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## A PATIENT WITH DEXTROCARDIA AND CHAGAS DISEASE: CASE REPORT AND LITERATURE REVIEW

**Keywords:** Dextrocardia; Chagas Disease; American trypanosomiasis; Situs inversus.

**Palabras clave:** Dextrocardia; Enfermedad de Chagas; Tripanosomiasis americana;  
*Situs inversus.*

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## ABSTRACT

**Introduction:** About half a million patients in Colombia are currently infected with *Trypanosoma cruzi*. However, little is known about patients with Chagas disease and anatomical defects such as dextrocardia.

**Case presentation:** A 52-year-old male patient with a 4-year history of dyspnea, chest pain, lower limb edema and syncope (requiring hospitalization), arrhythmias and dextrocardia, underwent serological tests for *T. cruzi* that were positive. A literature review was conducted to find case reports of patients with dextrocardia or situs inversus and Chagas disease in order to determine the proper treatment.

**Conclusion:** Cases of patients with dextrocardia and Chagas disease are rare. Besides the reported case, only three other cases were found in the literature, which were relatively similar, although they could be considered more severe. According to the findings, the use of etiological treatment is acceptable in patients with coronary anatomic abnormalities and *T. cruzi* infection. The present case draws attention to the importance of adequately approaching and monitoring this type of patient.

## RESUMEN

**Introducción.** En la actualidad, en Colombia hay aproximadamente medio millón de personas infectadas con *Trypanosoma cruzi*; sin embargo, no hay mucha información sobre pacientes que viven con enfermedad de Chagas y anomalías anatómicas como la dextrocardia.

**Presentación del caso.** Paciente masculino de 52 años con cuadro clínico de aproximadamente cuatro años de evolución consistente en

disnea, dolor torácico, edema de extremidades inferiores, síncope (que requirió hospitalización), arritmias y dextrocardia, a quien se le practicaron pruebas serológicas para *T. cruzi* que resultaron positivas. Con el fin de establecer el tratamiento adecuado, se realizó una revisión de la literatura buscando reportes de casos de pacientes con dextrocardia o situs inversus y enfermedad de Chagas.

**Conclusión.** Los casos de pacientes con dextrocardia y enfermedad de Chagas son poco frecuentes: además del caso reportado, en la literatura solo se encontraron tres reportes adicionales, los cuales fueron relativamente similares, aunque podrían considerarse más severos. Según los hallazgos, el uso de tratamiento etiológico es adecuado en pacientes con anomalías anatómicas cardiovasculares e infección por *T. cruzi*. El presente caso llama la atención sobre la importancia de tener un enfoque y seguimiento adecuados en este tipo de pacientes.

## INTRODUCTION

At least 4.8 million people in Colombia are at risk of contracting Chagas disease, and almost half a million are currently infected (1). Several meta-analyses recently estimated the prevalence of the disease with a range between 2-4% (2,3). Unfortunately, according to the consolidated information from the data published in the 2016 epidemiological weeks and data from the public health surveillance system, screening tests have not been widely performed and between 2008 and 2015, only 65 000 tests were performed among the population at risk, representing only 1.35% of that population. Of the taken tests, approximately 10% were positive (4).

Furthermore, according to data consolidated and provided by the Red Nacional de

Bancos de Sangre (Colombian National Blood Network in internal conferences) in 2016 and based on information from the public health system, the network tested over 5 million blood units in 2014 and 2015 and less than 10% were positive. However, in 2018, this national network confirmed that 10% of total donors in 2016 tested positive for molecular markers of Chagas disease (5). Regardless, this is not a representative sample because most blood units were collected from major city health centers, which may not reflect the actual distribution of the disease.

A flaw of this screening process is that there are no records regarding the follow-up of these patients (2). Another worrying aspect is that the National Clinical Guideline, which has not been revised since its creation, has a poor to moderate overall quality; this is also true for several other epidemiological reports of the disease (6,7). Another significant problem is that not all public health laboratories have the installed capacity to perform the diagnostic tests and not all laboratories can carry out the three recommended tests (8). Therefore, the country had to modify the diagnostic algorithm to eliminate this diagnostic access barrier (9).

