CLINICAL ARRHYTHMIA
Case Report
https://doi.org/10.24207/jca.v34i1.3414

# Dilated Cardiomyopathy Compatible With Sarcoidosis Presenting with Syncope Due to Torsades de Pointes: a Case Report

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## ABSTRACT

Sarcoidosis is a multisystemic noncaseating granulomatous disease of unknown etiology. Cardiac sarcoidosis clinical presentation is diverse, and syncope is one of the possible primary events. Due to its variable natural history and initial presentation associated with lacking sensitive and specific diagnostic tests, it still represents a challenging diagnosis. This article presents the case of a 51-year-old female patient with intermittent syncope events associated with torsades de pointes and dilated cardiomyopathy compatible with sarcoidosis.

**KEYWORDS:** Sarcoidosis; Syncope; Cardiac arrhythmias; Magnetic resonance imaging.

## INTRODUCTION

Sarcoidosis is a rare systemic inflammatory noncaseating granulomatous disease of unknown etiology that usually affects adults between the ages of 25 and 45[1]. Basic pathogenesis involves resolving inflammation areas that tend to evolve to myocardial scarring tissue, providing the substrate for reentry circuits[2]. Upon this scenario, the inflammatory affection of myocardial tissue stablishes cardiac sarcoidosis (CS), that might present with electrical abnormalities, including ventricular arrhythmias and atrioventricular (AV) blocks[3], but also syncope[4–7], heart failure and even cardiac tamponade[8]. The most common electrical abnormality is third degree AV block, followed by ventricular tachycardia (VT)[2].

The exact prevalence of isolated cardiac sarcoidosis is uncertain[9]. It is estimated that up to a quarter of patients with sarcoidosis might present CS[10], but only 5% manifest cardiac involvement clinically[4]. In parallel, up to 20% of CS patients

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**Received:** Aug 12, 2020 | **Accepted:** Dec 07, 2020

present a clinically silent disease[11] with asymptomatic cardiac involvement, not identified by diagnostic criteria. Cardiac sarcoidosis patients may present with higher morbidity and mortality rates, with overall 5-year survival around 60%[12].

A recent study showed that sudden cardiac death (SCD) constitutes up to 14% of the presenting manifestations of CS and as many as 80% of all fatalities in that group. It also states that almost 66% of fatalities occur suddenly, due to undiagnosed intracardiac granulomas[13], thus configuring SCD as one of the most feared clinical implications of this disease.

Although at present there is no specific optimal screening or risk stratification strategy for SC patients[12], guidelines refer to clinical, radiologic, and immunohistologic criteria for diagnosing cardiac sarcoidosis[1], which might be established on a histological or clinical basis. Considering iatrogenic risks related to endomyocardial biopsy[13] and its low sensitivity[14], individualized diagnostic approach and accurate noninvasive diagnosis is desirable.

If there is no previous diagnosis of extracardiac sarcoidosis, clinical suspicion should occur if the patient is below 60 years and has no prior history of sarcoidosis but presents: (a) Mobitz II AV block; or (b) third degree AV block; or (c) sustained VT; or (d) heart failure with reduced or preserved left ventricle ejection fraction (LVEF) of unclear etiology[15].

The objective of this report is to present a case of a 51-year-old patient with syncope events associated with torsades de pointes identified in the 24-hour Holter and dilated cardiomyopathy compatible with CS.

## CASE REPORT

A 51-year-old white female patient, with no previous comorbidities, presented to an outpatient cardiology clinic with a complaint of a 4-month intermittent repeated syncope. The events were preceded by dizziness. Sporadic episodes of palpitation and vertigo have also been reported. She was not taking any cardioactive medications. The family history was negative for SCD.

Electrocardiogram showed sinus rhythm, complete right bundle branch block, left anterior hemiblock associated with ventricular ectopic beats. On 24-hour electrocardiogram (ECG) Holter monitoring (Fig. 1), it was found that a syncope event was preceded by a torsades de pointes that degenerated into ventricular fibrillation.

