Case report

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First case report of eosinophilic meningitis associated with cerebral toxoplasmosis in an HIV-positive patient

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Abstract

Cerebral toxoplasmosis is the most common cause of focal brain lesion in people living with HIV (PLWH) and usually causes multifocal encephalitis with little or no meningeal involvement. Classically, only subtle cerebrospinal fluid (CSF) abnormalities are described. There are no prior case reports in the literature on eosinophilic meningitis associated with cerebral toxoplasmosis in PLWH. We report on an HIV-positive man from Brazil who presented to the emergency department with headache, nausea, vomiting, and hemiparesis. He had a T-CD4+ lymphocyte count of 145 cells/mm^3, and antiretroviral failure was identified. Brain computed tomography showed a contrast-enhancing lesion with mild mass effect and trimethoprim–sulfamethoxazole and dexamethasone were started. Examination of CSF showed 194 cells/mm^3 (74% eosinophils, 18% lymphocytes, 4% monocytes, and 2% neutrophils), protein = 83 mg/dL, and glucose = 49 mg/dL. Detection of *Toxoplasma gondii* on CSF by polymerase chain reaction confirmed the diagnosis of cerebral toxoplasmosis. An exhaustive laboratorial investigation excluded other possible etiologies. After 14 days, the patient showed complete resolution of neurological and CSF alterations and substantial improvement in the brain lesion and was discharged home. We suggest that eosinophilic meningitis should be included in the spectrum of manifestations of HIV-related cerebral toxoplasmosis, especially in countries with high prevalence of toxoplasmosis in the general population.

Keywords

Cerebral toxoplasmosis, meningitis, eosinophils, human immunodeficiency virus, Brazil

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Introduction

The availability of combination antiretroviral therapy (cART) has significantly decreased the incidence of opportunistic infections.[1–4] Despite this, cerebral toxoplasmosis continues to be the most common cause of focal central nervous system disease and a common cause of important mortality and morbidity among people living with HIV (PLWH) from resource-limited settings.[5]

HIV-related cerebral toxoplasmosis usually causes multifocal encephalitis with little or no meningeal involvement. For this reason, manifestations such as focal deficits are frequent and meningism, nausea, and vomiting are uncommon.[6,7] Basic cerebrospinal fluid (CSF) characteristics from patients with cerebral toxoplasmosis are usually not relevant.[8] In addition, cerebral toxoplasmosis, in contrast to other parasitic

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diseases, is usually not included as a cause of eosinophilic meningitis or meningoencephalitis.[9]

Herein, we report an HIV-positive patient with eosinophilic meningitis associated with cerebral toxoplasmosis.

Case report

A 21-year-old man living with HIV infection and having experienced antiretroviral failure was admitted to our hospital with a holocranial headache, nausea and vomiting for three weeks. The patient had been treated for pulmonary tuberculosis seven years ago. He had always lived in an urban neighborhood in the state of São Paulo and denied travel out of this state in the last 3 years. In addition, there was no report of ingestion of raw molluscs or manipulation of snails and slugs during gardening. On physical examination, neck stiffness was not observed and the single alteration was mild right hemiparesis. Brain computed tomography (CT) showed a left nucleo-capsular contrast-enhancing lesion, associated with a mild mass effect. Trimethoprim–sulfamethoxazole and dexamethasone were initiated. Examination of CSF showed cells 94 cells/mm^3 (74% eosinophils, 18% lymphocytes, 4% monocytes, and 2% neutrophils), protein = 83 mg/dL, and glucose = 49 mg/dL. Cultures of blood and CSF for bacteria, fungi, and mycobacteria did not show any growth. The complete blood count and biochemical tests were normal. Peripheral eosinophilia was not observed. The patient had a T-CD4+ lymphocyte count = 145 cells/mm^3 and HIV-1 RNA = 1315 copies/mL. Blood enzyme-linked immunosorbent assay (ELISA) for *Toxoplasma gondii* showed reactive IgG antibodies. Polymerase chain reaction (PCR) was positive for *T. gondii* in CSF. The finding of a high percentage of eosinophils in CSF led to the investigation of unusual microorganisms in PLWH. Blood antibody detection immunoassays for *Trypanosoma cruzi* (ELISA and indirect hemagglutination assay), schistosomiasis (ELISA), cysticercosis (ELISA), and angiostrongyliasis (ELISA) were non-reactive. Direct examination for larvae in CSF was also negative. PCR ELISA for toxocariasis, schistosomiasis, cysticercosis, and angiostrongyliasis were non-reactive in the CSF. Three stool ova and parasite tests and one stool culture were all negative. After seven days of treatment with trimethoprim–sulfamethoxazole and dexamethasone, the headache had resolved and the hemiparesis improved. A new brain CT was performed after 14 days of treatment, and it revealed substantial improvement in the lesion and mass effect. Another lumbar puncture was performed showing no cells /mm^3, protein = 23 mg/dL, and glucose = 51 mg/dL. A new ELISA for angiostrongyliasis was non-reactive in the CSF. The patient showed complete resolution of the hemiparesis and was discharged to home to complete eight weeks of treatment. Two years after hospital discharge, the patient was asymptomatic, on new cART and with T-CD4+ lymphocyte count = 581 (19%) cells/mm^3 and HIV-1 RNA < 40 copies/mL.

