Transactions of the Royal Society of Tropical Medicine and Hygiene 104 (2010) 447–452

Contents lists available at ScienceDirect

Transactions of the Royal Society of Tropical Medicine and Hygiene

journal homepage: http://www.elsevier.com/locate/trstmh

Chagas' disease and HIV co-infection in patients without effective antiretroviral therapy: prevalence, clinical presentation and natural history

Eros A. Almeida[a,*], Josué N. Lima[a], Eliane Lages-Silva[b], Maria E. Guariento[a], Francisco H. Aoki[a], Ana E. Torres-Morales[c], Rogério J. Pedro[a]

[a] Alexander Fleming 40, Faculty of Medical Sciences, University of Campinas – Campinas, São Paulo, Brazil. CEP 13083-970
[b] Federal University of Triângulo Mineiro – Uberaba, Minas Gerais, Brazil
[c] Faculty of Medicine, Regional University of Blumenau – Blumenau, Santa Catarina, Brazil

ARTICLE INFO

Article history:
Received 13 May 2009
Received in revised form 10 February 2010
Accepted 10 February 2010
Available online 19 March 2010

Keywords:
Chagas' disease
American trypanosomiasis
HIV
AIDS
Co-infection
reactivation

ABSTRACT

The objectives of this study were to establish the prevalence of Chagas' disease among HIV seropositive patients and to define the clinical profile of co-infected cases. Cross-sectional study: the prevalence of co-infected subjects was 1.3% and there was no significant difference between co-infected and non co-infected patients relative to race, birthplace, home address and CD4 T cells. The co-infected group comprised predominantly women and mean age and median viral load were higher. Longitudinal study: included 20 patients (12 women) and described the clinical presentation and natural history of concomitant infections. The mean follow-up time was 35.8 months, mean age was 43 ± 8.7 years and 60% of patients were white. During the follow-up, a total of 113 serological tests for Chagas' disease were performed: 89 (78.8%) were reactive/positive, 21 (18.6%) were doubtful and three (2.6%) were non-reactive/negative. Positive results for xenodiagnosis were high (81%). At the baseline evaluation, thirteen patients had the indeterminate form of Chagas' disease and seven cardiopathy. One patient developed from indeterminate to digestive form, three had a reactivation of Chagas' disease in the central nervous system, all had parasitological confirmation and received specific treatment. There were 11 deaths. Thus, HIV-infected patients should be tested for Chagas' disease when epidemiologically relevant.

1. Introduction

Chagas' disease is caused by the *Trypanosoma cruzi* protozoan and is transmitted to humans mainly by hemipterous insects[1] and through blood transfusions, blood products and through congenital transmission. Vectorial transmission of *T. cruzi* is quite prevalent in many countries, though in Brazil this route of infection has ceased to be an issue.[2] Infection by blood transfusion remains an undesirable possibility, however, thanks to strict safety measures established in blood banks it is increasingly infrequent. Despite all efforts to mitigate its presence, human infection by *T. cruzi* remains prevalent throughout Brazil and approximately 5 million Brazilians were chronically infected.[3] The disease is divided into acute and chronic phases and approximately one-third of individuals with chronic Chagas' disease develop a cardiac or digestive pathology, resulting in high disease-related morbidity and mortality.[4]

National surveillance studies estimate that there are 660 000 people between the ages of 15 and 49 years living with HIV (PLWH) in Brazil, representing a national prevalence of 0.65%.[5] In recent years, changes in the

* Corresponding author. Tel.: +55 19 35217803/92579269; fax: +55 19 35217878/32894107.
E-mail address: eros@fcm.unicamp.br (E.A. Almeida).

0035-9203/$ – see front matter © 2010 Royal Society of Tropical Medicine and Hygiene. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.trstmh.2010.02.004

epidemiological profile of HIV have shifted the burden of disease to the interior of the country, affecting primarily poor people and heterosexual women.[6] This profile is quite similar to that of individuals infected with *T. cruzi* and there is a large overlap in the geographic distribution of the two diseases.[7]

To date, the prevalence of Chagas/HIV co-infection in Brazil and other Latin American countries remains unknown and difficult to establish. Cases of co-infection are identified at routine outpatient follow-up visits and the clinical course of co-infection, as observed in these individuals, is thought to be a natural evolution of both diseases: a chronic disease profile.[8-14] Laboratory studies, however, have demonstrated a higher load of *T. cruzi* organisms on parasitological exams (xenodiagnosis and blood culture) among co-infected patients as compared to those with only chronic Chagas' disease.[15,16]

Reactivation of Chagas' disease represents a deviation from the normal clinical course of the disease and it occurs primarily in immunosupressed patients.[17] It presents most frequently with meningo-encephalitis and acute myocarditis. In AIDS patients, while serious, it is less likely to occur in individuals with less advanced disease or on highly active antiretroviral therapy (HAART) due to better immunologic function.[18] Considering the large number of PLWH in Brazil and Latin America unaware of their HIV-status and not receiving ART, there is still a substantial risk of encountering Chagas' disease reactivation.

