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Case Report

REACTIVATION OF CHAGAS DISEASE IN THE POSTOPERATIVE PERIOD OF HEART TRANSPLANTATION

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Abstract

Reactivation of chronic Chagas disease is a serious complication that usually occurs in states of immunosuppression after transplants, malignant tumors, severe infections and chemotherapy. Cases of cutaneous manifestation of Chagas disease reactivation are less frequent than post-reactivation cardiac changes. We report the case of a 64-year-old chagasic patient undergoing heart transplantation and immunosuppressive therapy, who exhibited reactivation of Trypanosoma cruzi infection, manifested exclusively by erythesic skin lesions, arranged on the lateral and posterior side of the left leg, with the presence of histiocytic reaction in the dermis and the presence of intracellular Trypanosoma cruzi amastigote forms. Cases of Chagas disease reactivation in cardiac transplant patients, who may have an asymptomatic course or present several manifestations, including the appearance of skin lesions characterized by erythesia nodules that may ulcerate with local sensitivity, located in general in the lower limbs and whose histopathological aspect of inflammation extends to the subcutaneous cellular tissue, is described in the literature. Skin and subcutaneous tissue biopsies show nonspecific inflammatory infiltrate and numerous nests of amastigotes. In many cases of Chagas disease reactivation, the parasite has not been found in peripheral blood and the diagnosis of reactivation is made by finding the parasite on histopathological examination of the skin. It should be emphasized the importance of the morphological characterization of the Trypanosoma cruzi (size, shape of the parasite), as well as the need for special stains and immunohistochemical examination, aiming at the differential diagnosis with other microorganisms that have the shape and size similar to Trypanosoma cruzi such as Leishmania sp, Leishmania donovani, Toxoplasma gondi and Histoplasma capsulatum.

Keywords: Chagas disease; Heart transplantation, Trypanosoma cruzi

Abbreviations

CD: Chagas disease
ECMo: Extracorporeal Membrane Oxygenation
EMB: Endomyocardial Biopsy
Tc: Trypanosoma cruzi

Patient E.F.S, male, 64 years old.

Pre-transplant diagnostics

- Decompensated heart failure in profile C → Left Ventricle Ejection Fraction 17%
- Intra-Aortic Balloon 24/01
- Extracorporeal Membrane Oxygenation (ECMo) venoarterial 21/02
- Chagas cardiomyopathy
- Cardiorenal syndrome - chronic kidney disease: basal creatinine.1,60 (06/08/21)

Background

- Multisite Cardiodefibrillator Implant → Electrode fracture (19/03/21)
- Chagas disease (CD)
- Systemic Arterial Hypertension
- Implantable cardiodefibrillator/ablation
- Cardiac arrest - 2015
- Dyslipidemia
- Hypothyroidism

Heart Transplant

- Blood typing O/PRA 25/10 - 0/0
- Serologies → Positive immunoglobulin G (IgG) Toxoplasma, IgG positive cytomegalovirus, Chagas reagent, Human Immunodeficiency Virus (HIV) negative, Hepatitis negative
- Orthotopic heart transplant bicaval (22/02)
- Prioritized by ECMo

- Negative virtual and real crossmatch
- Donor
- 38 years, 80 Kg /180 height
- Cause of death: head trauma on 13/02
- Negative serologies

Post-transplant complications

- Skin CD reactivation (01/05): skin biopsy 05/05 - presence of intracellular parasites → positive for Chagas
- Discrete dysfunction of the right ventricle
- Cytomegalovirus
- Abscess in inguinal region (Surgical Wound Cannulation ECMo) (06/03)
  - Klebsiella β-lactamases of extended spectrum: treated with ertapenen
  - Fast-growing mycobacterium
  - Surgical debridement + VAC 23/03
  - New approach 30/03
- Pericardial effusion: drained 30/03; drain ed 04/04
- Diarrhea → worsens 25/04 (clostridium +)
- Acute cholecystitis - cholecystectomy surgery by laparoscopy video 19/5 - Enterococcus faecalis multis in bile fluid culture