Depending on the stage of the disease, two separate methods for diagnosing Chagas disease must be used. The first one is utilized in the acute phase, where confirming the presence of the parasite in peripheral blood is critical (10). The second strategy must be used during the chronic phase, when indirect assays have more sensitivity; two or more types of tests (Immunofluorescence Assay, Hemagglutination Assay, or ELISA) must be used at the same time when they are used (11).

Once diagnosed, treatment, which presents barriers to access as well (8,12), can be started. Currently, two medications are being used. The first one is nifurtimox (13), which is

given in doses of 8-10mg/kg/day for 60-90 days (14). Despite its side effects, this drug is relatively effective in children in the chronic phase of the disease; therefore, its use is advisable in this population (15). Anorexia, nausea, weight loss, anxiety, excitability, psychological alterations, nausea, vomiting, diarrhea, among others, are some of the side effects associated with this medication (16). The second drug is benznidazole (13). Its efficacy is comparable to nifurtimox, but with a lesser number of adverse effects (17) and more effective in the acute phase. However, its cure rate is low in the chronic phase (18,19). The recommended dose ranges between 5-10 mg/kg/day for 60 days. Side effects include skin alterations, bone marrow depression, thrombocytopenic purpura, agranulocytosis, kidney failure, liver failure, gastrointestinal effects, among others (14).

In Colombia, the indications to start treatment are: 1) all cases in the acute phase, 2) congenital infection, 3) all diagnosed patients under 18 years of age, 4) patients in the chronic phase with disease reactivation, and 5) accidental exposure (20).

Although knowledge of Chagas disease is always increasing, little is known about patients living with it and congenital anatomic abnormalities such as dextrocardia, situs inversus totalis, or others. This could be explained because it is a relatively rare condition; for example, its prevalence in the United States is estimated at about 2 patients per 10 000-20 000 inhabitants (21).

The most common type of dextrocardia is mirror image, in which the morphology and anatomy of the various parts of the heart are normal, but they are not in their usual position (right to left reversal). Changes in electrocardiography and imaging scans are helpful diagnostic aids, but clinical approach, clinical judgment and suspicion are also needed

(22,23). Inverted P, QRS, and T waves in D1, as well as a progressive increase in R waves in precordial leads, are common electrocardiographic findings (21).

Patients with Chagas disease and dextrocardia may present with syncope, palpitations, chest pain, anxiety, dyspnea, and reduction of functional class (22,24,25). Clinical findings include bradycardia, tachypnea, ventricular tachycardia, mitral systolic murmur, right bundle branch block, antero-superior left bundle branch block, cardiomegaly, atrioventricular block, among others. Negative waves (P, QRS, and T) can be detected in D1 on the electrocardiogram (22,24,25). These signs and symptoms are somewhat similar to those that Chagas disease patients typically experience.

The present article reports the case of a patient with dextrocardia and *Trypanosoma cruzi* infection.

## CASE DESCRIPTION

### Medical history until 2017

This is a 52-year-old mestizo male patient from the department of Santander, Colombia, who works as a dealer of various products and comes from a middle-income family (level 3 on a stratification scale from 1 to 6). He denies any relevant family history. His medical history includes hypertension, currently treated with enalapril 20mg P.O. per day since being diagnosed four to five years ago. Moreover, he was diagnosed with dextrocardia when he was 20 years old. His physical examination was normal, with a heart rate of 66 heartbeats per minute, respiratory rate of 18 breaths per minute, blood pressure 124/82, and temperature 36.5°C.

