Case Report

Cardiac Sarcoidosis as a Cause of Total Atrioventricular Block: Importance of Differential Diagnosis

Sarcoidose Cardíaca como Causa de Bloqueio Atrioventricular Total: Importância do Diagnóstico Diferencial

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Introduction

Sarcoidosis is a systemic granulomatous disorder of unknown cause that can affect virtually any organ. The extracardiac forms are usually benign and subjected to spontaneous remission. However, the prognosis may be unfavorable in case of cardiac involvement.

Symptomatic cardiac sarcoidosis (CS) is diagnosed in approximately 5% of patients with sarcoidosis.[1] However, based on some autopsy series, the prevalence of subclinical CS can reach 25–30%.[1]

Cardiac involvement is mainly characterized by compact non-caseous epithelioid cell granulomas that, depending on their extent and location, can lead to heart failure (HF) or cause potentially lethal arrhythmias, particularly ventricular, such as ventricular tachycardia (VT) and ventricular fibrillation (VF), and atrioventricular (AV) conduction disorders. The etiological diagnosis of CS can be of extreme clinical importance, especially in cases of advanced AV block (AVB), changing therapeutic measures and presenting significant prognostic implications.[1,2]

Case report

A 39-year-old man with a 3-month history of progressive tiredness and dizziness was referred for permanent cardiac pacemaker (PM) implantation due to a complete atrioventricular block (CAVB) on electrocardiography (Figure 1A) and New York Heart Association functional class III HF. Echocardiography showed dilation of the four cardiac chambers and significant left ventricular dysfunction with a left ventricular ejection fraction (LVEF) of 34%. Cardiac magnetic resonance confirmed the echocardiographic findings and showed a myocardial infiltrative aspect with delayed enhancement diffusely affecting the right ventricle (RV) and several left ventricular (LV) segments, such as the mesocardium and sub-epicardium, in addition to significant septal involvement.

To confirm the CS criteria, the patient underwent chest computed tomography, which showed which multiple lymph nodes, peri-lymphatic and mediastinal nodules, and peri-bronchial interstitial thickening compatible with the diagnostic hypothesis (Figure 2).

As recommended in the Heart Rhythm Society (HRS) guidelines for CS,[1] the patient received an implantable cardioverter-defibrillator (ICD), and immunosuppressive treatment with corticosteroids was promptly started. His condition progressed with a significant improvement in ventricular function, functional class, and pulmonary changes; subsequently, the conduction disorder regressed to a first-degree AVB.

After approximately 8 months, the patient presented with new disease activity, an episode of appropriate ICD therapy in the VF zone (Figure 1B). Considering the presence of methotrexate-induced hepatotoxicity, azathioprine was added to the corticosteroid treatment to stabilize the disease. Months later, he presented with symptomatic atrial fibrillation (AF) and was treated with rivaroxaban anticoagulation and subsequent electric cardioversion (ECV).

Since then, the patient has been clinically stable in functional class II (NYHA) with an LVEF of 40% and is receiving bisoprolol, amiodarone, spironolactone, furosemide, and rivaroxaban. As for the arrhythmic condition, he started to present significant sinus dysfunction (sinus frequency < 30 bpm), a new CAVB dependent on artificial cardiac stimulation, and recurrent AF (new ECV).

Discussion

The case described emphasizes the importance of the etiological diagnosis of an advanced AV conduction disorder (CAVB) associated with HF in a young patient who was previously asymptomatic and had no comorbidities. In this case, the CS diagnosis impacted his early treatment, with immunosuppressive therapies and the choice of the implanted device. In this case, the implantation of an ICD instead of a conventional PM as the primary method of preventing sudden cardiac death according to the recommendations of the Japanese Circulation Society and the HRS guidelines.[1,3] It is noteworthy that the patient had an episode of ventricular arrhythmia (VF range) in the follow-up period that was treated by the device.

The occurrence of CAVB in young patients is a warning

Keywords

Arrhythmogenic right ventricular cardiomyopathy/dysplasia; Atrioventricular block; Diagnosis; Sarcoidosis; Sudden death; Ventricular tachycardia.

