

Case Report

Chagasic cardiomyopathy and Pompe disease: case report

Rafael OB de Morais¹, Ândrea V Chaves-Markman^{1,2}, Anna PP Miranda³, Ingrid G Amorim⁴, Maria da GA de M Cavalcanti¹, Manuel Markman¹, Brivaldo Markman-Filho²

¹Hospital Agamenon Magalhães, Department of Cardiology, Brazil; ²Hospital das Clínicas da UFPE, Department of Cardiology, Brazil; ³Hospital das Clínicas da UFPE, Department of Neurology, Brazil; ⁴Hospital Maternidade Divino Amor, Brazil

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Abstract: Background: Pompe disease is a lysosomal storage disease with an autosomal recessive inheritance characterized by an insufficient activity of the acid alpha-glucosidase enzyme. The incidence varies from 1:40000 to 1:200000 live births and cardiac involvement in adults is rare. Chagas disease is an infection caused by the protozoan *Trypanosoma cruzi*, in which one-third of the cases progress to the chronic form, and may lead to cardiac involvement, usually from the fifth decade of life onwards. We report a case of a patient with Chagas and Pompe diseases who had early cardiac involvement and rapid evolution to heart failure. Case report: A 43-year-old male patient with a history of ischemic stroke at 28 years with gait ataxia sequelae. A few years after the episode, he experienced gait impairment and difficulty climbing stairs, attributed to stroke. A family screening for Pompe disease was carried out years later, and thus the diagnosis was made. As for Chagas disease, the investigation was performed because the patient lives in an endemic area. The cardiovascular physical examination did not show significant changes. The electrocardiogram showed sinus rhythm with left bundle branch block and first-degree atrioventricular block; the transthoracic echocardiogram demonstrated left ventricular systolic dysfunction; the Holter monitoring showed several episodes of ventricular tachycardia. The patient is undergoing optimized treatment for heart failure and enzyme replacement therapy for Pompe disease. Conclusion: Cardiomyopathy with early onset and with rapid evolution suggests overlap of the two diseases.

Keywords: Pompe disease, Chagas disease, heart failure

Introduction

Pompe disease (PD), also known as glycogenosis type II, is an autosomal recessive lysosomal storage disease caused by a decrease in the activity of the acid alpha-glucosidase (AAG) enzyme. Its deficiency results in inadequate accumulation of intra-lysosomal glycogen in several organs, resulting in a broad clinical spectrum [1]. There are two types of PD, the infant and the adult form. The first has a progressive course in the first year of life and mainly affects cardiac and musculoskeletal systems with evolution to heart failure (HF) [2]. The second one involves a wide variety of signs and symptoms, but cardiac involvement is a rare manifestation in this phase, with up to 10% of patients with cardiovascular symptoms [3, 4].

Chagas disease (CD) is an infection caused by a protozoan parasite called *Trypanosoma cruzi*,

found in feces of hematophagous insects of the Triatominae subfamily [5]. The disease consists of two phases: acute and chronic. The chronic form can still be divided into indeterminate, cardiac, digestive and mixed (cardiac and digestive). About 30-40% of patients reach the cardiac stage after two decades of acute infection [6]. This involvement is of major relevance, given its severity, and affects mostly age groups around 55 years [7]. We will describe a case of a patient with Chagas and Pompe diseases with early signs and symptoms of ventricular dysfunction.

Case report

A 43-year-old male from Santana dos Garrotes (Paraíba), the northeastern region of Brazil, presented a sudden lowering of the level of consciousness associated with dizziness, dysarthria, and loss of strength in the four limbs at

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Table 1. Cronology of clinical events and diagnosis

| Clinical Event | Symptoms | Diagnosis |
|---------------------------|---|--|
| Ischemic stroke at age 28 | Gait ataxia and left hemiparesis | Chagas cardiomyopathy disease by two serologic tests |
| At age 34 | Worsening in the gait, difficulty climbing stairs, and difficulty standing up | - |
| At age 39 | Worsening of the neurologic symptoms | Familial screening for Pompe disease. Heart failure |

