



Cerebral toxoplasmosis in patients with acquired immune deficiency syndrome in the neurological emergency department of a tertiary hospital



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ABSTRACT

Introduction: Cerebral toxoplasmosis is the most common cause of space occupying brain lesion in patients with HIV/AIDS in Brazil. In the post-HAART era, it is responsible for high rates of morbidity and mortality worldwide.

Materials and methods: This study consists of a case series of 56 patients diagnosed with cerebral toxoplasmosis whose clinical features, brain imaging and cerebrospinal fluid aspects were analyzed.

Results: Cerebral toxoplasmosis led to the diagnosis of infection by the human immunodeficiency virus (HIV) in 27 (48.2%) of the patients, while 29 (51.2%) others already knew to be HIV seropositive. However, at the time of diagnosis of cerebral toxoplasmosis, only 9 (16.6%) reported being under antiretroviral therapy and 5 (8.9%) were receiving primary prophylaxis for toxoplasmosis. Headache, strength deficit and fever were the most frequent signs and symptoms throughout the study. Fifty-three patients showed changes consistent with toxoplasmosis in CT or MRI. Thirty-four (60.7%) CSF samples were positive in the indirect haemagglutination test and for the reaction of *Toxoplasma gondii* IgG ELISA, while 31 (55.4%) were positive in the direct haemagglutination test. Fifty (89.3%) patients underwent first-line treatment for toxoplasmosis.

Conclusion: Cerebral toxoplasmosis is still a very relevant neurological disease in individuals with AIDS admitted to neurology emergency departments. Early diagnosis and initiation of empiric treatment and antiretroviral therapy are important for good prognosis.

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1.3. Introduction

Cerebral toxoplasmosis is one of the most common causes of central nervous system (CNS) infection and a frequent cause of space occupying brain lesion in patients with acquired immune deficiency syndrome (AIDS) in Brazil; it is typically the result of reactivation of chronic *Toxoplasma gondii* infection due to changes in cellular immunity [1,2]. Cerebral toxoplasmosis is currently the third-most prevalent AIDS-defining illness in Brazil, after tuberculosis and *Pneumocystis jirovecii* pneumonia [2]. An estimated 30% to 50% of HIV-seropositive individuals infected with *T. gondii* develop cerebral toxoplasmosis, which also has a high mortality [3,4].

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Introduction of highly active antiretroviral therapy (HAART) resulted in significant worldwide reduction in morbidity and mortality of individuals living with human immunodeficiency virus (HIV)/AIDS [5]. The incidence of opportunistic CNS infections has also declined compared to levels in the pre-HAART era [6]. However, cerebral toxoplasmosis persists in some geographic regions, such as Brazil, with delayed diagnosis of protozoan infections and difficulty in accessing specialized treatments [7].

The definitive diagnosis of cerebral toxoplasmosis requires histological or cytological examination of affected tissues or fluids (i.e., brain biopsy). Therefore, most physicians treat it presumptively based on a focal neurological clinical syndrome history compatible with intracranial lesions, reduced level of consciousness accompanied by brain images showing mass effect (ring enhancement on magnetic resonance imaging [MRI] or computed tomography [CT] with or without injection of contrast media), and serological findings [8].

In this study, we report a series of patients with AIDS and cerebral toxoplasmosis treated in a neurology emergency room. Most of the cases of cerebral toxoplasmosis occurred in individuals who knew they were seropositive for HIV.

2. Materials and methods

This study was conducted in the neurology emergency department at the Hospital da Restauração Governador Paulo Guerra, the largest tertiary healthcare center in the state of Pernambuco, with more than 704 beds, and a reference hospital for emergency cases.

A prospective cross-sectional study was conducted between December 2013 and January 2015. The sample included individuals positive for HIV who were admitted to the neurological emergency department with cerebral toxoplasmosis.

The data used for analysis were medical records from the inpatient unit of the emergency department, which included biological, demographic, clinical, radiological, and laboratory data. Neuroimaging (CT and MRI) results were examined for brain lesions, topography, perilesional edema, and midline deviation.

Cerebrospinal fluid (CSF) was examined to determine white blood cell count; levels of proteins, chloride, and glucose; and immune response to *T. gondii* (enzyme-linked immunosorbent assay (ELISA) measuring immunoglobulin G and M [IgG, IgM] levels, and hemagglutination tests); *Treponema spp* (Venereal Disease Research Lab [VDRL]) and HIV (ELISA) were also measured, along with testing for *Cryptococcus neoformans* (India ink and Crypto-la test).

