Case Report

Cardiac Sarcoidosis and Complex Arrhythmias

Anna Luiza Souza,[1] Renata dos Santos Oliveira,[1] Ana Paula Lindoso Lima Barreiro,[1] Mauricio Lopes Prudente,[1] Rodrigo Paashaus de Andrade,[1] Giulliano Gardenghi[1]

Hospital ENCORE,[1] Aparecida de Goiânia, GO, Goiás – Brazil

Introduction

Sarcoidosis is a multisystem inflammatory granulomatous disease of unknown cause, related to genetic factors, with an incidence of 1 to 30 cases/100,000 people, and is more prevalent in women over 50 years of age. The formation of scar tissue characterizes it and can affect any organ, with a predilection for the lungs in approximately 90% of cases. Patients with cardiac involvement are mainly male and, in general, have a worse prognosis, with high mortality rates observed in this population (85% of deaths).[1,2]

The scar substrate in the myocardium, which presents as multifocal and heterogeneous, is related to several cardiac manifestations. Among the most common, we can mention left ventricular dysfunctions, atrioventricular conduction abnormalities, and ventricular and supraventricular arrhythmias, such as ventricular tachycardia and atrial fibrillation, which can lead, in some cases, to sudden death.[1] In view of this, the use of antiarrhythmic drugs is necessary in clinical practice in most patients, aiming at the control of arrhythmias, especially those of ventricular origin, and consequently improving the quality of life and reducing mortality.[2] In this work, we report the therapeutic management of a case of cardiac sarcoidosis associated with prolonged QT interval that evolved with complex ventricular tachycardia (VT).

This study was approved by the Ethics Committee of the Hospital de Urgências de Goiás under number CAAE: 82840424.9.0000.0033.

Case Report

A 41-year-old male patient with systemic sarcoidosis with cardiac involvement was admitted to the emergency department after an episode of sudden death aborted by an appropriate shock from an implantable cardioverter-defibrillator (ICD), despite drug treatment with metoprolol 50 mg/day, amiodarone 100 mg/day, azathioprine 100 mg/day, methotrexate 20 mg/week, and prednisone 5 mg/day. His past medical history included a similar event with ICD shocks, ablation of ventricular extrasystoles (VE) in the septal portion of the right ventricle (RV), and treated pulmonary thromboembolism. He was sedentary and denied alcoholism, drug use, or smoking.

On physical examination, he was oriented and communicative, with no signs of respiratory distress at rest and oxygen saturation of 98%, hemodynamically stable, blood pressure of 124/79 mmHg, heart rate of 100 bpm. Respiratory and cardiac auscultation were within normal limits. The peripheral pulses of the four limbs were palpable and symmetrical.

Biochemical tests did not show electrolyte alterations, and thyroid function was normal. The electrocardiogram (ECG) revealed sinus rhythm with VE (Figure 1). Coronary angiotomography showed a calcium score of zero and the absence of atherosclerotic lesions.

Intravenous amiodarone and magnesium were administered in the ICU, the dose of metoprolol was increased to 100 mg/day, and the usual immunosuppressants were maintained. A transthoracic echocardiogram showed moderately depressed global and segmental right ventricular (RV) systolic function (FAC 21%). Mild dilatation of the right chambers (RV diastolic diameter of 49 mm, indexed right atrial volume of 35 mL/m^2) and indirect signs of pulmonary hypertension (TAC 98 ms). Mild to moderate tricuspid regurgitation secondary to dilatation. Left ventricle with normal dimensions and ejection fraction of 63% with asynchronous movement of the interventricular septum.

The 24-hour Holter showed 3,754 EV (4%), of which 168 were episodes of VT, the largest of which was 69 bpm and the fastest was 250 bpm. It also revealed a prolonged QT interval (QTc 470 ms), as shown in Figure 2, in addition to sustained VT, *Torsades de Pointes,* and ventricular flutter (Figure 3), which were interrupted by a new appropriate shock from the ICD, even with the use of high-dose antiarrhythmic drug therapy during hospitalization.

Positron emission tomography with 18F-Fluorodeoxyglucose (18F-FDG PET/CT) was performed to evaluate the reactivation of sarcoidosis; however, no inflammatory activity was observed in the skeleton, lung, liver, heart, or lymph nodes (Figure 4). From this, the relationship between the current condition and the progression of the disease was ruled out.

Given this scenario, we discussed it with the Heart Team. We concluded that the complex ventricular arrhythmias were probably due to the proarrhythmogenic effect of amiodarone due to the prolongation of the QT interval, favoring the occurrence of the R on T phenomenon. We then decided to

Keywords

Sarcoidosis; Cardiac Arrhythmias; Long QT Syndrome.

