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Case Report

# Trypanosoma cruzi Myocardial Infection Reactivation after Heart Transplant: A Case Report

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**Abstract**

Chagas Disease is a parasitic disease caused by the Protozoan *Trypanosoma cruzi*, characterized by a variable spectrum. Amongst infected individuals, about 30-40% will have heart involvement throughout life, and in those who develop ventricular dysfunction, the disease usually has a progressive course with evolution to advanced heart failure. In these cases, heart transplant is a good treatment option. Despite the proven benefits, transplant is associated with several complications – such as infectious, autoimmune and neoplastic.

In this study, we present a case of a 57-year old male patient, with Chagas cardiomyopathy who underwent heart transplantation due to end stage heart failure. After transplant, he was readmitted with the hypothesis of acute graft rejection. The endomyocardial biopsy showed reactivation of Chagas Disease. Anti-parasitic treatment was started and the patient had a good clinical evolution.

## ABBREVIATIONS

NYHA: New York Heart Association; PCR: Polymerase Chain Reaction; *T. cruzi: Trypanosoma cruzi.*

## INTRODUCTION

Chagas Disease is a parasitic disease with a two-phase clinical course (acute phase and chronic phase) caused by the Protozoan *Trypanosoma cruzi*, characterized by a variable clinical spectrum, and may be asymptomatic or manifest itself mostly through cardiac or gastrointestinal tract involvement. It's an endemic disease in Latin America, and in Brazil it is estimated that 1.9 to 4.6 million people are infected by the parasite [1]. Amongst infected individuals, about 30% will have the heart involvement throughout life, characterized by arrhythmias, heart failure and thromboembolic phenomena [1]. In patients who develop ventricular dysfunction, the disease is usually progressive with evolution to advanced heart failure. In these cases, heart transplant is a good treatment option. However, this procedure is associated with several complications - infectious, autoimmune and neoplastic. We present a case of myocardial reactivation of Chagas Disease in a patient undergoing heart transplant due to end stage heart failure.

## CASE PRESENTATION

57-year-old male patient with Chagas Disease and ventricular dysfunction (left ventricle ejection fraction: 30%), persistently symptomatic with minimal exertion (New York Heart Association - NYHA – Heart Failure Functional Class III) evolved with worsening of symptoms and was admitted at the Heart Institute Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo in April 2011 with acute decompensation of chronic heart failure (Hemodynamic profile Wet and Cold). Vasoactive drugs were needed during the hospitalization but the patient remained refractory to clinical treatment. He underwent to bicaval orthotopic heart transplant in November 2011 due to end stage heart disease. Postoperative recovery went well and he was discharged from the hospital after 3 weeks, asymptomatic and using immunosuppressive therapy (Azathioprine + Cyclosporine + Prednisone).

In January 2012, the patient was readmitted with a 2-day history of hyporexia, increase of abdominal girth, dyspnea and fever (axillary temperature 38.3°C). Electrocardiogram at admission showed a junctional rhythm with bradycardia and the first hypothesis was acute graft rejection. Pulse therapy (with methylprednisolone) was initiated and the patient went to the Intensive Care Unit. Transthoracic Echocardiogram at admission did not reveal any significant changes in ventricular function. Two days after the admission, the patient presented important clinical worsening, with signs of hemodynamic collapse with

refractory bradycardia and temporary pacemaker was indicated in addition to high doses of dobutamine and adrenaline. New Transthoracic Echocardiogram showed significant dysfunction of the right ventricle. Endomyocardial biopsy was performed and it revealed Chagas Disease reactivation, with numerous *T. cruzi* amastigotes nests in the myocardium and severe myocarditis (Figure 1,2).

Benznidazole was promptly started and the patient evolved with progressive hemodynamic improvement. He was discharged on May 2012 with the same immunosuppressive therapy scheme (Cyclosporine + Azathioprine + Prednisone).

## DISCUSSION

Chronic chagasic cardiopathy is amongst the leading causes of heart failure in Brazil and, in recent years, due to the intense migration of Latin Americans, the disease has spread through several countries in the world. In the United States it is estimated that more than 300,000 people are infected by *T. cruzi* [2], and in the world it is estimated that 6 to 7 million people are infected [3]. Because of the progressive course of the disease, patients with chronic chagasic cardiopathy present worse prognosis than other cardiomyopathies [4]. Heart transplantation is a treatment option in advanced cases of the disease, demonstrating effective modification of the natural history of the illness [5]. Observational studies have shown that patients with chronic chagasic cardiopathy have better survival rates after heart transplant compared to other etiologies (ischemic and non-ischemic) [6], despite of the possibility of reactivation of Chagas Disease in these patients.

