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Case Report

Kidney Transplantation Patient with Discordant Diagnostic Tests for Chagas Disease: Case Report

Juliana J G Ferreira[1], Glaucia B Marcon[2], Luiz Claudio Martins[1], Sandra C B Costa[1], and Eros A Almeida[1]*

[1]*Departament of Medical Clinic, Medical Sciences School, Campinas State University, Brazil*

[2]*Oswaldo Cruz Foundation, Brazil*

***Corresponding author**

Eros A Almeida. Campinas State University. Medical Sciences School, 126, Tessália Vieira de Camargo Street, zip code: 13083-970, Campinas, São Paulo, Brazil, Tel: 55-19-3521-7603. Fax: 55-19 3289-4107; Email: eros@fcm.unicamp.br

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Abstract

In Brazil, the Chagas disease is among the parasitic diseases which takes part in screening pre-transplant on the donor and recipient, because in case of positive results it is indicated the anti-parasitical therapy. The immunosuppressive therapy in kidney transplantation patients could take to opportunistic diseases or reactivation of latent infection. In the Chagas disease, is characterized by high parasitaemia and organs involvement as a cardiac or nervous system. It has been reported a case a patient with chronic renal failure secondary to pyelonephritis which undergone kidney transplantation, presented cardiac clinical manifestations of Chagas disease with discordant laboratory results. The patient has received anti-parasitical therapy, with improvement of cardiac condition, but evolved with graft loss.

ABBREVIATIONS

CD: Chagas Disease; DNA: Deoxyribonucleic Acid; ELISA: Enzyme-Linked Immunosorbent Assay; IIF: Indirect Immunofluorescent; Igg: Immunoglobulin G; NPCR: Nested Polymerase Chain Reaction; PCR: Polymerase Chain Reaction; Qpcr: Quantitative Polymerase Chain Reaction

INTRODUCTION

Chagas disease (CD) is caused by flagellated protozoan *Trypanosoma cruzi* and presents a complex cycle, which involves triatomine bugs vectors. In some countries, this transmission path was considered controlled by control measures of the domiciliary vector. Nowadays, it is been given great attention to the form of transmission: congenital, transfusion, organs transplants, oral and laboratory accidents. The serological screening is used since then in blood banks and before the organ transplant [1]. An estimated 6 to 7 million of people are infected worldwide and each year 10,000 people die in consequence of CD, being 25 million of people are at risk of acquiring the disease [2]. On the acute phase of the disease, there is the presence of circulating parasites in the blood and usually manifests nonspecific symptoms such as fever, diarrhea, vomiting, headache and others. When it evolves into the chronic phase, the amount of circulating parasites decreases and there is the presence of IgG antibodies. It is possible to have the absence of symptoms or the presence of specifics symptoms the cardiac and/or digestive system, which decrease the quality and life expectancy of patients. Patients with an impaired immunity, such as transplantation patients, the risk of reactivation of the disease increases and results in severe clinical manifestations that affect the heart or nervous system [3]. In order to monitor the CD reactivation in the kidney transplantation patients and those subject to immunosuppressive therapy, it is recommended direct parasitological tests, with microscopic analysis of blood in thick drop or smears, called direct fresh test, analysis of cream leukocyte after centrifugation [4], microhematocrit and histopathological examination of tissue lesions [5]. The molecular assay polymerase chain reaction (PCR) has been used as an auxiliary method it has been proved to be a technical with good sensibility and specificity, capable of detecting the DNA of parasite in peripheral blood [6]. The specific treatment for the CD with benzolidazole, allopurinol or association of two medicaments decreases the parasitaemia in episodes of CD reactivation [7-9].

CASE PRESENTATION

Man, 33 years old, natural and resident in the State of São Paulo/Brazil. Hypertensive patient started the dialytic process when he has 14 years old due chronic renal failure secondary to pyelonephritis. He held four blood transfusions, the last one

in 1998. He was registered on the list for kidney disease, which occurred in April/2001 (cadaver donor). The pre-transplants serological tests was discordant for the CD, being ELISA test (enzyme-linked immunosorbent assay) nonreactive and the IIF (indirect immunofluorescent) reactive in title 1/160. After the transplant, the serological tests became nonreactive, the direct parasitological tests (fresh blood, coloring, and Strout), as a xenodiagnostic were negative and the *nested* polymerase chain reaction (NPCR) was positive in two samples collected on different dates (Figure 1). The serological results for leishmaniasis were nonreactive. Five months post-transplant, the patient presented cardiac manifestations of moderate mitral insufficiency, interpreted as CD reactivation. The specific treatment for the *Trypanosoma cruzi* happened with allopurinol (8mg/kg/60 days). The immunosuppressive therapy consists in variable doses of prednisone and azatioprina (subsequently replaced by mycophenolate mofetil) [10]. In 2003, the serological tests continued negative. At the end of the same year, he presented manifestations of acute rejection the transplanted kidney. In 2004, he was diagnosed with mesangial proliferative glomerulonephritis. Even with increased the corticoids, in 2005 the patient lost the graft and returned to dialysis.