Induction immunosuppression

- Mycophenolato 720 mg
- Methylprednisolone 1g

Immunosuppression in use

- Tacrolimus 2 mg/day
- Azathioprine 50 mg/day
- Predinisone 5 mg/day

Treatment of cutaneous Chagas

- Benzonidazole - 03/05 to 03/07

Endomyocardial Biopsies (EMB)

- EMB: 03/03 - 0R / pAMR0
- EMB: 23/03 - 0R / pAMR0
- EMB: 20/05 - 1R / pAMR0
- EMB: 03/07 - 0R / pAMR0

Complementary Exams

- 04/08/22 - Transthoracic ECHO:
  - Ejection fraction 0.75, left atrium with normal dimensions.
  - Indexed volume of 34 ml/m2 (VR < 35 ml/m2).
  - Left ventricle with normal dimensions, systolic function of the left ventricle preserved.
  - Right ventricle with borderline normal dimensions, preserved systolic function. Systolic pressure in the pulmonary artery estimated at 34 mmHg (VR <35 mmHg).
- 03/12/22: Cardiac scintigraphy with Gallium citrate-67: no scintigraphic evidence of active cardiac inflammatory/infectious process.
- 22/11/22: Renal Function: Cr - 1.37.

Discussion

In the discussion: CD reactivation was reactivation, 60 days after the onset of immunosuppression. Reactivation of chronic CD is a serious complication that usually occurs in states of immunosuppression after transplants, malignant tumors, severe infections and chemotherapy [1].

Cases of cutaneous manifestation of CD reactivation are less frequent than post-reactivation cardiac changes. The above description shows a 64-year-old chagasic patient undergoing heart transplantation and immunosuppressive therapy, who exhibited reactivation of Trypanosoma cruzi (Tc) infection, manifested exclusively by erythesic skin lesions, arranged on the lateral and posterior side of the left leg, with the presence of histiocytic reaction in the dermis and the presence of intracellular Tc amastigote forms. Cases of CD reactivation in cardiac transplant patients, who may have an asymptomatic course or present several manifestations, including the appearance of skin lesions characterized by erythesia nodules that may ulcerate with local sensitivity, located in general in the lower limbs and whose histopathological aspect of inflammation extends to the subcutaneous cellular tissue, is described in the literature [2]. Skin and subcutaneous tissue biopsies show nonspecific inflammatory infiltrate and numerous nests of amastigotes. In many cases of CD reactivation, the parasite has not been found in peripheral blood and the diagnosis of reactivation is made by finding the parasite on histopathological examination of the skin [3]. It should be emphasized the importance of the morphological characterization of the Tc (size, shape of the parasite), as well as the need for special stains and immunohistochemical examination, aiming at the differential diagnosis with other microorganisms that have the shape and size similar to Tc such as Leishmania sp, Leishmania donovani, Toxoplasma gondi and Histoplasma capsulatum [4]. Once the diagnosis is performed, trypanomycin treatment has been shown to be quite effective [5]. A good response of 30-60 days of benznidazole treatment has been reported, with adequate patient survival. Mortality related to CD reactivation was 0.3%, and survival rates are not different from those of other heart transplant recipients [5].

We believe that the importance of reporting this case is to draw attention to the possibility of reactivation of chronic diseases in immunosuppressed individuals, as well as the need for a detailed physical examination of the skin and pathological study of their skin lesions. Such procedures are not at risk, can be performed on an outpatient basis, are low operational cost and allow accurate diagnosis in 48 hours, thus enabling a specific and effective treatment of the etiological agent. The development of skin lesions and nodosed erythemas are highly suggestive of cutaneous manifestations of CD reactivation after immunosuppression in cardiac transplant patients and in other transplants such as bone marrow and renal bone marrow.

Table 1 shows a suggestion of a protocol of clinical, laboratory and histological monitoring for patients undergoing heart transplantation and etiological treatment of acute CD reactivation, according to the 3rd Brazilian Heart Transplant Guideline [5].

Table 1: Clinical and laboratory monitoring of trypanosoma cruzi infection reactivation after heart transplantation in Chagas disease and etiological treatment.