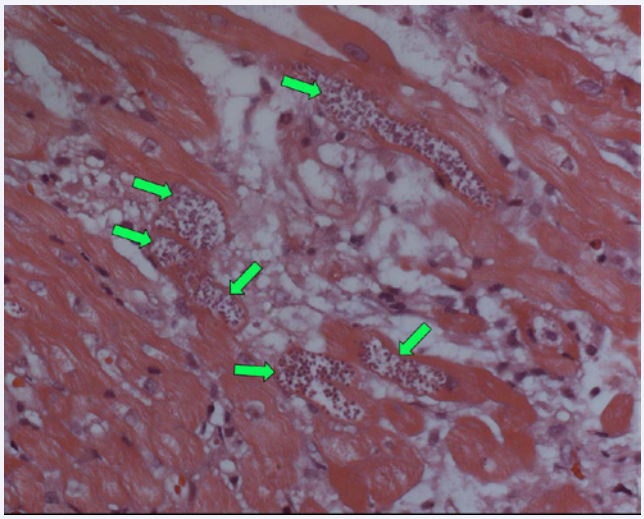

**Figure 1** Histological section of the myocardium showing nests of *T. cruzi* (amastigote form) inside myocardial cells (arrows) and inflammatory cells at the interstitium. Hematoxylin & eosin staining.

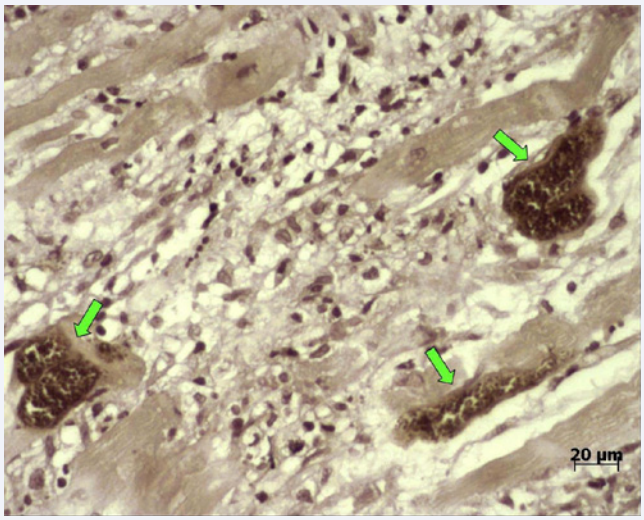


**Figure 2** Histological section of the myocardium with positive immunostaining for *T. cruzi* inside myocardial cells (arrows).

Patients undergoing heart transplant receive immunosuppressive therapy for prevention and control of episodes of rejection. Treatment including corticosteroids, calcineurin inhibitor and an antiproliferative agent is the most used [7]. In addition, patients often receive steroid pulse therapy during episodes of rejection. The immunosuppressive therapy predisposes the patient to infectious complications, including the possibility of reactivation of Chagas Disease, which is more common in the first few months after the transplant, when immunosuppression is more intense.

Some studies have shown that reactivation of the infection by *T. cruzi* can occur in 21-45% of the transplanted patients [2], commonly in the period from 1 to 24 months after the surgery, and frequently they present more than 2 episodes of reactivation [8]. The use of mycophenolate mofetil in immunosuppression, neoplasms and multiple episodes of rejection are factors that have been associated with higher rates of reactivation [9].

The reactivation of the infection by *T. cruzi* often manifests by panniculitis or myocarditis. The myocarditis can lead to congestive heart failure or arrhythmias and is present in 11 to 75% of the patients with reactivation of the disease [10]. The diagnosis of reactivation is made through the identification of the parasite in the myocardium, in blood samples or samples of any tissue that might be affected by the infection. The use of the Polymerase Chain Reaction (PCR) for *T. cruzi* has also shown benefit in diagnosis of reactivation. Other laboratory tests (e.g. serological tests) are not recommended for this purpose [5].

When the diagnosis of reactivation is performed, treatment with anti-parasitic drugs (benznidazole or nifurtimox) must be started immediately to reduce the chances of sequels or unfavorable prognosis. Benznidazole therapy is able to eliminate the circulating parasites in 2 weeks and should be administrated for 60 days [5]. Currently, mortality associated with *T. cruzi* infection reactivation is close to 0.7% [10].

Because of the high rates of reactivation, prophylaxis with anti-trypanosomal therapy has been used in some centers, but the results did not demonstrate benefits with this approach [2]. Early reduction of immunosuppressive therapy and the replacement of mycophenolate mofetil by azathioprine have been recommended as strategies to reduce the possibility of reactivation.

Monitoring reactivation of *T. cruzi* infection, before and after heart transplant, whether clinical or histological, is essential due

to inherent risks, including the possibility of transmission of the infection. However, there is no standardization of frequency and methods for monitoring the reactivation of *T. cruzi* infection [1].

## CONCLUSION

Chagas Disease may have a progressive course leading to end stage heart failure. Heart transplant turns to be a valuable option for these cases. Despite the proven benefits, the transplant is associated with several complications, including the possibility of reactivation of *T. cruzi* infection, which should be promptly recognized and treated.

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