

Prolonged survival and immune reconstitution after chagasic meningoencephalitis in a patient with acquired immunodeficiency syndrome

Sobrevida prolongada e reconstituição imunológica depois de meningoencefalite chagásica de um paciente com síndrome de imunodeficiência adquirida

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ABSTRACT

We report a case of cerebral meningoencephalitis due to *Trypanosoma cruzi* in a patient with acquired immunodeficiency syndrome. The patient presented with seizures and focal neurological signs. Definitive diagnosis of chagasic meningoencephalitis was made by demonstration of free trypomastigote forms in the cerebrospinal fluid. Benznidazol was prescribed with clinical and neurological improvement. Antiretroviral drugs improved cellular immunity and three years later the patient presents a good clinical condition with immune reconstitution and undetectable viral load. Chagasic meningoencephalitis has a poor prognosis when specific treatment is not initiated or is delayed. A high index of diagnosis is necessary for early diagnosis and treatment, especially in endemic areas for *Trypanosoma cruzi* infection.

Key-words: Chagas' disease. *Trypanosoma cruzi*. Meningoencephalitis. AIDS

RESUMO

Relatamos um caso de meningoencefalite devida ao *Trypanosoma cruzi* em um paciente com síndrome de imunodeficiência adquirida. O paciente apresentou convulsões e sinais neurológicos focais. O diagnóstico definitivo de meningoencefalite chagásica foi feito pela demonstração de formas tripomastigotas livres no líquido. Foi iniciado benznidazol com melhora clínica e neurológica. As drogas antiretrovirais melhoraram a imunidade celular e três anos mais tarde o paciente tinha uma boa condição clínica com reconstituição imunológica e carga viral indetectável. A meningoencefalite chagásica tem um prognóstico ruim quando o tratamento específico não é iniciado ou quando há demora para substituí-lo. É necessário um alto índice de suspeita para o diagnóstico e tratamento precoces, especialmente em áreas endêmicas para a infecção pelo *Trypanosoma cruzi*.

Palavras-chaves: Doença de Chagas. *Trypanosoma cruzi*. Meningoencefalite. SIDA.

Chagas' disease or American trypanosomiasis is an anthroponosis, endemic in Latin America and is caused by the flagellated protozoan *Trypanosoma cruzi*, transmitted to humans and animals by a family of *haematophagus triatominae* insects. Human beings may also acquire the infection by blood transfusions, transplacental route, infected transplanted organs or contaminated food².

In Latin America, the disease affects about 25% of the population, with 16 to 18 million people infected and about 100 million at high risk of infection².

The population with chronic infection is 7.2%² in Argentina.

The progressive increase of Chagas' disease cases in urban populations as a result of massive migration from rural areas to major cities, associated with widespread infection caused

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by human immunodeficiency virus (HIV), have created the conditions for the emergence of a large number of coinfection cases¹.

Chagas' disease can reactivate in patients with severe immunodeficiency associated with acquired immunodeficiency syndrome (AIDS) and generally presents with neurological compromise as brain mass lesions or acute diffuse meningoencephalitis (75 - 90% of cases)^{5,6}. The central nervous system (CNS) tumor-like lesion is the most common manifestation; less frequently this reactivation may also present as episodes of a diffuse meningoencephalitis with trypomastigotes in the cerebrospinal fluid (CSF)^{2,11,14}.

We report a case of chagasic meningoencephalitis with focal brain lesions in a patient with AIDS who remains in good clinical condition three 3 years after diagnosis.

CASE REPORT

A 32-year-old man infected with the human immunodeficiency virus was admitted to our unit of AIDS-related opportunistic infectious diseases with fever, fatigue, headache and some seizure episodes. Physical examination revealed fever (38°C), tachycardia (102 beats/min), hypotension (100/60mmHg) and weight loss of (approximately 10kg in the three months prior to admittance). The patient also presented sensory compromise with obnubilation and a focal neurological syndrome consistent with hemiparesis with weakness of the face, arm and leg on the right side of the body. Lung auscultation was normal; the abdominal examination revealed hepatomegaly (4cm below the right costal margin); the spleen was not palpable.

Relevant laboratory findings were anemia with hematocrit 31%, hemoglobin 9g/uL, leucocytes 4,100/mm³ (76% of PMN), platelet count 131,000/mm³ and CD4 T cell count of 42 (4%) cell/uL. The plasma viral load RNA-HIV was 71,188 copies/mL. Liver enzymes levels, coagulation tests and chest radiograph were normal. Blood, urine and sputum cultures for bacterial, mycobacterial and fungus were all negative. The anti-toxoplasma IgM was negative and IgG titer was positive 1/512; serological assay for *Trypanosoma cruzi* (indirect immunofluorescence, passive hemagglutination and enzyme linked immunoassay) were reactive. The echocardiogram was normal.