Mailing Address: Giulliano Gardenghi •
Rua Gurupi, Quadra 25, Lote 6 a 8. Postal Code 74905-350, Vila Brasília, Aparecida de Goiânia, GO – Brazil
E-mail: coordenacao.cientifica@ceafi.edu.br
Manuscript received October 09, 2024, revised manuscript November 22, 2024, accepted December 08, 2024
Editor responsible for the review: Luis Beck-da-Silva

DOI: https://doi.org/10.36660/abchf.20240062i

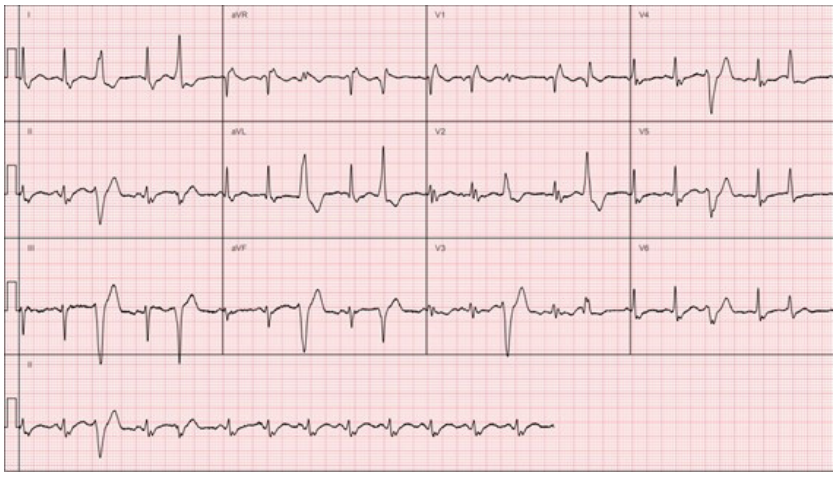

Figure 1 – *Electrocardiogram with isolated ventricular extrasystoles after sudden death aborted by ICD shock and corrected QT interval of 430 ms.*

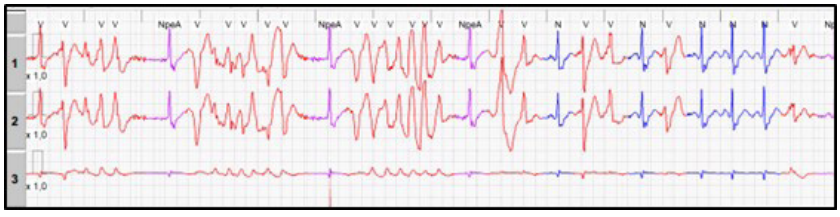

Figure 2 – *24-hour Holter monitoring showing non-sustained ventricular tachyarrhythmias and corrected QT interval of 470 ms.*

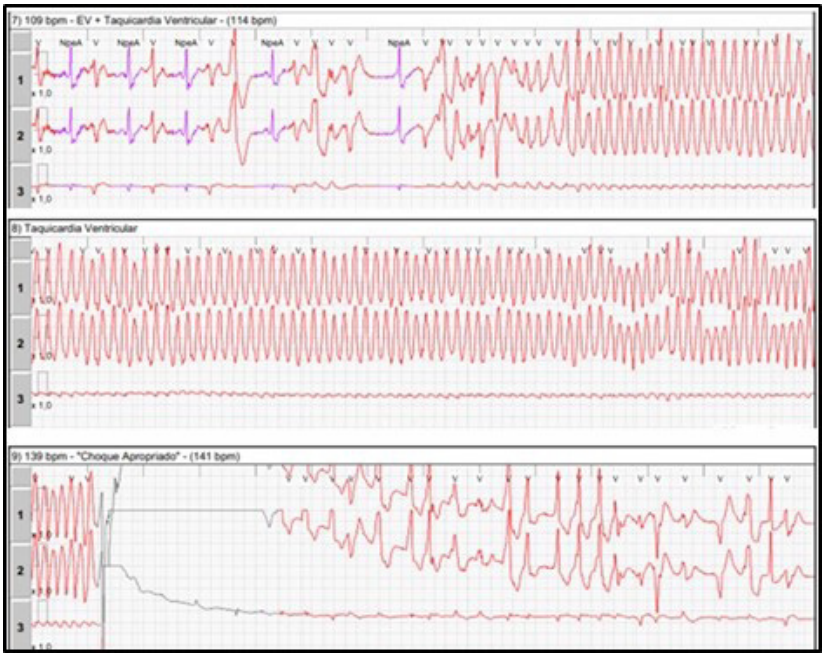

Figure 3 – *24-h Holter analysis showing ventricular arrhythmias interrupted by appropriate ICD shock.*

suspend amiodarone and replace metoprolol with propranolol at a dose of 240 mg/day. Initially, the pacemaker was adjusted to a rate of 60 bpm; however, the patient began to present frequent signs and symptoms of low output. In view of this and considering his BMI of 34.4 kg/m², our team decided to reprogram the pacemaker to a rate of 75 bpm, which evolved with good tolerance. In addition, the team raised the possibility of ablating the arrhythmogenic focus. However, upon achieving electrical stability, we decided to reevaluate the indication for such a procedure after hospital discharge.

