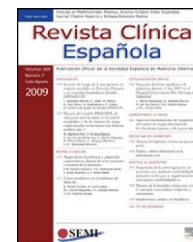




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Chagas disease reactivation in a patient non-Hodgkin's lymphoma



Reactivación de la enfermedad de Chagas en un paciente con linfoma no Hodgkin

M.H. Vicco^{a,b,*}, L.I. César^c, H.M. Musacchio^a, D.O. Bar^c, I.S. Marcipar^a, O.A. Bottasso^d

^a Laboratorio de Tecnología Inmunológica, Facultad de Bioquímica y Ciencias Biológicas, Universidad Nacional del Litoral, Ciudad Universitaria, Santa Fe, Argentina

^b Servicio de Clínica Médica, Hospital J. B. "Iturraspe", Santa Fe, Argentina

^c Servicio de Hematología, Hospital J. B. "Iturraspe", Santa Fe, Argentina

^d Instituto de Inmunología, Facultad de Medicina, Universidad Nacional de Rosario, Santa Fe, Argentina

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Chagas disease is a chronic infection caused by the protozoan *Trypanosoma cruzi* (*T. cruzi*). It has a worldwide distribution affecting at least 8–10 million people. In non-endemic countries, Chagas disease is an emerging illness and has become a public health problem. Most of the patients are asymptomatic, but about 30% of the individuals infected with *T. cruzi* develop clinically relevant syndromes involving the gastrointestinal tract and the heart.¹ Actually, another important complication with poor prognosis is Chagas disease reactivation in relation with immunosuppressive states.²

A 65-year-old man was hospitalized because of multiple bilateral, and painful cervical, axillary and inguinal lymphadenopathies, fever, night sweats and weight loss of two months evolution. In addition to positive serology for *T. cruzi* infection, he suffered arterial hypertension that was treated with angiotensin-converting enzyme inhibitors and chronic Chagas heart disease. He had not received treatment with

anti-*T. cruzi* compounds. Vital signs were within normal range. Routine laboratory tests showed normal hemogram, renal and liver function tests, except increased lactate dehydrogenase (1280 UI/L) and decreased serum albumin levels (2.6 g/dL). Serological tests for HIV were negative. Chest X-ray examination was normal. A twelve-lead electrocardiogram revealed persistent precordial S waves. A 2D and M mode echocardiogram only indicated mild left ventricular hypertrophy. A lymph node biopsy was performed and a diagnosis of non-Hodgkin lymphoma was established. Pre-chemotherapy treatment with dexamethasone (16 mg/day) was instituted. Ten days later the patient suddenly worsened with oligoanuria, hypotension and sustained ventricular tachycardia. New laboratory tests revealed renal failure with normal values of serum potassium, sodium, calcium and phosphorus. Blood and urine cultures were negative. Direct search for *T. cruzi* in peripheral blood was performed through microscopic examination of buffy coat, yielding positive results. The patient died one day after. Autopsy was not performed.

On admission, a serum sample was collected to assess the levels of antibodies against anti-homogenate parasite, anti-FRA (flagellar repetitive antigen of *T. cruzi*), anti-p2β

* Corresponding author.

E-mail addresses: mvicco@santafe-conicet.gov.ar, mhvicco@outlook.com (M.H. Vicco).

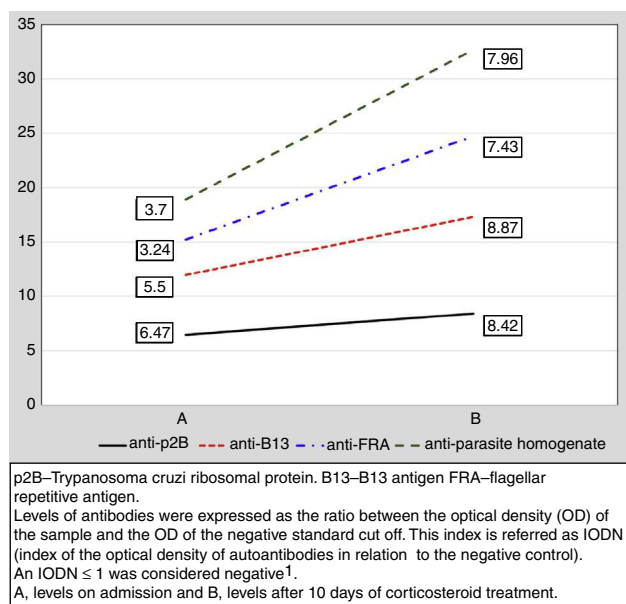


Figure 1 Antibody levels after 10 days of immunosuppressive treatment initiation.

