunately, in most cases the variety is not 
known, since the performance of polymerase chain 
reaction and ELISA is not common practice. Currently,
cases of asymptomatic pulmonary cryptococcosis and pulmonary infection-secondary meningoencephalitis have been reported without pulmonary clinical or radiologic data and, in these cases, the pulmonary infection is controlled by granulomas that disappear after weeks or months. Cryptococcosis presentation in the CNS can be as cysts in the cerebral cortex with granulomatous meningeal reaction, or granulomas in the white matter known as cryptococcomas, which were not detected in our patient; her medical condition precluded the performance of magnetic resonance.

Cryptococcosis clinical manifestations appear at 1 to 2 weeks after exposure to spores in bird feces, plants (eucalypts) and animals (e.g., koalas). Immunocompetent patients can develop symptoms after months or with slow progression. Initial symptoms include progressive holocranial headache, general deterioration and fever that only occurs in 50% of cases. As for neurological symptoms, higher prevalence and more intensity have been observed in immunocompetent patients, with local or general manifestations depending on the area affected by the yeasts. In our patient, the first CT was normal; however, it has been documented that CT can be normal or show cryptococcomas in 38-58%, cerebral edema, hydrocephaly or meningeal enhancement. Magnetic resonance is more sensitive to detect nodules within the cerebral parenchyma; meninges, basal ganglia and mesencephalon are abnormal in 40% of patients with the infection typical presentation. CSF cytological examination shows lymphocytic pleocytosis, hyperproteinorachia and hypoglycorrhachia, and the Indian ink test is positive in 50% of patients without AIDS. The most widely used diagnostic method is Cryptococcus culture (90% sensitivity); however, latex agglutination has been reported to be the diagnostic test with the highest sensitivity and specificity with titers higher than 1:2048.

Regardless of patient neurological and immune status, the recommended treatment for cerebral cryptococcosis is with amphotericin B (0.7-1.0 mg/kg per day IV) plus flucytosine (100 mg/kg per day by oral route, in four divided doses) for at least 4 weeks, and when there are complications (intracranial hypertension, among others), 6 weeks of induction therapy are recommended to subsequently start consolidation with fluconazole (400 mg/day) for 8 weeks. After induction and consolidation therapy, maintenance therapy is established with fluconazole, at 200 mg per day for 6-12 months.

Prognosis is poor in immunodepressed and immunocompetent patients without treatment; with treatment, worldwide-reported mortality in immunocompetent patients is 27%, and in immunodepressed subjects it is 32%. Cerebral cryptococcosis in immunocompetent patients is infrequent; however, it can have a fatal evolution in spite of currently recommended antimicrobial treatment.

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References