The patient progressed well clinically, and after four days of adjustments, a new 24-hour Holter analysis revealed 11,040 EV (10%), including two episodes of VT, the largest of which was 3 bpm and the fastest of which was 141 bpm. The ECG showed a corrected QT of 446 ms (Figure 5). He was discharged asymptomatic, with maintenance of immunosuppressants, propranolol 240 mg/day, and magnesium for outpatient follow-up.

Discussion

The genesis of ventricular arrhythmias in patients with cardiac sarcoidosis is multifactorial. In addition to the fibrotic arrhythmogenic substrate of granulomatous disease and the inflammatory activity itself, the occurrence of polymorphic VT, *Torsades de Pointes*, resulting from QT prolongation exemplifies a consolidated fact: antiarrhythmic drugs can have proarrhythmic effects through different mechanisms.[2,3] In the present case, the discontinuation of amiodarone and metoprolol associated with the prescription of propranolol and the adjustment of the pacemaker frequency resulted in normalization of the QT interval and improvement of VT.

Amiodarone, a class III antiarrhythmic drug according to the Vaughan Williams classification, is widely used to suppress VT and is the drug of choice for patients with structural heart disease and left ventricular dysfunction, as are beta-blockers. It is important to emphasize that its use is not free from side effects.[4] In patients with persistent ICD and sustained VT, the adjunctive pharmacological treatment aims to reduce the frequency of shocks since they are directly related to increased morbidity and mortality.[4,5] Combination therapy with beta-blockers has been shown to be superior to monotherapy, sotalol, or beta-blockers in reducing shocks.[4]

Among beta-blockers, nadolol and propranolol are considered the most effective in managing QT interval prolongation. Propranolol is the most commonly used drug in clinical practice, at 2 to 3 mg/kg per day, with higher doses acceptable for severe cases. Metoprolol is considered less effective and has been associated with recurrent arrhythmias when compared to propranolol and nadolol. This difference between the drugs, although not well established, appears to be linked to their distinct roles in blocking ion channels.[6-8] Class IB antiarrhythmics, such as lidocaine and mexiletine, have the property of selectively blocking sodium channels and acting to reduce the QTc interval. Although they were not used in the reported case, they have proven to be safe options as adjuvant treatment for persistent ventricular arrhythmias.[8]

In patients with heart failure or coronary disease, pacemaker implantation for therapeutic support has already been validated despite the chronic use of beta-blockers. Artificial cardiac stimulation at a frequency above the usual sinus rate can prevent sympathetic action, favoring the control of electrical storms.[9] In the present case, the frequency of the electronic device was adjusted in order to maintain the cardiac output necessary for daily activities since high doses of propranolol were required.

Yafasova et al. observed, in a cohort study, that patients with sarcoidosis had a significantly higher risk of the composite outcome of ICD implantation, ventricular arrhythmias, and cardiac arrest compared to the control group. In this same study, it was also seen that patients with sarcoidosis who developed heart failure had higher mortality than those who had heart failure without a history of sarcoidosis.[6]

Faced with this disease, considered enigmatic, the presence of complex arrhythmias, electrocardiographic

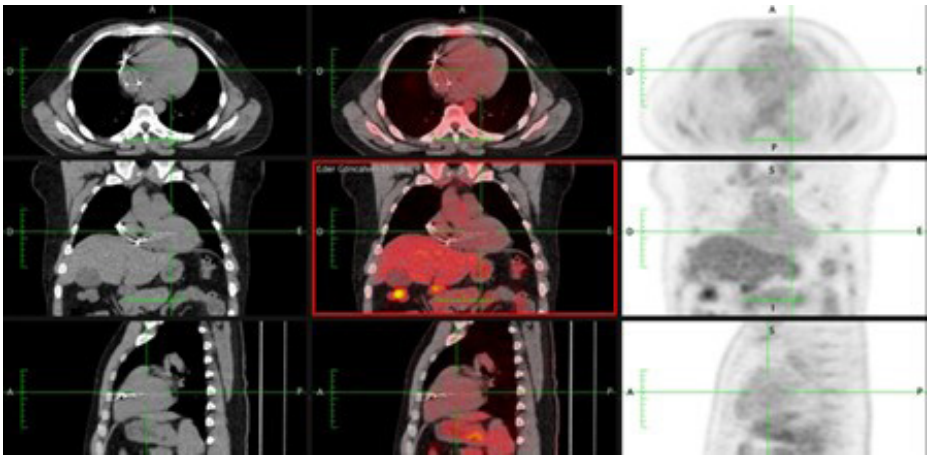

Figure 4 – *Positron emission tomography with 18F-Fluorodeoxyglucose with the absence of inflammatory activity due to sarcoidosis.*