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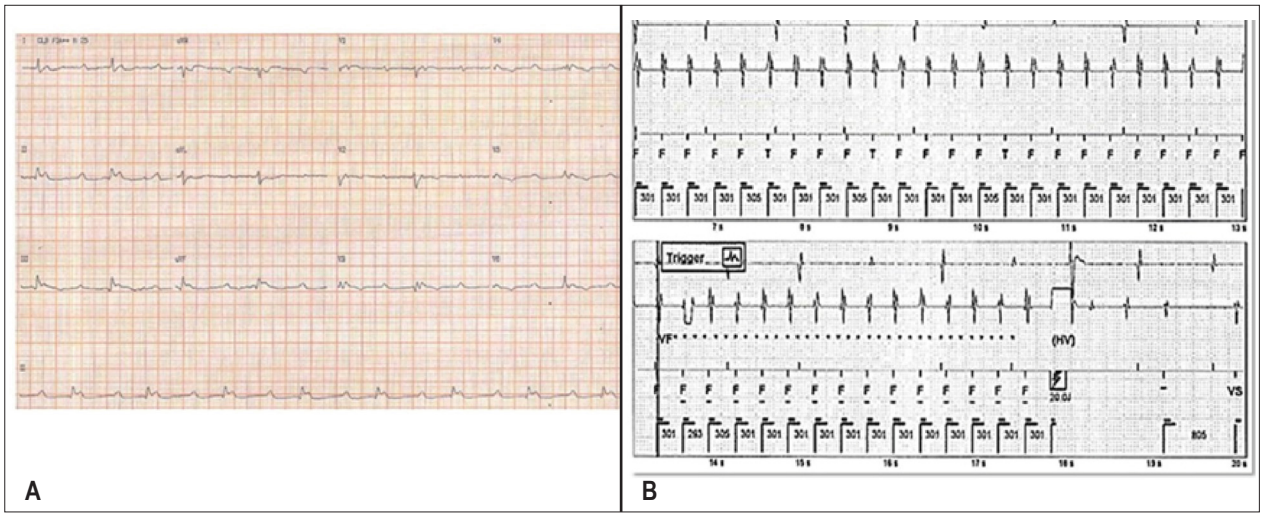

Figure 1 – *(A) Complete atrioventricular block. (B) Telemetry record of the device showing an episode of ventricular tachycardia (approximately 300 ms/200 bpm cycle) with effective therapy.*

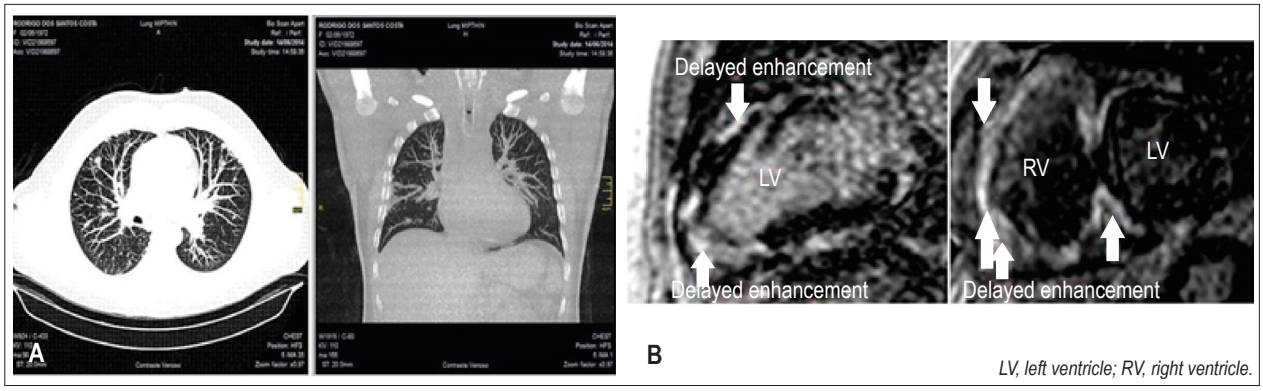

Figure 2 – *(A) Chest computed tomography image showing multiple lymph nodes, peri-lymphatic and mediastinal nodules, and peri-bronchial interstitial thickening. (B) Delayed enhancement diffusely affecting the right ventricle and several segments of the left ventricle in addition to significant septal involvement.*

factor for severe forms of heart disease requiring more detailed screening, particularly CS.[1,3,4] Kandolin et al. used endomyocardial biopsy to investigate 72 patients (aged < 55 years) with AVB of unknown etiology and reported findings compatible with CS in 14 of them (19%) and "probable" CS in four (6%) cases. In 44% of cases, symptomatic AVB was the first clinical sign of CS. Sarcoidosis patients had a significantly worse prognosis than those with idiopathic AVB.[5] The same was observed in a prospective Canadian study that diagnosed CS in 34% of patients (18–60 years old) presenting with advanced AVB.[6] These findings are extremely important considering that about half of the young patients without a definitive diagnosis can receive a PM implant.[1]

As a result, the HRS expert consensus recommends that patients < 60 years of age with high-grade idiopathic AVB should be routinely evaluated for CS.[1]

One of the fundamental aspects in making the differential diagnosis, with relevant clinical impact, is the possible clinical presentation overlap between CS and arrhythmogenic RV cardiomyopathy (ARVC/D),[2] which leads to the need to be familiarized with certain progressive characteristics, possibly distinct, between the two pathologies.