(*T. cruzi* ribosomal protein), and anti-B13. A blood sample was also investigated for the direct presence of *T. cruzi*, revealing no parasites. Another blood sample was taken after 10 days of immunosuppressive treatment initiation. Protein expression, purification and measurement of antibodies by immunoassay were performed as described elsewhere.¹ Serum levels of antibodies are shown in Fig. 1.

Chagas disease reactivation is defined as an increase in parasitemia detected by direct parasitological techniques in patients with chronic Chagas disease.² Most common clinical presentations include heart failure due to acute myocarditis, acute onset of malignant ventricular arrhythmias, meningoencephalitis, fever, and involvement of the esophagus, colon and liver. The few reports of Chagas disease reactivation in hematologic neoplasms are mostly associated with blood transfusion administration. Rassi et al.³ described changes in the course of *T. cruzi* infection but only after long-term corticosteroid therapy (46–60 days).^{2–5} Table 1 summarizes published cases reported of Chagas disease reactivation related with hematological neoplasms under chemotherapy.

Non-Hodgkin lymphoma might induce several immunological disturbances affecting cellular and humoral immune response, which might induce Chagas disease reactivation. However, there is no evidence to support oncohematological diseases as a risk factor.² The relevance of our report relies mainly on the rapid onset of Chagas disease reactivation, just after 10 days of corticosteroid treatment, and its poor clinical course. Moreover, this is the first description that refers to the levels of anti-p2β, anti-B13, anti-parasite homogenate and anti-FRA, during Chagas disease reactivation. Anti-p2β and anti-B13 have been shown to play a pathogenic role in the development of heart tissue lesions.¹ While not routinely employed, these antibody measurements may be useful for assessing Chagas disease staging, prognosis and treatment response.^{12–14}

Table 1 Characteristics of reported cases of Chagas disease reactivation in patients with hematological neoplasms undergoing chemotherapy.

Case report	Age (years)	Sex	Underlying neoplasm	Chemotherapy	Length of time for reactivation	Treatment	Outcome
Franca ⁶	65	Male	LL	NM	N/A	-	Death
Kohl et al. ⁷	14	Female	LL	NM	One month after the first cycle of chemotherapy	Nifurtimox	Survival
Metze ⁸	46	Female	HL	NM	During the induction phase	-	Death
Salgado ⁹	73	Male	LL	Chlorambucil	N/A	Benznidazole	Survival
Fontes Rezende ⁵	42	Female	NHL	CHOP + BLEO	1 month after the last cycle of chemotherapy	Benznidazole	Death
Cohen ¹⁰	16	Female	LL	NM	2 years after the last cycle of chemotherapy. In maintenance therapy with methotrexate and 6-mercaptopurine	Benznidazole	Survival
Oliveira ¹¹	67	Female	NHL	CHOP	After the fourth cycle of chemotherapy	Benznidazole	Death

NM: not mentioned; ALL: acute lymphocytic leukemia; HL: Hodgkin lymphoma; NHL: Non-Hodgkin lymphoma; CHOP: cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone; BLEO: bleomycin.

N/A: not applicable, in both cases the diagnosis of "acute" Chagas disease was done concomitantly with the oncohematological disease.

As depicted in Table 1, Chagas disease reactivation usually occurs during chemotherapy, even during the induction phase, like in this case. Only two cases developed Chagas disease reactivation after chemotherapy completion.

There are no consensus guidelines about how to monitor patients with hematological neoplasms with *T. cruzi* infection. Although some authors recommend the use of quantitative polymerase chain reaction (qPCR) for earlier diagnosis of *T. cruzi* reactivation,^{15–17} these studies have been performed in HIV patients and/or in immunosuppressive states due to organ transplantation. Furthermore, qPCR should be validated in large clinical trials.¹⁸ On the other hand, *Argentine consensus on Chagas disease management* does not recommend qPCR for the monitoring of Chagas disease reactivation in patients with malign hematological disorders.¹⁹

The possibility of rapid fatal outcome, as in our case, in patients with Chagas disease reactivation raises the possibility of early treatment with benznidazole or nifurtimox in all patients with positive serology for *T. cruzi* and clinically significant immunosuppression. Anyway, Chagas disease reactivation should always be taken into account if the patient presents compatible symptoms.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

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