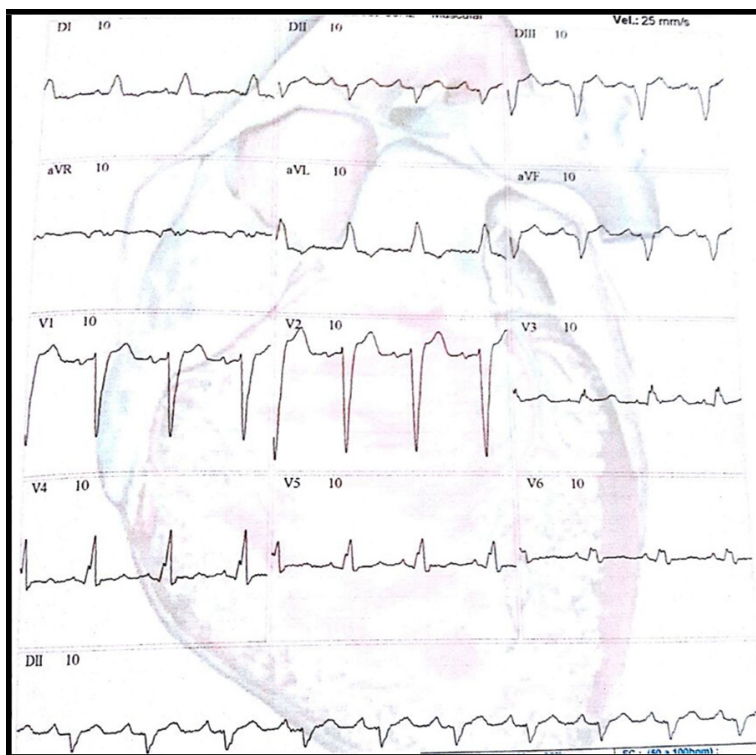


Figure 1. Electrocardiogram -Sinus rhythm, left axis deviation (-60°), first-degree atrioventricular block, left bundle branch block. Heart Rate: 78 bpm.

the age of 28. He was attended at an emergency department and diagnosed with ischemic stroke, which led to the sequela of gait ataxia and left hemiparesis, with sequelae of gait ataxia and left hemiparesis. At the same time he was diagnosed with Chagas disease through serological tests, and the ischemic event was attributed to the cardioembolic cause.

He remained stable for six years, but afterwards presented worsening in the gait, difficulty climbing stairs, and difficulty standing up. During that period, his mother was diagnosed with PD, and her family members underwent genetic screening. The patient had a confirmed diagnosis of PD, with AAG enzyme dose of 0.4

$\mu\text{mol/l/h}$ (Reference: $\geq 3.9 \mu\text{mol/l/h}$) and the following mutations: c.-32-13T>G and c.2501_2502delCA p.T834Rfs*49. The chronology of the events are summarized in **Table 1**.

He is currently in good condition with regular heart rhythm, normophonic heart sounds without murmurs and symmetrical pulses. Upon neurological evaluation, there is a weakness in the flexor muscles of the head, rectus abdominis, and pelvic and scapular waist. The patient also presents anserine gait with a broad base and macroglossia.

The drugs in use are metoprolol, enalapril, spironolactone, amiodarone, and aspirin. The features of the electrocardiogram (ECG) are shown in **Figure 1**. The transthoracic

echocardiogram shows dilatation of left cavities and severe left ventricular (LV) systolic dysfunction (ejection fraction 0.20) with apical aneurysm (**Figure 2**). The 24-hour Holter monitoring revealed complex ventricular arrhythmias (**Figure 3**).

The evaluation of lung function through the manovacuometer presented the following result in the first consultation: Vital capacity (VC): 2320 ml (55%); Supine CV: 1150 ml (36%).

These results were consistent with diaphragmatic weakness, and the use of nocturnal Bilevel Positive Airway Pressure (BIPAP) was indicated.