Unlike CS, high-grade AVB is rare in patients with ARVC/D dysplasia (ARVC/D).[2] A series of 113 patients with ARVC/D followed up for 10 years showed that none of them had a conduction disorder greater than first-degree AVB.[7] A good proportion of reported cases of severe AV conduction disorder attributed to ARVC/D were diagnosed before the advent of advanced imaging methods other than echocardiography and ventriculography, which may have influenced the diagnosis of CS.

Thus, although CS can have a clinical presentation that mimics the ARVC/D criteria, the simple presence of advanced AVB should support its diagnosis.[2]

In this regard, magnetic resonance imaging (MRI) can show greater basal septal impairment (presence of delayed enhancement) in patients with CS (unusual finding in ARVC/D) in addition to extracardiac abnormalities such as mediastinal lymphadenopathy and pulmonary changes.[1-2]

It is essential to establish the differential diagnosis between these two pathologies because the general features (i.e., CS immunosuppression and family screening for ARVC/D) and the specific conduction (conduction disorder) of the two clinical conditions are distinct.[1,2]

Another issue is the appropriate response to corticosteroid therapy in the acute phase of CS. Early treatment can lead to significant improvement or even prevent cardiomyopathy, suppress ventricular arrhythmia and, perhaps, decrease mortality.[1,3,8] Unfortunately, its use at a later stage and in the presence of advanced ventricular dysfunction does not seem to decrease morbidity or mortality, and it may even expose patients to unwanted side effects such as infection and complications related to implantable devices.[1]

The role of steroids in AVB is questionable. Although an initial meta-analysis showed that about half of AVB cases improved with steroids, device implantation is recommended because reversibility is unpredictable.[1] Even after an acute AV conduction recovery, myocardial inflammation can result in fibrosis and subacute/chronic healing of the exciting-conductor system.[1,3,8] The question is not whether it is possible to reverse CAVB with corticosteroid therapy, but whether the AV conduction disorder occurs more frequently in cases of greater myocardial impairment and an increased risk of ventricular tachyarrhythmia, as seen in the present case.

The most common CS presentation is symptomatic high-grade AVB, which is usually associated with ventricular dysfunction and arrhythmia.[1,9] The consensus of HRS specialists on arrhythmias in CS recommends ICD implantation in all CS patients with indications for permanent cardiac stimulation (class IIa).[1]

The recent registry study on Myocardial Inflammatory Diseases in Finland showed that high-grade AVB in CS is not a benign condition, even when it is the only sign of cardiac involvement. This was demonstrated by a 34% risk of sudden death within 5 years with the association of AVB and ventricular and/or VT dysfunction, and from 9% to 14% in cases of isolated AVB or mild LV dysfunction.[9]

The present case shows that the wide cardiac involvement caused by the disease can result in the coexistence of atrial and ventricular arrhythmias in the same person.[1,3] Compared to ARVC/D patients, the incidence of AF/atrial flutter and sinus dysfunction with the need for atrial stimulation is much higher in CS.[2] Thus, the implantation of a bicameral ICD would have several advantages, such as the maintenance of AV synchronism, AF detection, atrial stimulation, and electrogram interpretation of tachyarrhythmia events.[1]

Finally, the establishment of the differential diagnosis before device implantation is essential due to an MRI contraindication in most cases. Fortunately, this situation has improved with the availability of conditioned devices to perform MRI using 1.5-Tesla systems.[1-2] Otherwise, the use of positron emission tomography is recommended to diagnose and monitor patients with unconditioned devices.[1]

Authors' contributions

Manuscript writing: J Elias Neto; data collection: J Elias Neto, RR Kunyoshi, G Futuro, ES Merçon, MA Silva, PS Grativvol; manuscript review: J Elias Neto, MA Silva; figure preparation: FC Pedroti.

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Conflict of interest

The authors have declared that they have no conflict of interest.

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