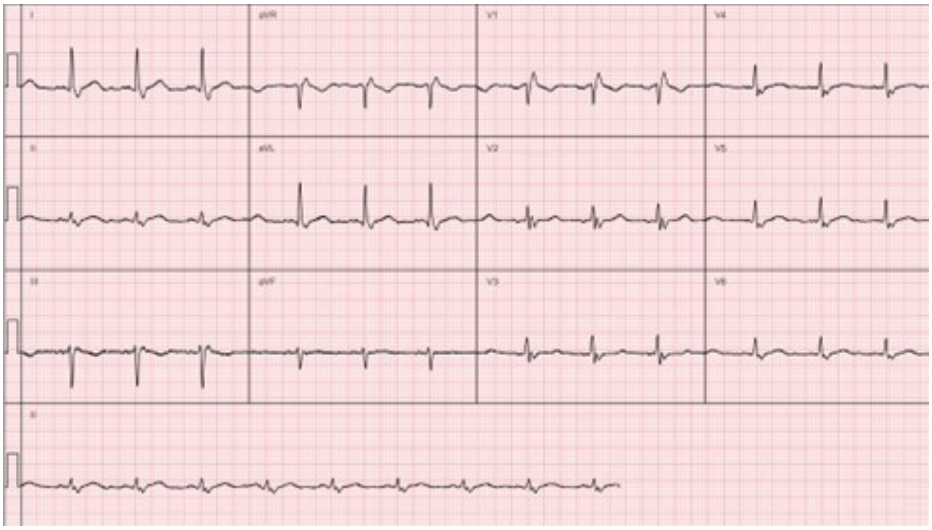

Figure 5 – *Electrocardiogram showing evidence of corrected QT of 446 ms after therapeutic adjustment.*

and echocardiographic alterations, as well as clinical worsening, necessarily imply evaluating the inflammatory activity and progression of sarcoidosis. The 2022 Brazilian guideline recommends performing 18F-FDG PET/CT for this purpose, which has an important prognostic value, combined with whole-body PET/CT, which allows the identification of extracardiac disease activity.[2] An active area of cardiac sarcoidosis is characterized by the uptake of the radiopharmaceutical associated with the perfusion defect, considered a typical finding (mismatch pattern), helping to determine the treatment.[2,3]

The treatment of cardiac sarcoidosis is based on immunosuppressants and depends on clinical experience and expert opinion due to the scarcity of randomized studies, with corticosteroids being considered the first line of therapy.[2] In the report described above, the PET/CT was negative, and for this reason, the doses of immunosuppressants were maintained. From this, we then prioritized the management of complex arrhythmias.

In cases of refractory VTDespite immunosuppressive and antiarrhythmic therapy, with or without ICD shocks, catheter ablation may be considered,[7] configuring an alternative for patients with the abovementioned condition. In selected patients who did not respond to the previous measures, bilateral cardiac sympathectomy may also be considered.[7] In a systematic review conducted by Papageorgiou et al., it was shown that catheter ablation of VT in patients with cardiac sarcoidosis can result in the absence of recurrence in almost 55% of cases and a reduction of the burden of arrhythmias in 88% of patients. It is important to emphasize that more than 30% of patients will need to repeat the procedure. Among the major complications (8% of cases) are electromechanical dissociation requiring a biventricular assist device, heart transplantation, coronary sinus perforation, and total occlusion of a small branch of the coronary artery.[1]

The management of cardiac arrhythmias resulting from sarcoidosis is challenging. Therapy with antiarrhythmic drugs can have repercussions such as prolongation of the QT interval, increasing the risk of electrical events. Due to side effects and potential proarrhythmic effects, they should be used with caution and with adequate control.[4]

Author Contributions

Conception and design of the research: Andrade RP; Acquisition of data: Souza AL, Oliveira RS, Andrade RP; Analysis and interpretation of the data: Barreiro APLL; Writing of the manuscript: Souza AL, Prudente ML, Gardenghi G; Critical revision of the manuscript for content: Oliveira RS, Barreiro APLL, Prudente ML, Gardenghi G.

Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

Sources of funding

There were no external funding sources for this study.

Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital de Urgências de Goiás under the protocol number CAAE:82840424.9.000090033. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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