He reported a 4-year history of dyspnea (functional class II/IV), fatigue, dizziness, chest pain, lower limb edema, and syncope that re-

quired hospitalization. Complementary tests were conducted during his hospital stay, including a 12-lead electrocardiogram, two-dimensional echocardiography, 24-hour Holter monitoring, and a chest X-ray. The electrocardiogram showed ventricular extrasystoles and supraventricular tachycardia. Chest X-ray (25/07/2018) showed dextrocardia (Figures 1 and 2). Serologic testing for *T. cruzi* was positive, leading to the diagnosis of chronic Chagas disease (anti-*T. cruzi* IgG ELISA with whole extract and synthetic peptide-based ELISA) (13,26).

Table 1. Findings in echocardiogram and Holter monitoring.

Echocardiogram	24-hour Holter monitoring
<b>27/07/2017</b> Dextrocardia, situs inversus totalis. Right atrium to the left. Left cavities to the right. Apex pointing to right. LVEF: 60%. Left ventricle end-diastolic diameter: 5.0cm (3.7-5.6); Left ventricle systolic diameter: 2.9 (2.0-3.8)	<b>27/07/2017</b> First-degree atrioventricular block, occasional monomorphic ventricular extrasystoles, occasional conductive atrial extrasystoles. QTc Interval 413mseg. Normal ST segment
<b>07/07/2018</b> LVEF: 65%. First-degree diastolic dysfunction, minimum tricuspid insufficiency. Left ventricle systole: 2.7cm. Left ventricle diastole: 4.2cm.	<b>09/07/2018</b> Mild ventricular and supraventricular arrhythmia.
<b>08/08/2019</b> Dextrocardia, apex pointing to right. Adequate biventricular function. First-degree aortic valve insufficiency. Upper limit of the ascending aorta. LVEF: 60%. Left ventricular systole: 2.5cm. Left ventricular diastole: 4.3cm.	<b>15/08/2019</b> High-grade ventricular arrhythmia. Mild ventricular and supraventricular arrhythmia

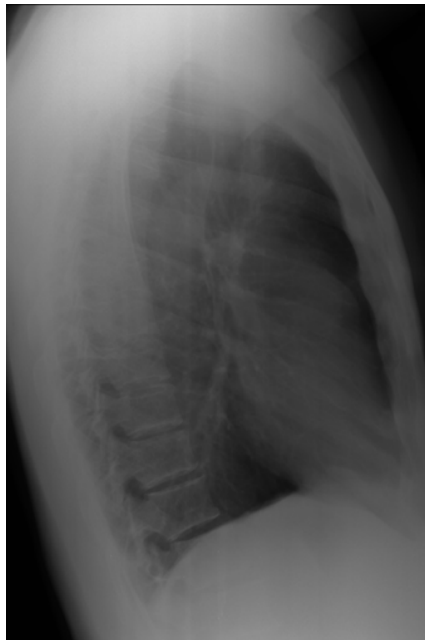
LVEF: left ventricular ejection fraction; QTc: corrected QT interval.

Source: Own elaboration.



**Figure 1. Anteroposterior projection of chest X-ray. Dextrocardia is clearly visible.**

Source: Chest X-ray taken by health services. Obtained during the course of the study.



**Figure 2. Lateral projection of chest X-ray.**

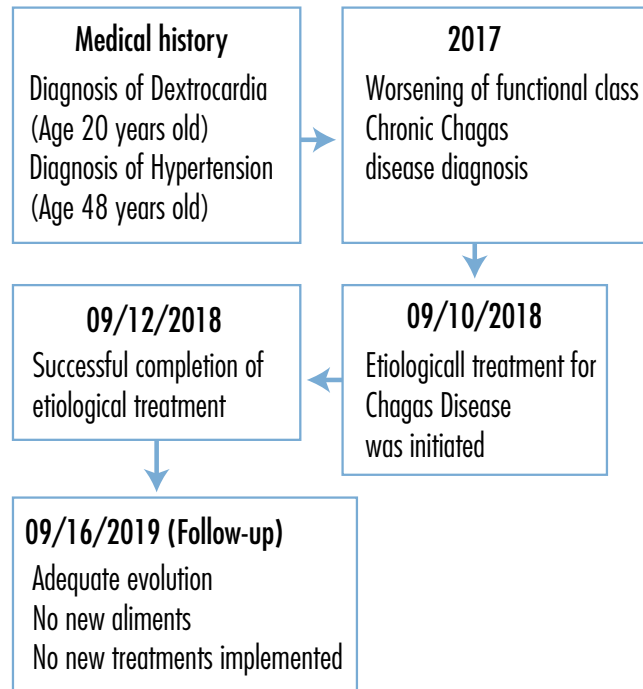
Source: Chest X-ray taken by health services. Obtained during the course of the study.