Recommendation Class	Indication	Level of Evidence
Monitoring		
	Before the transplant	
	Two serological tests for Chagas disease, performed by different methods, for the potential recipient and potential donor	
After transplant		

I	Periodic clinical consultations with attention to signs/ symptoms of reactivation, including electrocardiogram and echocardiogram	C
	Trypanosoma cruzi routine blood research (smear, blood culture and xenodiagnosis) for diagnosis of infection reactivation	
	Routine periodic endomyocardial biopsies, with study by Trypanosoma cruzi by histology	
	Routine endomyocardial biopsies, with research of Trypanosoma cruzi by immunohistochemistry when there is moderate inflammation	
	Trypanosoma cruzi research in tissues (skin, bone marrow, etc.) in a framework compatible with reactivation of Trypanosoma cruzi infection	
IIa	Routine periodic endomyocardial biopsies, with study by Trypanosoma cruzi by polymerase chain reaction	C
IIb	Trypanosoma cruzi research routinein the blood by qualitative or quantitative polymerase chain reaction	C
Treatment		
I	Benzonidazole 5 mg/ kg/day for 60 days	C

There is no evidence to support the prophylactic anti-Tc treatment strategy of reactivation. Anti-Trypanosoma medications have important side effects and do not lead to cure of chronic infection, in addition to which a patient may have more than one episode of reactivation after treatment. Therefore, it is necessary to maintain reactivation monitoring even after treatment of CD [6] reactivation.

Conclusion

The immunosuppressive therapy instituted increases the risk of reactivation of Tc infection, whose incidence after heart transplantation ranges from 21 to 45% [6]. Considering morbidity and potential mortality, the diagnosis and appropriate management of CD reactivation in the context of organ transplantation are extremely important. This procedure should be performed within a structured clinical and laboratory protocol to monitor the reactivation of the infection and its subsequent treatment [7].

The diagnosis of reactivation is based on clinical signs and symptoms and/ or presence of parasites in the blood, liquor, bone marrow or other tissues [8]. Currently, post-transplant skin manifestations should be on the diagnostic spectrum of CD reactivation for appropriate etiological treatment.

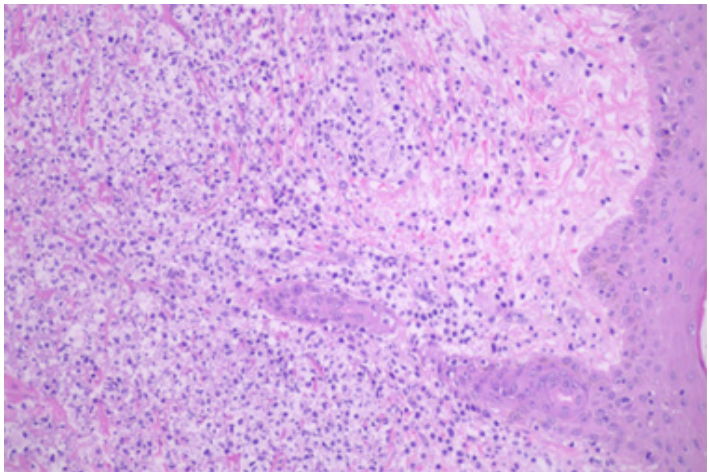

Figure 1. Skin photomicrography with dense histiocytic inflammatory process in the dermis (HE AO 100X).

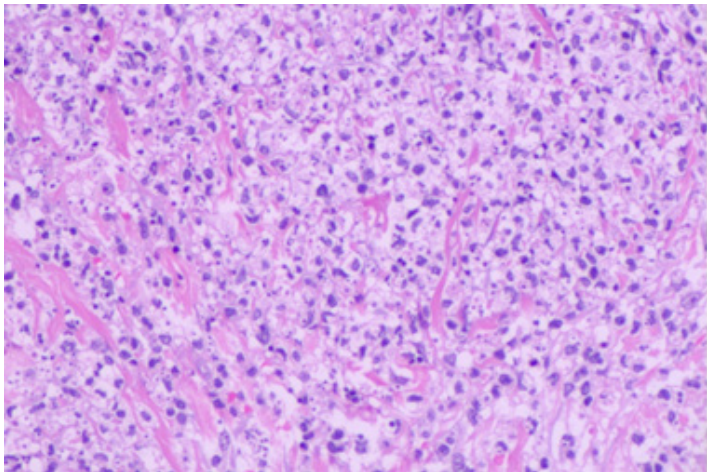

Figura 2. Skin photomicrography shows in detail the dense histiocytic inflammatory infiltrate into the dermis. Histiocytes are voluminous, containing a large number of amastigote forms of Trypanosoma cruzi in the cytoplasm (HE AO 200X).