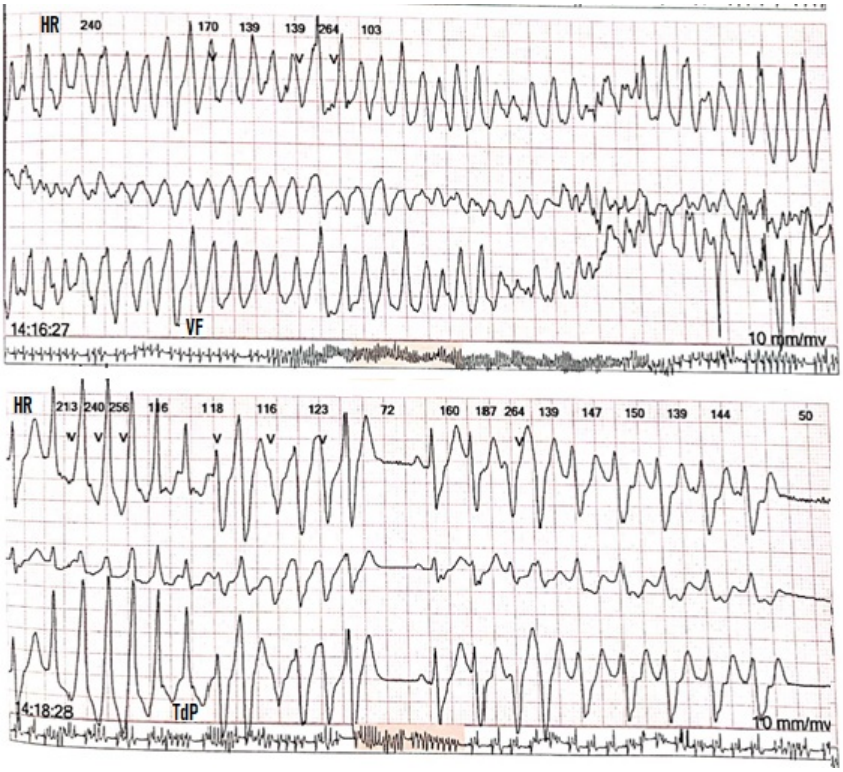


**Figure 1**. 24-hour ECG Holter. 24-hour Holter monitor records of torsade de pointes (TdP). HR: heart rate; VF: ventricular fibrillation.

Cardiac magnetic resonance imaging (MRI) (Fig. 2) was also performed, showing: (1) mild left atrium dilation (2) mild systolic LV dysfunction; (3) akinesia of the (a) inferior, septal and basal; and (b) inferior, septal and medial segments; (4) delayed enhancement pattern of moderate degree in mesocardium, with transmural involvement of the above-mentioned segments, favoring CS diagnosis. The $^{67}$gallium scintigraphy was inconclusive.

Transthoracic echocardiography (TTE) identified a dilated cardiomyopathy with left atrium enlargement, diffuse hypokinesia and mild to moderate left ventricle (LV) dysfunction with an LVFE of 45%. Laboratory tests showed no abnormalities. At this point, the patient received a target dose prescription of sacubitril/valsartan, bisoprolol and amiodarone and an indication of implantable cardioverter-defibrillator (ICD).

Based on these findings, the diagnostic hypothesis was nonischemic myocardial injury, consistent with CS or previous episode of myocarditis. Thus, the patient underwent ICD implantation. Three episodes of sustained ventricular arrhythmias were documented in the first six months after ICD implantation and no new episodes of syncope were registered or reversed six months before this report. Although endomyocardial biopsy is required for histopathological confirmation of CS, the patient opted not to undergo the procedure due to the related iatrogenic risks.

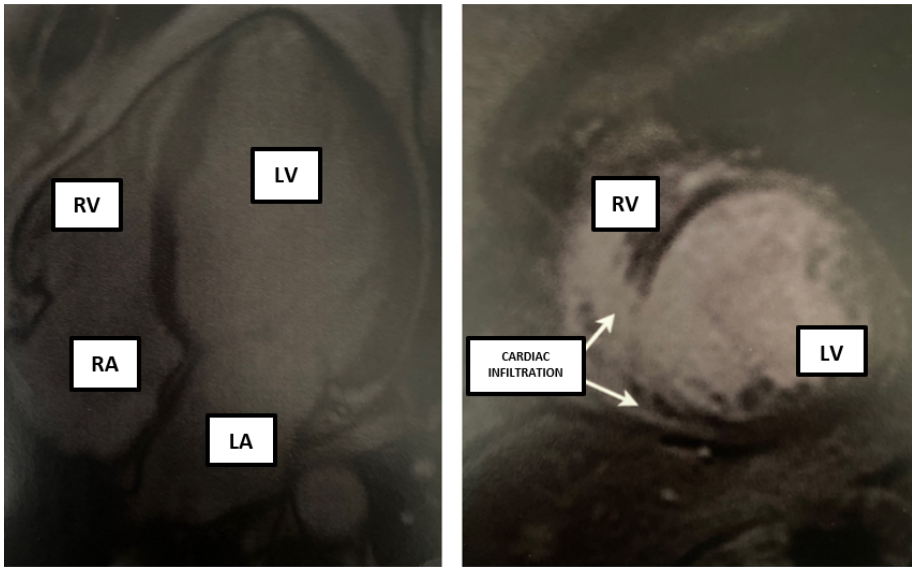


**Figure 2.** Cardiac magnetic resonance imaging. CMRI: moderate heterogeneous late enhancement of inferior, septal and basal mesocardium segments. RV: right ventricle; LV: Left ventricle; RA: right atrium; LA: Left atrium.

# DISCUSSION

Although endomyocardial biopsies (EMBs) may provide a definitive SC diagnosis, it presents practical limitations related to the focal nature of the disease and to the method itself, such as poor sensitivity (with diagnostic yield varying from 13 to 35%, among studies), high false negative rates, invasiveness and complications associated with tissues sampling[3,13,14,16–18].