**10/09/2018:** The patient reported dyspnea (functional class II/IV) and thoracic pain. Dextrocardia was discovered during clinical examinations. Etiological treatment for Chagas disease (benznidazole 5 mg/kg/day for 60 days) was started and completed successfully. Treatment was temporally suspended for 5 days from day 12 due to gastrointestinal manifestations (severe nausea, vomit, and diarrhea) that limited his activities of daily living. He also experienced fatigue and weakness. The patient presented a pruriginous rash that was treated with antihistamines. Afterwards, treatment was continued without further complications. The patient lost 4kg due to the side effects of the treatment.

**16/09/2019:** The patient claimed that his condition had not worsened at the follow-up appointment. He had no pain and no further alterations in his functional class. No other member of his family has been diagnosed with Chagas disease. He has not acquired a new illness, nor has he undergone any extra therapies or procedures. His condition was defined as stable, with a favorable prognosis and a long-life expectancy. Furthermore, it was made clear that a lifelong follow-up was needed to avoid complications and further deterioration of his condition. The timeline of the case is presented in Figure 3.

### Search strategies

PubMed, Scopus, SciELO, Redalyc, Lilacs, and Google Scholar were used to conduct the literature review. Five terms related to the patient's condition were combined in the search strategy: 1) Chagas disease, 2) Dextrocardia, 3) Humans, 4) Situs inversus, and 5) Situs solitus. The search included all studies conducted up until November 19, 2019, with no date restrictions.



**Figure 3.** Timeline of the clinical evolution of the patient.

Source: Own elaboration.

## Study selection and data extraction

Cases or series of cases of dextrocardia or situs inversus and Chagas disease with at least one patient were eligible for inclusion. If a study described a single case, it was classified as a case report, and if it described more than one patient, it was classified as a series. Publications not written in English, French, Spanish, or Portuguese were excluded. Two reviewers independently screened the search results for inclusion and extracted data using a standardized data extraction form. Disagreements were resolved through discussion until consensus was reached. Information about first author, country, year of publication, number of patients, sex, clinical manifestations, treatment, characteristics of the report and outcome was extracted.

## Quality analysis

Each study was subjected to a quality assessment. To that end, both reviewers used a standardized data extraction form to extract the data. Coherence, findings, discussion, conclusion, the manner in which the case was reported, and diagnostic reasoning was evaluated.

The literature review yielded 230 studies (Figure 4) and 27 duplicates were removed. After screening titles and abstracts, 196 studies were excluded, for a total of 7 full texts evaluated. 3 of these studies met the inclusion criteria (Table 2). The 3 reported cases were female, with a mean age of  $37.3 \pm 1.2$ . Dyspnea and syncope were the two most common symptoms. Table 3 shows other characteristics.