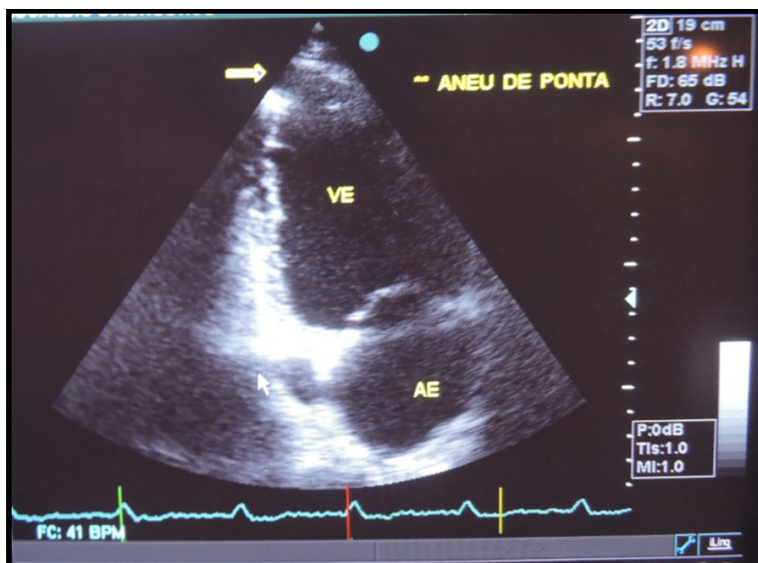


Figure 2. Transthoracic Echocardiogram - left chambers dilatation with apical left ventricular aneurysm. VE: Left Ventricle. AE: Left Atrium. Aneu de Ponta: Apical left ventricular aneurysm.

The patient is on Enzyme replacement therapy (ERT) [8], BIPAP, respiratory physiotherapy and optimized treatment for heart failure (HF).

Discussion

The case report presents a patient with the late-onset form of PD and chronic chagasic cardiomyopathy (CCC), stage C [7].

PD is a rare condition and it is usually unthinkable. After confirmation in the mother, the patient and the family members were investigated. Two siblings were positive, one of whom was also diagnosed with the indeterminate form of CD. Neurological signs were initially attributed to the sequelae of the IS. The presence of malignant arrhythmias in advanced HF is not frequent in the late phase of PD and, thus, Chagas cardiomyopathy would be the most likely diagnosis. CCC is usually manifested around the fifth or sixth decade of life [9, 10], because chronic heart failure usually appears 20 or more years later after the infection [11]. CCC involvement before the age of 30 is more usual in vertical transmission, an alternative that was rejected due to the negative serology for Chagas in the patient's mother.

The frequent commitment of the sinus node, the atrioventricular node and the bundle of His can lead to sinus dysfunction and various atrioventricular and intraventricular blocks. The

right bundle branch and left anterior-superior bundle are more vulnerable and more frequently affected. Thus, complete right bundle branch block associated with left anterior or hemiblock is the most frequent alteration observed in cases of CCC (>50.0% of patients). The involvement of the left bundle branch or left posterior bundle is rare [11]. The patient's ECG has a first-degree atrioventricular block and complete left bundle branch block, probably due to advanced systolic dysfunction. Although there are no clinical manifestations or alterations in complementary pathognomonic examinations of CCC, the serological confirmation of the disease in a

patient with HF constitutes the diagnostic sequence in most cases. Right bundle branch block associated with left anterior hemiblock in the ECG is highly suggestive of CCC in patients from the endemic area, whereas left bundle branch block makes chagasic etiology less likely. The echocardiogram of chagasic patients with ventricular dysfunction and ventricular arrhythmias may present apical aneurysms in the LV (80%), sparing the septum, which represents in some papers a marker of the disease [12, 13]. The authors raise the possibility of PD and CD have led to the early and rapidly progressive involvement of cardiomyopathy.