The primary objectives of this study were to establish the prevalence of Chagas' disease and to define the clinical profile of co-infected cases among HIV seropositive patients enrolled in care and treatment at the HIV/AIDS Clinic, Hospital of Campinas University, São Paulo, Brasil.

2. Methods

2.1. Cross-sectional study

A cross-sectional study was performed to define the Chagas' disease prevalence among HIV patients enrolled in care and treatment at the HIV/AIDS clinic at the Clinical Hospital of Campinas State University, from 1994 to 2001. HIV infection was diagnosed by ELISA and confirmed by western blotting. Chagas' disease was diagnosed using at least two of the following serological tests: indirect immunofluorescence assay (IFA) and/or enzyme-linked immune-sorbent assay (ELISA) and/or complement fixation (CF) reaction**.** The following data was assessed for this group: race, birthplace, location of residence, CD4 T cell count and HIV viral load. Individuals identified as co-infected were then contacted and asked to participate in the longitudinal study, after obtaining their informed consent.

2.2. Longitudinal study

A longitudinal study group was set up to describe the clinical presentation and natural history of concomitant infections. This included all the co-infected patients identified from cross-sectional study and others selected from non-HIV/AIDS clinics, from 1991 to 2001. The demographic data, clinical and epidemiological history of both HIV and Chagas' disease, and results from a physical examination were obtained and registered on the first visit. Mantoux test, serologic tests for syphilis (VDRL and TPHA or FTAbs), toxoplasmosis, cytomegalovirus, hepatitis B/C were also done on the first visit. All subjects also underwent laboratory analyses periodically including: complete blood count, renal and liver panels, chemistries, CD4 T cell count and HIV viral load. Apart from the first visit, Chagas' disease serological tests were also periodically repeated during the follow-up period. At the start of the follow-up and at yearly intervals, the cardiac status was evaluated by chest radiography; resting 12-lead electrocardiogram; two-dimensional cardiac echocardiography; and continuous electrocardiography (Holter system) for 24 hours. When clinical evidence of dysphagia or chronic constipation were found, the digestive system was evaluated with specific focus on the esophagus and colon, using barium swallow or enema x-ray.

Trypanosoma cruzi parasitemia was evaluated using xenodiagnosis and blood cultures. Xenodiagnosis was primarily artificial, carried out using techniques described by Silva et al.[19] All natural xenodiagnosis was performed using the Schenone[20] technique. In both, stage III or IV nymphs of *Triatoma infestans* were used, and then examined at 30 and 60 days. The presence of at least one *trypomastigote* form of *T. cruzi* was considered a positive result. The quantitative evaluation was carried out based on the number of positive *Triatoma infestans* nymphs in relation to the total amount examined. The blood cultures were done according to standard technique[21] using 30 ml of venous blood which was then divided into ten tubes after homogenization in half LIT (Liver Infusion Tryptose). Microscopic examination of the tubes was carried out at 30, 60 and 90 days. If *trypomastigote* forms of *T. cruzi* were present in any one of the ten tubes, the test was considered positive.

All of the individuals were staged for both HIV and Chagas' disease status at enrollment and follow-up. HIV staging was done according to standard 'AIDS Surveillance Case Definition for Adolescents and Adults' (Centers for Disease Control and Prevention, 1993). Chagas' disease staging was done as described by Macedo et al.[22] and patients were assigned to one of four categories: indeterminate, cardiopathy, digestive, and cardiopathy associated to digestive. Chagas' disease reactivation was defined when rare clinical manifestations of this disease, not observed in immunocompetent individuals with chronic forms, was seen and *T. cruzi* was found in biological samples of peripheral blood or other fluids (cerebrospinal fluid, pericardial, peritoneal effusion, etc) detected by direct microscopical examination, or those found to have high burdens of *T. cruzi* amastigotes in histopathological studies (biopsy or autopsy)[23]

The data set for the Cross-sectional Study was analyzed using the Epi-Info 6.0 statistical program (CDC, Atlanta, GA, USA). The results were shown through the mean and median. The statistical evaluation used χ^2 or Fisher's exact test where appropriate. The means were compared using the T-test.