ORIGINAL ARTICLE PARASITOLOGY

Immunosuppression and Chagas disease; experience from a non-endemic country

F. Salvador[1], A. Sánchez-Montalvá[1], L. Valerio[2], N. Serre[3], S. Roure[2], B. Treviño[3], D. Pou[3], E. Sulleiro[4], C. Bocanegra[3] and I. Molina[1]

1) *Department of Infectious Diseases, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona, PROSICS Barcelona,* 2) *North Metropolitan International Health Unit, PROSICS Metropolitana Nord,* 3) *Special Programme for Infectious Diseases Vall d'Hebron-Drassanes and* 4) *Department of Microbiology, Vall d'Hebron University Hospital, PROSICS Barcelona, Barcelona, Spain*

Abstract

Reactivation of Chagas disease in the chronic phase may occur when immunosuppression is established, sometimes resulting in high parasitaemia and severe clinical manifestations such as meningitis and meningoencephalitis. Although this situation is being increasingly described, there is still scarce information. This retrospective observational study was performed in three Tropical Medicine Units of Barcelona (Spain) included in the International Health Programme of the Catalan Health Institute (PROSICS). The objective of the study was to describe epidemiological, clinical, microbiological, prognostic and therapeutic data from patients with Chagas disease and any kind of immunosuppressive condition attended in these three institutions from January 2007 to October 2014. From 1823 patients with Chagas disease attending these three centres during the study period, 38 (2%) had some kind of immunosuppressive condition: 12 patients had human immunodeficiency virus infection, 8 patients had neoplasia, 4 patients underwent organ transplantation and 14 patients had an autoimmune disease. Eight (21.1%) patients had cardiac involvement, and six (15.8%) patients had gastrointestinal involvement. Acute *Trypanosoma cruzi* infection was detected in two Spanish patients. Thirty-one (81.6%) patients received treatment with benznidazole, of whom 17 (54.8%) had some kind of adverse event. No patient had a severe manifestation or reactivation of Chagas disease. Patients with Chagas disease under immunosuppressive conditions are being increasingly described, especially in non-endemic countries. More information about this topic is required and international consensus in the diagnosis, treatment and follow up of these patients must be established to reduce the morbidity and mortality.

Keywords: Chagas disease, human immunodeficiency virus, immunosuppression, transplantation, *Trypanosoma cruzi*
Original Submission: 23 March 2015; **Revised Submission:** 5 May 2015; **Accepted:** 27 May 2015
Editor: E. Bottieau
Article published online: XXX

Corresponding author: F. Salvador, Infectious Diseases Department, Vall d'Hebron University Hospital, Pº Vall d'Hebron 119-129, 08035 Barcelona, Spain
E-mail: fmsalvad@vhebron.net

Introduction

Chagas disease is caused by *Trypanosoma cruzi*, a haemoflagellate protozoa mostly transmitted through the faeces of haematophagous triatomine vectors and congenitally from mother to child. Other transmission routes include blood transfusion and organ transplantation from infected donors, transmission among injecting drug users and oral consumption of contaminated food. The acute phase of the infection is either asymptomatic or presents with non-specific symptoms (fever, malaise, lymphadenopathy). After the acute phase, a subsequent usually asymptomatic chronic stage (or indeterminate phase) takes place over years; after 20–30 years, up to 30–40% of patients develop the symptomatic chronic phase, with cardiac and/or digestive involvement [1].

http://dx.doi.org/10.1016/j.cmi.2015.05.033

Reactivation in the chronic phase (detection of trypomastigotes in blood and other body fluids) may occur when immunosuppression is established, sometimes resulting in high parasitaemia, and severe clinical manifestations such as meningitis and encephalitis, acute myocarditis and skin lesions (panniculitis and subcutaneous nodules) [2,3]. Human immunodeficiency virus (HIV) infection has been the immunosuppressive condition most described in patients with Chagas disease, and meningoencephalitis is the most prevalent clinical manifestation of Chagas disease reactivation in HIV-infected patients [4,5]. Nevertheless, Chagas disease reactivation is increasingly described in other immunosuppressive conditions, such as organ transplantation, neoplastic diseases and new immunosuppressive therapies [6,7].