One way to improve EMBs indicators is to associate electroanatomic voltage mapping (EVM). The largest cohort of patients undergoing EVM-guided EMB compared it with a cardiac magnetic resonance (CMR) guided approach. It was pointed out that EVM presents similar sensitivity rates to CMR (74% versus 77%), with higher specificity levels (70% versus 47%). On the one hand, it is suggested that EVM accuracy rate is close to CMR and that such methods combined grant EMB a positive predictive value of 89%, with low complication rates. On the other hand, it is pointed out that the absence of pathological findings at CMR and EVM does not reliably exclude CS[19].

In clinical practice, relatively few cases are definitively diagnosed through histologic parameters[20]. Since early diagnosis is of paramount importance to best prognosis, imaging represents vital noninvasive and sensitive methods[17] and there are

some available modalities[18]. In this scenario, a combination of clinical, electrocardiographic and imaging criteria seems to be desirable and can be relied upon to provide probabilistic diagnosis[16].

In the past few years, many studies have shown the diagnostic utility of 2-deoxy-2-[fluorine-18]fluoro-D-glucose, or $^{18}$F-FDG PET/CT, in patients with CS[21]. A recent systematic review with meta-analysis revealed the sensitivity of the method was 84% (95% confidence interval [95% CI] 0.71-0.91) with specificity of 83% (95% CI 0.74–0.89) for detection of cardiac sarcoidosis[22]. Compared to MRI, the advantages of $^{18}$F-FDG PET/CT are: (1) provision of metabolic information; (2) detection of active inflammation; (3) potential for determine cardiac and extracardiac involvement; and (4) contemplation of patients with implantable cardiac devices, non-MRI compatible, or chronic renal failure[23]. Despite both methods seem to be effective for the detection of CS, there is no formal consensus on which imaging modality is preferred[18].

The Japanese Circulation Society (JCS) suggests an innovative strategy that enables the establishment of clinical diagnosis of CS without any histopathological evidence of sarcoidosis[14]. For such, patients must present "CS-specific cardiovascular findings" and histopathological or clinical diagnosis of extracardiac sarcoidosis and F-FDG PET is considered mandatory[24]. The patient presented in this case report showed two criteria of primary findings: (1) clinical evidence of cardiac manifestation, such as torsades de pointes; and (2) late gadolinium enhancement (LGE) with CMR. Although it is not possible to establish a diagnose of CS based on such parameters, since FDG PET criteria were not established. Nonetheless, the existence of criteria that prescind from histopathology emerges as a new paradigm on this scenario, that may be useful for other patients. Finally, CS screening tests should be developed to diagnose CS before it causes symptoms and important morbidity and mortality[18].

Implantable cardioverter-defibrillator implantation is a therapeutic mainstay for prevention of SCD in CS and some of the implantation criteria include: (1) sustained VT or survivors of sudden cardiac arrest (2) LVEF of 35% or less; (3) patients with LVEF greater than 35% who have syncope and/or evidence of myocardial scar by cardiac MRI or PET scan, and/or have an indication for permanent pacing implantation of an ICD reasonable; (4) patients with LVEF greater than 35%, in whom it is reasonable to perform an electrophysiological study and to implant an ICD, if sustained ventricular arrhythmias (VA) is inducible; (5) patients who have an indication for permanent pacing; (6) patients with frequent symptomatic VA and evidence of myocardial inflammation, immunosuppression in combination with antiarrhythmic medication therapy[25]. Based on that, the patient received an ICD implantation, with satisfactory results: no more syncope or SCD episodes have been registered 2 years later. It should also be noted that three episodes of sustained VT were reverted due to antitachycardia pacing therapies delivery on the same period.

## CONCLUSIONS

Cardiac sarcoidosis remains an enigma with an uncertain etiology and a challenging diagnosis, which leads to potentially serious adverse outcomes. Since the early diagnosis is of paramount importance to best prognosis and that, in clinical practice, relatively few cases are definitively diagnosed through histologic parameters, a combination of clinical, electrocardiographic and imaging criteria seems to be desirable and can be relied upon to provide probabilistic diagnosis. Prevention of SCD is a vital part of the conduct that also involves optimized pharmacological treatment and ICD implantation as a mainstay.

## AUTHORS' CONTRIBUTION

**Conceptualization:** Tinoco F. C., Branca N. R. P., Carvalho G. D., Faria L. S. P. and Nascimento E. A.; **Methodology:** Tinoco F. C., Branca N. R. P., Carvalho G. D., Faria L. S. P. and Nascimento E. A.; **Writing – Original Draft:** Tinoco F. C., Branca N. R. P., Carvalho G. D., Faria L. S. P. and Nascimento E. A.; **Writing – Review and Editing:** Nascimento E. A. **Supervision:** Nascimento E. A.

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