A brain magnetic resonance imaging (MRI) showed a large right cortico-subcortical parieto-occipital lesion, hypointense in T1 weighted and hyperintense in T2 and FLAIR, with enhancement after the administration of gadolinium and surrounding edema, without mass effect rise the midline (Figure 1).

A presumptive clinical and radiological diagnosis of toxoplasma encephalitis was made and empirical antitoxoplasma treatment (pyrimethamine, clindamycin, leucovorin, dexamethasone and anticonvulsivants) was initiated.

After three weeks of empirical treatment the patient's neurological condition did not show any sign of recovery with a decrease in consciousness. A lumbar puncture was performed; the CSF profile was completely normal, with

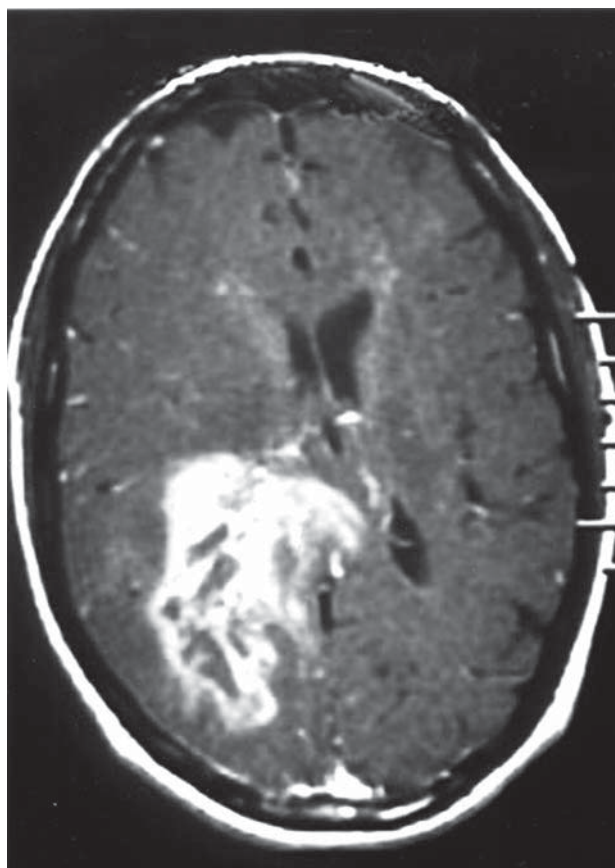


Figure 1 - Axial T1-weighted MRI showing a heterogenous right parieto-occipital lesion with irregular gadolinium enhancement and perilesional edema, before treatment.

1 leukocyte, a glucose level of 52mg/dL and a protein level of 32mg/dL. The results of bacterial, mycobacterial and fungus cultures were negative. Cryptococcal antigenemia was negative. PCR for JC virus and herpes neurovirus (Epstein-Barr virus, cytomegalovirus, varicella-zoster and herpes simplex virus) and VDRL in CSF were all negative. CSF smears with Giemsa stain demonstrated abundant free motile and flagellated trypomastigote forms of the protozoan *Trypanosoma cruzi*. Three buffy-coat smears were negative for parasitemia detection.

The patient was treated with the specific antitrypanosomal drug benznidazol at a dose of 5mg/kg/day twice daily, for 60 days with good clinical and neurological response. After, he received a secondary prophylaxis based on benznidazol at a dose of 200mg three times a week, and antiretroviral therapy based on zidovudine plus lamivudine plus efavirenz was initiated. Three years after the onset of neurological symptoms he remains in good clinical condition; the secondary prophylaxis was interrupted, the CD4 T cell count is > 250 cell/uL and the plasma RNA-HIV viral load is undetectable.

The last MRI scan of the brain demonstrated a right sequela atrophic cortico-subcortical parieto-occipital image, with partial cavitation, hypointense in T1, hyperintense in T2 and hypointense in FLAIR, consistent with gliosis. This lesion is associated with retraction of the brain ventricular system (Figure 2).