DISCUSSION

The high prevalence of the CD in the endemic countries and the migration of infected people for the non-endemic countries increase the attention for the not vectorial transmission of the disease, especially when the carriers are asymptomatic. The absence of a standard test which offers a good accuracy for the acute and chronic phases of the disease is a one of the factors which proves how the disease is neglected. In immunocompetent patients, the acute phase is diagnosed by parasitological tests which confirm the presence of the parasites on the blood. In the chronic phase, is used serological tests to identify antibodies, as in this phase is characterized by low parasitaemia. In immunosuppressed patients with suspected CD reactivation, it is used direct parasitological tests. The polymerase chain reaction (PCR) detected the DNA of the parasite and because this is considered more sensible in transplants patients [11]. Studies show that immunosuppression regimen assumed may interfere in the degree of reactivation of the disease. The Ministry of Health of Brazil [12] indicates the triple therapy with cyclosporine, prednisone and a third drug, azathioprine or mycophenolic acid precursors (mycophenolate mofetil or mycophenolate of sodium), which are used in specific cases of intolerance to azathioprine Cardiac transplanted patients who used azathioprine had less degree of reactivation of CD when compared to patients who use mycophenolate of mofetil [13]. Currently, the benzonidazole is a drug of the choice for prophylactic therapy or treatment of the disease, even presented frequent adverse events. Allopurinol has been as therapeutic option and was able to reduce symptoms associated to reactivation of the CD [14].

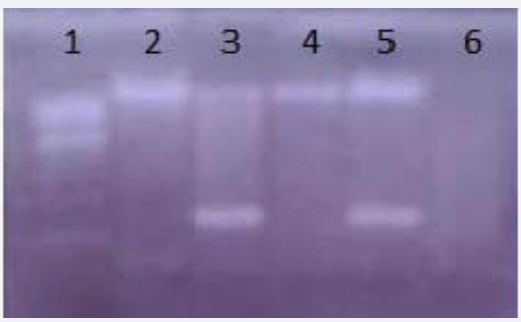

Figure 1 Results of N-PCR for TCZ 3 and 4 primers amplifying a 149 bp on 2% agarose gel. Line 1: DNA size marker 100 bp; Line 3: One sample of patient described in this case report; Line 5: Positive control; Line 6: Negative control; Lines 2 and 4: Others patients not included on the study. Bp: base pairs.

In the case described, the immunosuppression regimen assumed utilize as third drug the azathioprine, which was subsequently replaced for mycophenolate mofetil. The patient was treated with allopurinol, improving the cardiac symptoms. However, there is not parasitological confirmation of reactivation, because the parasitological results were negative before and after to start the allopurinol treatment. The serological results, which previously had been discordant, were negative after transplant. However, in this case, these results do not offer a good accuracy because the patient is immunosuppressed. In a previous report, as well as this, it has become evident how important is to considerer the immunosuppressed patient with negative serological tests for the CD, as a CD bearer, mainly if positive epidemiology. In this case, the suspicion is that the transmission of trypanosomiasis was by transfusion, once is not possible to make serological test in the patient's mother for confirmation or exclusion of congenital path. Besides that, it is suggested that etiological treatment must be performed before the transplant. The disagreement among the results by different tests in this patient, suggests that the laboratory diagnostic for the CD could present failures. In this case, CD reactivation was diagnosed with cardiac clinical signals. However, it is not confirmed by direct parasitological tests, which was not confirmed the *Trypanosoma cruzi* in the peripheral blood. Even with non-standardized technique, the NPCR demonstrated the presence of parasite DNA, however it did not do it in a quantitative way, which would be necessary to confirm reagudization. Currently, with the development of quantitative PCR (qPCR), these cases may have the parasitaemia monitored and so help in the implementation anti-parasitical therapy. This case is one among others that presents difficulties in the CD diagnostic and reactivation, which emphasizes the need of research on new methods that present more reliable results.

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