Discussion

To the best of our knowledge, this is the first case of eosinophilic meningitis associated with cerebral toxoplasmosis in PLWH. The definitive diagnosis of cerebral toxoplasmosis was based on compatible clinical and radiological findings and detection of *T. gondii* by PCR in CSF. In addition, resolution of clinical and CSF alterations was observed after sole anti-Toxoplasma therapy. An exhaustive investigation was performed, and no other concomitant diagnosis was identified.

Cerebral toxoplasmosis can manifest as multiple or single expansive brain lesions or rarely as diffuse encephalitis without evidence of focal brain lesions in imaging studies.[1,7] Historically, lumbar puncture was not routinely considered in the initial approach in PLWH with expansive brain lesions, and prompt empiric anti-Toxoplasma treatment was the rule.[10,11] However, when lumbar puncture is safe and feasible, this procedure should be performed in order to evaluate the presence of *T. gondii* DNA using PCR.[1] Thus, definitive diagnosis can be obtained with this less invasive strategy compared to neurosurgery.

Classically, only subtle CSF abnormalities such as normal or mildly elevated cell counts and protein values were described in PLWH-related cerebral toxoplasmosis.[12] Interestingly, toxoplasmosis is not included in most reviews about eosinophilic meningitis,[9,13–18] and more surprisingly, there are no reports in the literature involving PLWH. Anecdotally, Woods et al. reported a case of congenital toxoplasmosis, not related to HIV infection, with eosinophilic predominance in CSF analysis.[19] In addition, a recent study reported 8 cases of AIDS-related cerebral toxoplasmosis that presented eosinophils in the CSF.[20] The median and interquartile range (IQR) of CSF cellular characteristics were: WBC: 69 (42; 81) cells/mm^3; lymphocytes, 90% (87%; 98%) and eosinophils, 1% (1%; 2%). None of them had eosinophilic meningitis criteria and only one case had blood eosinophils > 5% (Sergio Monteiro de Almeida, personal communication). These results and our present case suggest a spectrum of previously unreported manifestations of cerebral toxoplasmosis in PLWH. Interestingly, in this study, the main cause of eosinophilic meningitis in PLWH was cryptococcosis, an unusual laboratory manifestation of this mycosis.[20] In the present case, it should be

noted that the only lesion identified on CT was not close to the meninges. Magnetic resonance imaging was not performed, therefore the existence of other lesions or meningeal enhancement can not be ruled out.

Parasitic infections are the most common cause of eosinophilic meningitis. In Southeast Asia, China, and Japan, angiostrongyliasis, gnathostomiasis and baylisascariasis are the principal etiologies. Other parasitic etiologies, including toxocariasis, cysticercosis, ascaridiasis, trichinosis, strongyloidiasis, echinococcosis, schistosomiasis, paragonimiasis, and fascioliasis, exist worldwide, but particularly in resource-limited settings. Tuberculosis, syphilis, coccidioidomycosis, lymphoma involving the meninges, and some drugs can occasionally cause CSF eosinophilia.[10,14-18] The diagnosis of eosinophilic meningitis is particularly challenging in tropical and subtropical countries where neuro helminthiasis is more prevalent and where appropriate testing is typically unavailable. In the present case, cerebral toxoplasmosis was postulated at admission based on clinical and radiological features. The identification of eosinophilic meningitis was an unexpected finding and an alternative or concomitant diagnosis was postulated. The possibility of the concomitant presence of *Angiostrongylus cantonensis* was a special concern. Globally, this parasite is the most frequent cause of eosinophilic meningitis[9,14,16] and several cases have been diagnosed in São Paulo.[21] Although the present case had some compatible clinical manifestations, prominent eosinophilia in the CSF and improvement after corticosteroids,[22] there was no consistent epidemiological history, no blood eosinophilia was observed and the immunological tests were negative in blood and CSF.[9,16,18] Therefore, the diagnosis of eosinophilic meningitis caused by *A. cantonensis*, concomitant with the diagnosis of cerebral toxoplasmosis, was considered unlikely.

In conclusion, we suggest that eosinophilic meningitis should be included in the spectrum of manifestations of PLWH-related cerebral toxoplasmosis, especially in countries with high prevalence of toxoplasmosis. Further studies are necessary to better understand the interface between eosinophils in the CSF, eosinophilic meningitis and cerebral toxoplasmosis in PLWH.

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