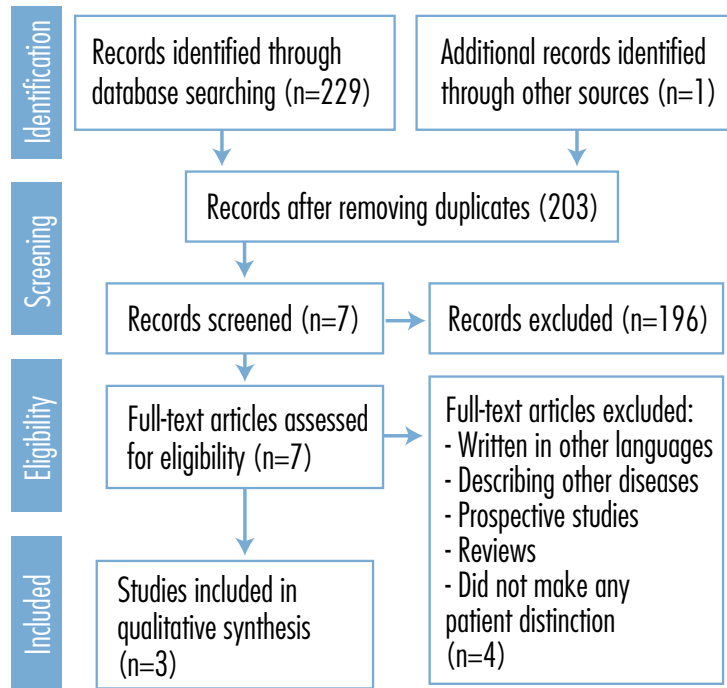


Figure 4. PRISM strategy.  
Source: Own elaboration.

Table 2. Case reports included after the systematic search of literature.

Ref.	Title	Year
(24)	Bloqueio atrioventricular total em dextrocardia e doença de Chagas: implante de marca-passo dupla-câmara com upgrade para estimulação biventricular	2015
(22)	Ablation of epicardial ventricular tachycardia in a Chagasic patient with situs inversus totalis: A case report	2017
(25)	Associação entre cardiomiopatia chagásica crônica e dupla lesão mitral reumática em uma paciente com situs inversus totalis	2012

Source: Own elaboration.

### Quality analysis results

Regarding the overall quality analysis, the results were fairly consistent. All the articles presented deficiencies in the reporting. However, follow-up and the use of different diagnostic aids were adequate in general. In general, however, follow-up and the use of various diagnostic aids were satisfactory. The studies omitted details

about the patients' demographics, medical and family history, and most of them did not explain the timeline according to the CARE guidelines, although they are not a quality assessment tool. Discussions were relatively solid, but they could be improved and extended. Patients' perspective was not described in any of the cases, and there was no explicit information on the patient's informed consent in some of the reports.



Table 3. Characteristics, symptoms and findings of the cases found in the literature search.

Ref.	Sex/ Age	Signs and Symptoms	MRI	EKG	RX	Echocar- diogram	Cineangi- ography	Other	Diag- nosis	Treatment	Out- come
(24)	F/38	Initial: Syncope, bradycardia	NA	Atrioven- tricular block, bra- dycardia. Negative P, QRS and T waves in D1	Car- diac apex point- ing to the right	LVEF: 60%, left ventricle 46mm x 30 mm and left atrium 35mm	Normal ventricular function and coronography. Dextrocardia.	NA	Chronic Chagas and dextro- cardia	Du- al-chamber peace- maker	Alive
		Subse- quent: Dyspnea, functional class III	NA	NA	NA	LVEF 28%, left ventricle 65.1 mm x 56.4 mm and left atrium 51.7 mm. Diffuse hypokinesis. Cardiac dysfunction	NA	NA	NA	Cardiac resynchro- nization therapy	
		Posttreat- ment: Functional class II	NA	NA	NA	LVEF 26%	NA	NA	NA	Adjust- ments in therapy. LVEF remained constant.	
(22)	F/36	Ventricular tachycar- dia and syncope	Dextro- cardia, left ventricle apex pointing to the right Position of the liver in- verted in relation to the heart.	Ventricu- lar tachy- cardia	NA	NA	NA	NA	Chronic Chagas and dextro- cardia	Epicardial ablation	Alive
(25)	F/38	Palpitations and dys- pnea. Mitral systolic murmur	NA	Function- al right bundle branch block Functional left ante- ro-superi- or bundle branch block	Car- diac apex point- ing to the right Cardio- megaly	LVEF 49%, left ventricu- lomegaly and atriomegaly, double mitral lesion with moderate stenosis and insufficiency	NA	NA	Con- genital Chagas and dextro- cardia	NA	Alive

Ref.: Reference number; LVEF: left ventricle ejection fraction; NA: not applicable.