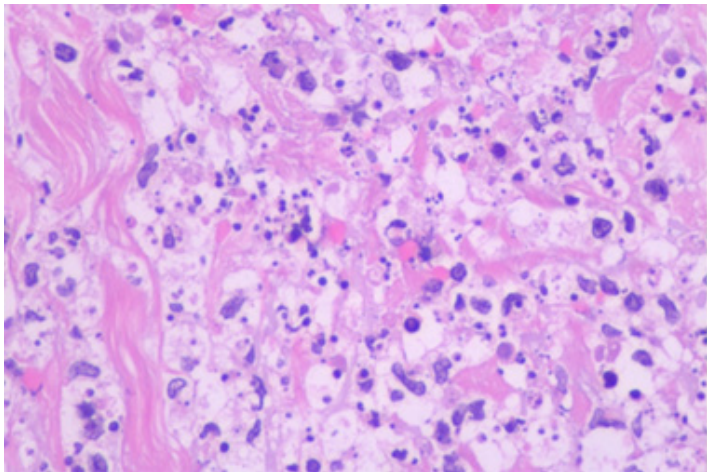

Figura 3. Skin photomicrography shows in detail the dense histiocytic inflammatory infiltrate into the dermis. Histiocytes are voluminous, containing a large number of amastigote forms of Trypanosoma cruzi in the cytoplasm (HE AO 400X).

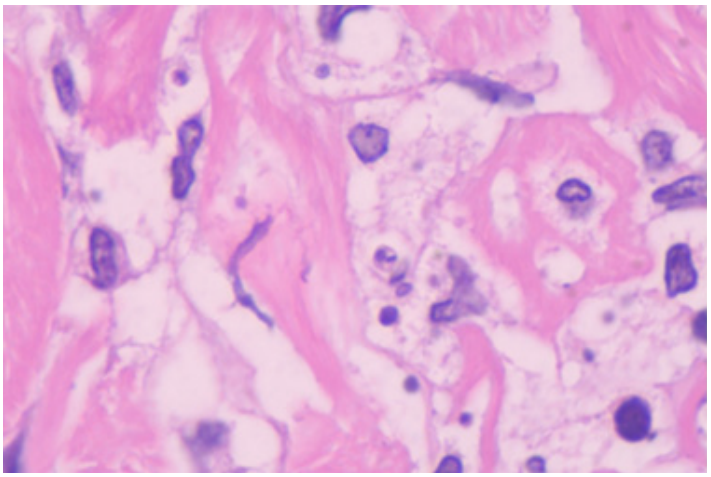

Figura 4. Skin photomicrography shows, in detail, voluminous histiocytes, containing amastigote forms of Trypanosoma cruzi in the cytoplasm. It is possible to identify the nucleus and kinetoplast of the parasite (HE AO 100X).

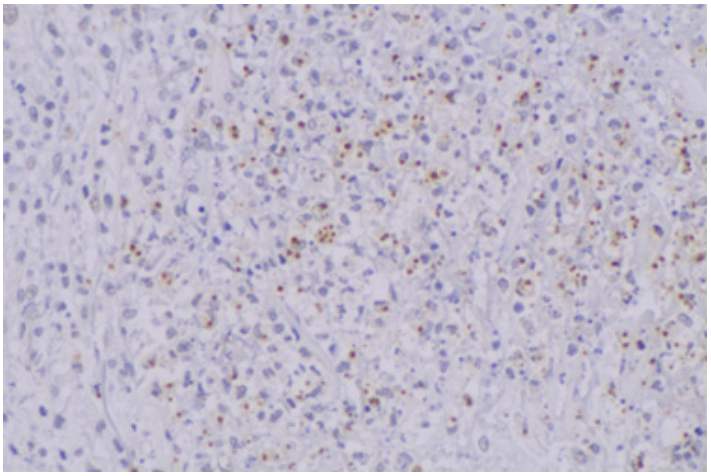

Figura 5. Skin photomicrography shows in detail the presence of a large number of amastigote forms of Trypanosoma cruzi in the cytoplasm of histiocytes (Immunohistochemistry for Trypanosoma cruzi AO 200X).

