EXACERBATION OF HIV VIRAL LOAD SIMULTANEOUS WITH ASYMPTOMATIC REACTIVATION OF CHRONIC CHAGAS' DISEASE

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Abstract. Chronic Trypanosoma cruzi infection can reactivate in patients with immunosuppression related to human immunodeficiency virus (HIV) infection, resulting in severe meningoencephalitis or myocarditis and high parasitemia. The effects of T. cruzi on HIV infection are unknown. We describe an HIV-infected patient with chronic Chagas’ disease who experienced an asymptomatic T. cruzi reactivation characterized by the finding of the parasite in direct microscopic examination of blood. The patient’s HIV viral load had increased simultaneously with the exacerbation of T. cruzi parasitemia and decreased to previous levels after successful antiparasitic treatment. This otherwise unexplained finding suggests that T. cruzi infection might up-regulate HIV replication, which may affect HIV disease progression. Asymptomatic reactivation of Chagas’ disease has not been reported before. This could mean that the severe clinical manifestations related to the reactivation of trypanosomiasis are just the tip of the iceberg.

INTRODUCTION

Reactivation of Chagas’ disease characterized by acute and severe clinical manifestations, mainly meningoencephalitis1,2 or myocarditis,1,3,4 and high Trypanosoma cruzi parasitemia has been reported in patients infected with human immunodeficiency virus (HIV) since the early 1990s. The effects of T. cruzi on HIV infection are less known. We describe an HIV-infected patient with chronic Chagas’ disease who had an asymptomatic reactivation of T. cruzi characterized by the finding of the parasite in direct microscopic examination (DME) of blood. His HIV viral load increased simultaneously with T. cruzi parasitemia exacerbation and decreased to the previous levels after successful antiparasitic treatment.

CASE REPORT

A 33-year-old man had lived 21 years in an endemic area for vectorial transmission of T. cruzi in Bahia, Brazil, then moved to São Paulo, a nonendemic area, where he had been living for 12 years. In November 1992, he presented with positive serologic tests for HIV antibodies (enzyme-linked immunosorbent assay [ELISA] and Western blot) and for Chagas’ disease (ELISA, indirect hemagglutination assay, and indirect immunofluorescence assay). He had a history of mild dysphagia, with barium esophagography showing megaesophagus, and an electrocardiogram (ECG) disclosed first-degree atrioventricular block, characterizing the chronic digestive and heart form of Chagas’ disease. In July 1993, the ECG showed isorhythmic atrioventricular dissociation, and in January 1995, a Holter monitor showed second-degree atrioventricular block during sleep and frequent polymorphic ventricular extrasystoles (114/hour) with bigeminy. Chest radiographs and a two-dimensional echocardiogram showed no abnormalities. In May 1996, because of a CD4+ T-cell count of 296 cells/mm³, the patient began antiretroviral therapy with zidovudine and didanosine, which was the antiretroviral regimen approved by the Health Ministry of Brazil for HIV asymptomatic patients with CD4+ T-cell counts >200 cells/mm³ at that time.

Blood parasitologic tests had been performed every 3 to 6 months since July 1993. Although T. cruzi parasitemia had been detected by indirect methods (xenodiagnoses* or blood cultures), the DME had been persistently negative until August 6, 1998, when T. cruzi trypomastigote forms were observed in the microhaematocrit test, characterizing the reactivation of Chagas’ disease. At that time, the patient had no new symptoms or signs, and the ECG, echocardiogram, and Holter monitor had not changed.

The patient was treated with benznidazole (6 mg/kg/day) for 53 days (from August 14 to October 5, 1998), which led to T. cruzi parasitemia control. His antiretroviral therapy (zidovudine and didanosine) was not changed. The results of CD4+ T-cell counts, HIV viral load, and parasitologic tests performed 6 months before, at the moment of the positive DME, and after treatment with benznidazole are shown in Table 1.

DISCUSSION

Unusually, this patient had no new symptoms and signs when T. cruzi was detected in the DME of blood. His HIV viral load increased simultaneously with the exacerbation of T. cruzi parasitemia and decreased to the previous levels after successful antiparasitic treatment.

During the chronic phase of T. cruzi infection, parasitemia can vary, even though it is always low and detected only by indirect methods, such as xenodiagnoses and blood cultures. The finding of T. cruzi in the DME has never been reported during the chronic phase of Chagas’ disease in immunocompetent patients even using sensitive methods such as the quantitative buffy coat.5,6

In immunocompromised patients with reactivation of Chagas’ disease, high T. cruzi parasitemia either can precede the clinical manifestations7 or can be a later finding,4 but it is always present. The finding of T. cruzi in the DME characterizes the reactivation of Chagas’ disease even if without clinical manifestations.

*In xenodiagnosis, the insect vector is used as a biologic culture medium for T. cruzi detection. Triatomine nymphs are fed on blood from the suspected patient, and 30 and 60 days after the blood meal, the parasite is sought in the intestinal contents of the insects.
The patient’s HIV viral load had increased significantly simultaneously with the exacerbation of *T. cruzi* parasitemia. The patient had adhered consistently to the antiretroviral therapy. He had not received any immunizations during the month before the reactivation of Chagas’ disease, and no other opportunistic disease was diagnosed. After anti-*T. cruzi* treatment, his HIV viral load decreased to the same levels he had before reactivating the trypanosomiasis, despite his antiretroviral therapy remaining unchanged. Although we cannot rule out the possibility of increased HIV viral load related to biologic variation, our data showing increased HIV viral load during *T. cruzi* parasitemia exacerbation and its control after successful antiparasitic treatment suggest that *T. cruzi* might up-regulate HIV replication.

Patients with chronic *T. cruzi* infection have chronic immune activation possibly resulting from low intermittent parasitemia. HIV-infected patients with chronic Chagas’ disease have higher *T. cruzi* parasitemia than HIV-negative individuals. The persistent immune activation induced by *T. cruzi* might lead to a sustained increase in the rate of HIV replication, which may affect HIV disease progression.

The results of an experimental study support this theory. Mice infected with *T. cruzi* and murine leukemia virus (MuLV), which causes an immunodeficiency similar to that caused by HIV in humans, had reactivation of chronic *T. cruzi* infection with high parasitemia and increased myocardium parasitism and inflammation. *T. cruzi* coinfection resulted in aggravation of MuLV infection when compared with mice infected only with MuLV.

This hypothesis raises the question of when to treat *T. cruzi* infection in HIV-coinfected (and other immunocompromised) patients. Chemotherapy for *T. cruzi* is still unsatisfactory. The efficacy of the only available drug (benznidazole) in chronic Chagas’ disease has not been shown. It has some efficacy in controlling parasitemia and clinical manifestations in patients with reactivation of Chagas’ disease, but the treatment should be initiated in the early stages of the reactivation process, when irreversible lesions have not occurred.

Considering this, HIV-coinfected patients with chronic Chagas’ disease who present with high parasitemia should receive specific anti-*T. cruzi* treatment even if asymptomatic.

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