Source: Own elaboration based on Craveiro *et al.* (24), Oliveira *et al.* (22) and Passos *et al.* (25).



## DISCUSSION

Chagas disease is one of the most prevalent parasitic diseases in the Americas (27). The present article reported the case of a patient with dextrocardia associated with Chagas disease. To date, there is not much information available on this type of patient. Not only situs inversus totalis is a rare condition (2 cases per 10 000 are estimated in the United States) (21), but co-infection with Chagas disease seems to be even rarer. The literature search yielded only three cases, which are relatively similar to the one presented in this article, although they could be considered more severe due to the characteristics of the clinical manifestations and the treatment required.

On the other hand, the present case was the only one that clearly stated that the patient received etiological therapy for Chagas disease and reported a male patient. It stands out because it emphasizes the difficulties and challenges that this condition poses for establishing a treatment. There is no clear care standard for this specific kind of patient, side effects could be severe, and adherence is challenging due to such side effects and therapy length.

Still, it is important to use and complete the etiological treatment in patients with abnormal cardiac anatomy. The treatment reported here was not only necessary but also appropriate, as it minimized the likelihood of potential complications, which could be fatal in patients with anatomical abnormalities. In the event of side effects, therapy may be temporarily suspended, or other solutions considered.

As stated above, unlike the other cases found in the literature, the patient reported here is a male. When comparing this patient's clinical evolution and symptoms to those described by Craveiro *et al.* (24), it was possible to establish that the clinical presentation of

our case was not as severe, whereas his young female patient required the implantation of a pacemaker. Nonetheless, her evolution was equally satisfactory. Regarding the case published by Oliveira *et al.* (22), which involved invasive procedures as treatment, she also had an adequate evolution. The last case (25) also had anatomical abnormalities that required other treatments and procedures to prevent complications and fatal outcomes.

As stated above, the findings of the overall quality analysis were relatively homogeneous. While these findings are similar to those reported in a study evaluating the consistency of evidence of acute outbreaks of Chagas disease, no other quality review of similar cases has been identified (7). The checklist used to evaluate the reviewed articles is not a quality assessment tool, which is a flaw in our approach to this case study (28). However, there was little knowledge on demographics, medical, and family history, and most of the cases lacked a timeline.

One difficulty of the quality analysis process was that there were several approaches. In a systematic review, Sanderson *et al.* (29) found 86 different tools, of which 48% were checklists, 38% scales, and 14% were summary judgement checklists. Moreover, some were created for general use, others for critical reading processes, and others were tools designed with a sole purpose in mind and can only be used in the original article. Since there are multiple tools, there is no consensus on their use (29). For example, the use of domains instead of checklists has been proposed by some organizations (30), especially as some checklist items are not justifiable and others are not related to quality or internal or external validity (30).

Finally, the strengths of this case report involve an extensive literature search, a thorough medical examination, the comprehensive assessment of the case, and the use of etiological

treatment. In contrast, the weaknesses include the lack of additional blood and laboratory tests, and other imaging studies to assess more exhaustively the clinical condition of the patient, for example, to assess the possibility of situs inversus totalis.

## CONCLUSION

This case highlights the importance of adequately approaching and treating patients with two conditions that can affect the cardiovascular system in particular and the whole anatomy in general. While this patient received sufficient follow-up, complications and challenges in this area are still a possibility and could hinder the comprehensive assessment of patients.

## ETHICAL CONSIDERATIONS

Written informed consent was obtained for the publication of this case, the photographs, and the pictures obtained during the course of the research.

## PATIENT'S PERSPECTIVE

The patient claims to be in good health. He understands both conditions and is aware that they are chronic. He says that will follow the recommendations and advice given to him.

## TRANSPARENCY

The authors declare that all the information contained in these pages is accurate, truthful, and transparent, that no important aspects of the case were omitted, and that all relevant characteristics or discrepancies were reported.

## CONFLICTS OF INTERESTS

None declared by the authors.

## FUNDING

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