Variables were presented as relative values; continuous variables were expressed as minimum, maximum, and arithmetic mean values.

3. Ethics

The institutional review boards of the Ethics Committees of the Hospital da Restauração Governador Paulo Guerra and the Fundação Oswaldo Cruz approved this study. All patients gave informed written consent.

4. Results

A total of 56 patients were enrolled during the 14-months study period, including 29 (51.8%) men. Their mean age was 39.1 years (23–61 years), and the majority, 46 (82.1%), lived in the Recife metropolitan region. Twenty-seven (48.2%) patients were diagnosed with AIDS at the time of admission to the emergency room, while 20 (35.7%) reported having known their HIV infection status for more than 2 years, and 9 (16.1%) for a period shorter than that.

Table 1
Signs and Symptoms in 56 Individuals with Cerebral Toxoplasmosis and AIDS.

Signs and symptoms	n (%)
Headache	39 (55.7)
Deficit force	38 (54.3)
Fever	25 (35.7)
Seizures	24 (34.3)
Altered level of consciousness	21 (30.0)
Dysphonia	16 (22.8)
Nausea	15 (21.4)
Vomiting	12 (17.1)
Visual Turbidity	4 (6.0)

Among the major signs and symptoms reported in the emergency room, most had headache (58.9%) and strength deficit (57.1%) in addition to fever (33.9%), one or more seizures (37.5%), and were confused (26.8%). Decreased level of consciousness occurred in 15 (26.8%) individuals, with Glasgow coma scale scores ranging from 10 to 14 points. Among patients with strength deficit, the upper limbs were the most commonly affected site, predominantly left limbs (Table 1).

CSF analysis revealed average white blood cell counts of 16.1 cells/mm³ (0–159 cells/mm³), total protein levels of 122.0 mg/dL (33–1,436.0 mg/dL), chloride levels of 693.9 mg/dL (631.0–750.0 mg/dL), and glucose levels of 56.8 mg/dL (29.0–84.0 mg/dL). Positive toxoplasmosis immunological reactions were observed in 60.7% (indirect haemagglutination test and ELISA IgG) and 55.4% (direct hemagglutination test) of patients. Twenty-eight (50%) patients had their CSF examined for the presence of immunological markers of HIV (CD4 cell and total lymphocyte counts), in addition to the serological confirmation, which applied to the 56 patients in the study, and all of these turned out positive. Markers for syphilis (VDRL) and *C. neoformans* (Crypto-LA[®] Test) were also searched and revealed positive in 2 (3.6%) and 1 (1.8%) cases, respectively. (Table 2).

Fifty-three (94.6%) patients underwent CT scans without contrast; of these, 22 (41.5%) and 31 (58.5%) had single and multiple lesions, respectively. Twenty-one (39.3%) patients underwent MRI, with single and multiple lesions visible in 5 (23.8%) and 16 (76.2%) of the cases, respectively. Perilesional edema and midline deviation were identified in 22 (39.3%) and 6 (10.7%) patients, respectively.

A combination of sulfadiazine and pyrimethamine was administered to 50 (89.3%) of patients in this study. Two (4%) patients switched to clindamycin due to the development of hypersensitivity. The corticosteroid dexamethasone or hydrocortisone was administered to 16 (28.6%) and 5 (8.9%) of patients, respectively, and 14 (17.9%) patients received anticonvulsants. Among cases in this study, only 9 (16.1%) reported receiving antiretroviral therapy at the time of emergency room admission.

5. Discussion

In the years that followed the introduction of HAART, a considerable decrease in the incidence of opportunistic infections and CNS disorders was observed worldwide [9–11]. It was not different for cerebral toxoplasmosis. The proportion of deaths associated with the disease reduced from 3.5% of all HIV-related death in 1992–1.9% in 1998, a reduction greater than in HIV-related deaths overall [12].

Despite this improvement in therapy, cerebral toxoplasmosis is still considered a major threat to the health of HIV-infected patients, especially in developing countries, the case of Brazil, where this study took place. In these places, the disease is responsible for a substantial proportion of mortality and morbidity [2,13].

The sample population had a mean age of 39.1 years with more than half of the individuals being males, similar to the distribution of AIDS cases in Brazil; in this country, there are 1.7 cases in

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