The clinical evaluation of the patient evidenced some classic symptoms of PD: weakness in the cervical, abdominal, and proximal muscles of the four limbs with predominance of the lower limbs and gait difficulty, besides the macroglossia. The important involvement of the diaphragmatic musculature was also evidenced by a spirometric test. After respiratory physiotherapy and non-invasive ventilation were applied through the use of BIPAP, respiratory function improved, as measured by vital capacity (CV) during lung function assessment. The patient is stable and optimized from a cardiological point of view.

A multidisciplinary follow-up is very important, with emphasis on psychological and social

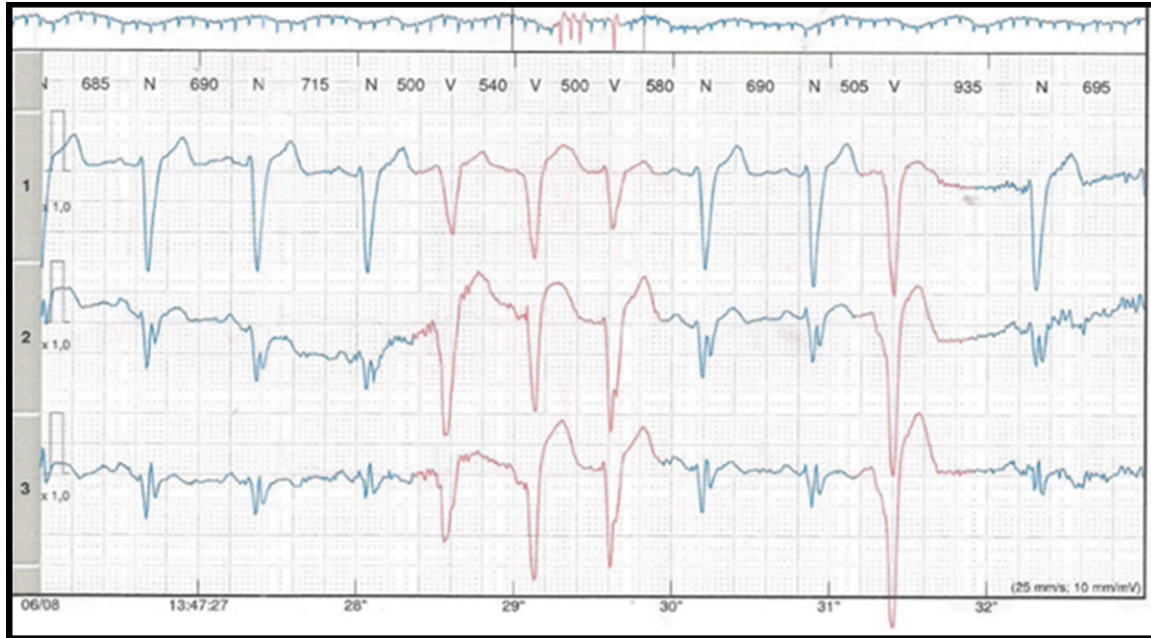


Figure 3. Holter 24 h monitoring-Non-sustained ventricular tachycardia and isolated ventricular extrasystoles.

aspects [14]. The neuromuscular disease has a progressive character, and periodic visits to the professional team are fundamental to allow the patient to understand his underlying disease and the need for commitment to treatment [15].

Conclusion

Cardiac involvement in CD varies from clinically unapparent abnormalities to severe forms such as heart failure, thromboembolic complications, refractory ventricular arrhythmias, and sudden death. [6] PD is rare, difficult to diagnose, and has initial symptoms that are largely non-specific.

In this case, the patient probably presents cardiovascular symptoms masked by neurological limitation. Cardiac involvement with rapid evolution may suggest an overlap of the two diseases.

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Disclosure of conflict of interest

None.

Address correspondence to: Rafael OB de Morais, Hospital Agamenon Magalhães, Department of Cardiology, Rua quarenta e oito, 1000, Apt 104. Espinheiro-Recife-PE. CEP. 52050-380, Brazil. E-mail: rafamorais.med@gmail.com

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