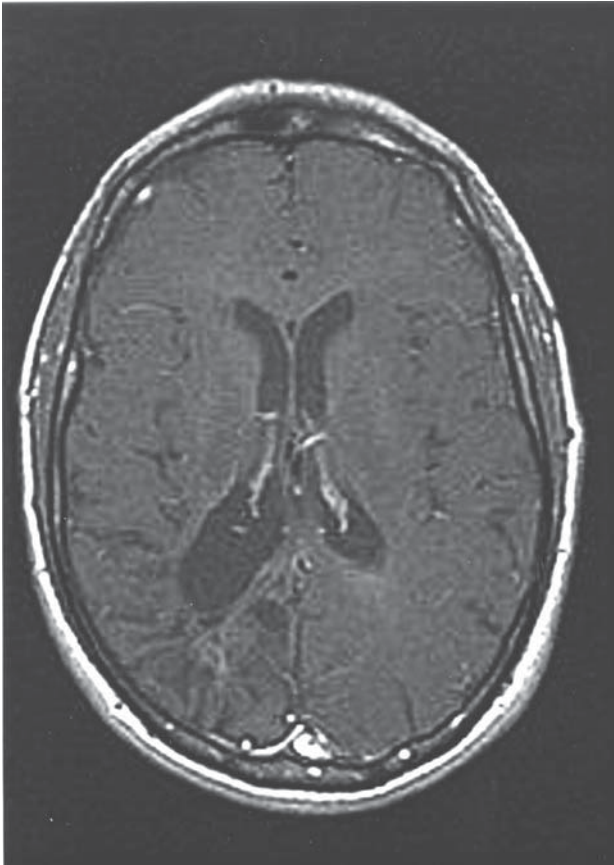


Figure 2 - Axial T1-weighted of the last MRI scan obtained three years after the diagnosis reveals a sequela lesion with partial cavitation, the degree of enhancement and brain retraction.

DISCUSSION

Neurological involvement in patients with AIDS is common. Approximately 40% to 60% of patients with AIDS develop some neurological disorder at some stage of the disease⁴. Acute exacerbation of chronic Chagas' disease can occur in immunocompromised patients, especially in individuals with the involvement of cellular immunity. In this context, patients with advanced HIV/AIDS disease can develop an acute diffuse meningoencephalitis or an intracranial mass lesion caused by *Trypanosoma cruzi*. Neuroimages including MRI and computerized tomography generally show single or multiple lesions with a hypodense or hypointense center, with or without contrast-enhancement and with or without mass effect, indistinguishable from that of *Toxoplasma gondii* encephalitis. The imaging pattern of brain chagoma is similar to that cerebral toxoplasmosis^{8 11 13}. Although primary central nervous system lymphoma and toxoplasma encephalitis continue to be the most common intracranial lesions in HIV-infected patients, other causes of cerebral mass lesions, such as tuberculosis, cryptococcosis, nocardiosis and Chagas' disease, should be considered in the differential diagnosis of enhancing lesions of the central nervous system in patients with AIDS^{4 7}.

In endemic areas for *T. cruzi* infection, all HIV patients presenting with cerebral brain lesions should be evaluated for specific anti-*T. cruzi* antibodies and for parasitemia¹.

The detection of parasitemia using the gross drop method to identify trypomastigotes are more frequent in HIV seropositive patients in comparison with seronegative people^{15 16}. Sartori et al¹⁷ emphasized the importance of routine detection of parasitemia in the reactivation of Chagas' disease in immunocompromised patients. The CSF profile may be normal, as in our patient, or can be associated with lymphocyte pleocytosis and hyperproteinorraquia. Also, CSF samples from AIDS patients with diffuse meningoencephalitis should be routinely sent to the parasitology laboratory for the detection of trypomastigotes, as was seen in our patient¹⁰. Centrifugation of the CSF enhances the sensibility of this test⁶.

When *T. cruzi* trypomastigotes cannot be demonstrated in the CSF, a cerebral biopsy of focal brain lesions may be necessary. Histopathological findings include focal necrotizing encephalitis with amastigotes of *T. cruzi* in Giemsa smears⁹.

Additionally, concomitant cardiac involvement with acute myocarditis suggests the possibility of the reactivation of Chagas' disease. Myocarditis is the second most frequent variation of Chagas' disease reactivation in patients with AIDS^{16 17}.

Fatal outcome is high in reported cases of AIDS associated chagasic meningoencephalitis³. Ferreira MS et al⁷ reported a short median survival (10 days) for these patients⁷. Sinagra and colleagues¹⁸ reported eight patients who died during benznidazol therapy and two other patients who died six to eight months after the reactivation of the disease.

In conclusion, Chagas' disease must be considered in the differential diagnosis of meningoencephalitis, with or without focal brain lesions, in AIDS patients. Sometimes, reactivation of *Trypanosoma cruzi* infection is the first AIDS - defining disease. A correct diagnosis based on epidemiological, clinical and serological information has a significant impact on patient survival. A poor outcome is related with a delay in establishing the correct diagnosis¹².

The potential impact of highly active antiretroviral therapy (HAART) and immune reconstitution in reactivation of Chagas' disease associated with AIDS remains to be established. Early diagnosis followed by specific therapy with benznidazol or nifurtimox and immune reconstitution associated with HAART should improve the survival rate of these patients, such as the case described. Long term secondary prophylaxis with benznidazol is necessary until the immune reconstitution associated with HAART.

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