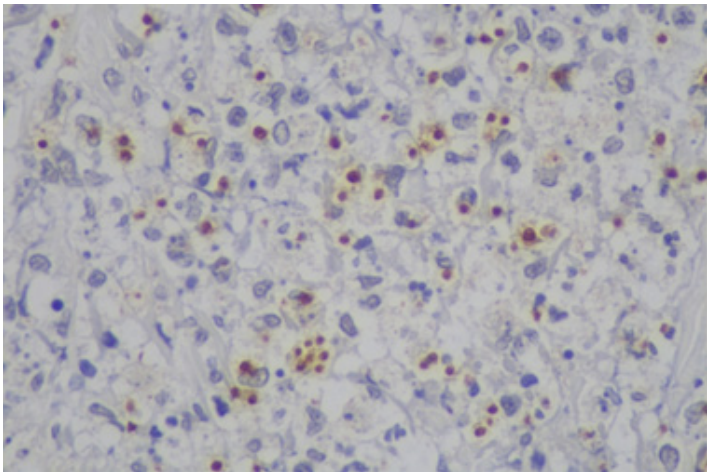

Figura 6. Skin photomicrography shows in detail the presence of a large number of amastigote forms of Trypanosoma cruzi in the cytoplasm of histiocytes (Immunohistochemistry for Trypanosoma cruzi AO 400X).

Acknowledgments

None.

Conflicts of interest

No conflict of interest.

References

1. Bacal F, Silva CP, Pires PV, Mangini S, Fiorelli AI, Stolf NG, Bocchi EA (2010). Transplantation for Chagas' disease: an overview of immunosuppression and reactivation in the last two decades. Clin Transplant. 24: 29-34. doi: 10.1111/j.1399-0012.2009.01202.x
2. Amato JGP, Amato Neto V, Amato VS, Duarte MIS, Uip DE, Boulos M (1997). Lesões cutâneas como únicas manifestações de reativação da infecção pelo Trypanosoma cruzi em receptora de rim por transplante. Rev Soc Bras Med Trop. 30: 61-63. https://doi.org/10.1590/S0037-86821997000100012
3. Ferraresso MG, Torre AC, Piva MMM, Barcan L (2018). Chagas disease reactivation: cutaneous manifestations in a transplanted patient. An Bras Dermatol. 93: 890-892. doi: 10.1590/abd1806-4841.20187855
4. Chocair PR, Sabbaga E, Amato Neto V, Shiroma M, Góes GM (1981). Transplante de rim: nova modalidade de transmissão da doença de Chagas [Kidney transplantation: a new way of transmitting chagas disease]. Rev Inst Med Trop Sao Paulo. 23: 280-282. https://pesquisa.bvsalud.org/portal/resource/pt/lil-3115
5. Bern C. (2011) Antitrypanosomal therapy for chronic Chagas' disease. N Engl J Med. 364: 2527-2534. doi: 10.1056/NEJMct1014204
6. Bacal F, Marcondes-Braga FG, Rohde LEP, Xavier Júnior JL, Souza Brito F, Moura LZ, et al. (2018) 3ª Diretriz Brasileira de Transplante Cardíaco. Arq Bras Cardiol. 111: 230-289. doi: 10.5935/abc.20180153
7. Bocchi EA, Fiorelli A. (2001) First Guideline Group for Heart Transplantation of the Brazilian Society of Cardiology. The Brazilian experience with heart transplantation: a multicenter report. J Heart Lung Transplant. 20: 637-645. doi: 10.1016/s1053-2498(00)00235-7
8. Moreira MDCV, Renan Cunha-Melo J (2020). Chagas Disease Infection Reactivation after Heart Transplant. Trop Med Infect Dis. 5: 106. doi: 10.3390/tropicalmed5030106

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