Chagas disease was originally an endemic disease of Latin America affecting rural and poor populations living in adobe houses. However, the increase of population mobility during last decades has lead to the spread of Chagas disease outside endemic countries [8]. This fact has changed the clinical profile of patients with Chagas disease in non-endemic countries, where patients may easily access newer therapies, including those causing immunosuppression [9].

In this study we describe epidemiological and clinical data of patients with Chagas disease with any kind of immunosuppression in a non-endemic country.

Patients and methods

This is a retrospective observational study performed in three Tropical Medicine Units of Barcelona (Spain) included in the International Health Programme of the Catalan Health Institute (PROSICS): the Infectious Diseases Department of the Vall d'Hebron University Hospital, the Special Programme for Infectious Diseases Vall d'Hebron-Drassanes and the North Metropolitan International Health Unit. Data were collected from clinical records of all patients diagnosed with Chagas disease attended in these institutions from January 2007 to October 2014. We included in the study all patients with Chagas disease with any kind of immunosuppressive condition.

Epidemiological and clinical data were collected from all included patients: age, gender, country of origin, time since arrival to Spain, data related to Chagas disease (cardiac and digestive involvement, severe clinical manifestation, microbiological results, treatment and follow up), and data regarding the immunosuppressive condition. Diagnosis of Chagas disease was based upon the positivity of two different serological tests according to WHO recommendations [10]; an ELISA with recombinant antigen (Bioelisa Chagas; Biokit, Lliçà d'Amunt, Spain), and an ELISA with crude antigen (Ortho *T. cruzi* ELISA; Johnson & Johnson, High Wycombe, UK or ELISA cruzi; bioMérieux, Marcy-L'Étoile, France). When possible, peripheral blood samples were collected and processed for *T. cruzi* PCR, as described elsewhere [11]. All patients were offered to receive treatment with benznidazole 5 mg/kg/day divided into two or three doses for 60 days following the current WHO recommendations [12]. We defined reactivation of Chagas disease during follow up as the positivity of *T. cruzi* PCR after treatment completion.

The objective of the study was to describe epidemiological, clinical, microbiological and therapeutic data from patients with Chagas disease and any kind of immunosuppressive condition, to contribute to increase the scarce information available in this area, and to propose strategies to improve the management of these patients.

The study protocol was approved by the Ethical Review Board of the Vall d'Hebron University Hospital (Barcelona, Spain). Procedures were performed in accordance with the ethical standards laid down in the Declaration of Helsinki as revised in 2000.

SPSS software for Windows (Version 19.0; SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Categorical data are presented as absolute numbers and proportions, and continuous variables are expressed as medians and ranges.

Results

Overall, 1823 patients with Chagas disease attended these three centres included in PROSICS during the study period; of these, 38 (2%) had some kind of immunosuppressive condition: 12 patients had HIV infection, 8 patients had neoplastic disease, 4 patients underwent organ transplantation, and 14 patients had an autoimmune or rheumatic disease that required immunosuppressive therapy. The main characteristics of all patients are described in Tables 1–4. The median age of patients was 37 (0–66) years and 25 (65.8%) were women. Most of them came from Bolivia (35 patients, 92.1%), and the median time of residence in our country at the time of Chagas disease diagnosis was 6 (1–12) years. Eight (21.1%) patients had cardiac involvement, all of them in the early asymptomatic cardiac stage of the disease (stage I of the Kuschnir classification), and six (15.8%) patients had gastrointestinal involvement (three patients with dolichocolon, two patients with megacolon, and one patient with low-grade oesophageal involvement). At the time of Chagas disease diagnosis, 11 of 26 (42.3%) patients had a positive *T. cruzi* PCR. No patient had a severe manifestation of Chagas disease.

Acute *T. cruzi* infection was detected in two Spanish patients. Patient 9 was a case of mother-to-child transmission of both Chagas disease and HIV infection. She was a preterm baby due

Please cite this article in press as: Salvador F, et al., Immunosuppression and Chagas disease; experience from a non-endemic country, Clinical Microbiology and Infection (2015), http://dx.doi.org/10.1016/j.cmi.2015.05.033