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Case Report

Cardiac Sarcoidosis Managed by Biventricular Pacing: A Case Report

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Abstract

Background: Cardiac sarcoidosis (CS) is a rare pathology that affects the middle-aged population. Its diagnosis, as well as its treatment, can be quite challenging, especially when dealing with device management. We hereby discuss a case of CS, managed by a biventricular pacemaker in a 43-year-old man.

Case Report: A 43-year-old male presented to the emergency department with a 15-day history of chronic cough and worsening dyspnea. On examination, he was found to be bradycardic in the context of a third-degree heart block on electrocardiography (ECG) as well as bilateral hilar lymphadenopathy on chest radiography. Based on these findings, cardiac sarcoidosis was suspected. A temporary right internal jugular transvenous pacemaker was implanted in the right ventricle and empiric corticosteroid management was started. Lung tissue biopsies were obtained via bronchoscopy and were positive for granulomas consistent with a diagnosis of sarcoidosis. Even though the patient showed a partial positive response to corticosteroid treatment, he required a permanent pacemaker. A dual-chamber implantable cardioverter-defibrillator (ICD) was implanted and the patient was discharged on prednisone. His follow-up plan consisted of serial echocardiography and consideration of a new coronary sinus lead in the event of left ventricular dysfunction in the future.

Conclusion: Cardiac rhythm management in the context of CS is often difficult, with decisions that need to be made between a pacemaker, a defibrillator, or a cardiac resynchronization device. The idea that biventricular pacing has a preventative role against heart failure in patients with normal left ventricular ejection fraction and CS deserves more attention and discussion.

Keywords: Cardiac sarcoidosis, Granulomatous disease, Atrioventricular block, Biventricular pacing, Case report.

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Introduction

Sarcoidosis is a systematic granulomatous disease of an unknown etiology. However, infectious, environmental, and occupational risk factors have been suggested [1]. It affects 10-40 per 100,000 persons in the United States and Europe [2]. There is little information regarding the prevalence of sarcoidosis in the Middle East region, and studies done were mainly case reports [3]. One of the large studies included 142 patients belonging to the Kuwaiti population [4]. Target organs include the lungs, eyes, skin, lymph nodes, and nerves [2].

CS is diagnosed in just 5% of patients with sarcoidosis [2]. However, there are many cases of subclinical CS, which are diagnosed only after autopsy [5]. The diagnosis of CS in a clinically suspicious patient is done by the integration of both imaging and pathological studies [6]. Several diagnostic methods have been proposed; cardiac magnetic resonance imaging (CMR) and fluorodeoxyglucose-positron emission tomography (FDG-PET). Endomyocardial biopsy is considered non-mandatory for the diagnosis of CS according to some guidelines [7].

Diagnosing CS is not an easy task considering that diagnostic tests such as echocardiography and ECG are non-specific and can be easily misdiagnosed as other cardiac pathologies [5]. Treatment of cardiac sarcoidosis is usually by immunosuppression (through corticosteroid, methotrexate) and antiarrhythmic drugs. ICD implantation was found to be beneficial, especially in patients with a history of heart attack, ventricular tachycardia, left ventricular ejection fraction (LVEF) lower than or equal to 35%, and life expectancy of more than 1 year [8]. According to a study by Zhou et al, the absence of an ICD or pacemaker was found to be associated with increased mortality in patients with CS [9].

We hereby report the case of a 43-year-old man diagnosed with CS that was managed by biventricular pacing.

Case Presentation

A 43-year-old male soldier, previously healthy, non-smoker, and non-alcoholic, presented to the emergency department complaining of intermittent non-productive cough of 15 days duration. He also reported, three days before presentation, mild dyspnea on exertion and fatigue while performing a 10 km ruck march. The patient has no relevant traveling history, no orthopnea, paroxysmal nocturnal dyspnea, chest pain, palpitations, fever, chills, night sweats, or history of syncope or lightheadedness. His family history was unremarkable.

On physical examination, the patient was bradycardic (46 beats per minute). Cardiac examination was normal, with no audible heart murmurs. No jugular venous distension or lower extremity edema was noted. Lungs were clear to auscultation. There was no skin rash, arthralgias, palpable lymph nodes, visual problems, weight or appetite changes.

Although pulmonary function tests were reasonable at this point, it was not performed due to a lack of resources in the institute. ECG revealed a complete atrioventricular (AV) block with ventricular escape rhythm at a rate of 46 beats per minute (Figure 1a), and intermittently captured beats with a right bundle branch block (RBBB) morphology (Figure 1b). Blood tests including troponin, calcium, angiotensin-converting enzyme (ACE), antinuclear antibodies (ANA), thyroid-stimulating hormone (TSH) were within normal ranges. Hepatitis B surface antigen (HBsAg), and hepatitis C virus (HCV) serologies were not reactive. Purified protein derivative (PPD) skin test was also negative. Chest radiography showed bilateral hilar lymphadenopathy which was further investigated through chest computed tomography scan revealing mediastinal, jugular, and carotid lymph node enlargement, in addition to several right lung 4mm parenchymal micronodules (Figure 2). Transthoracic echocardiography showed a

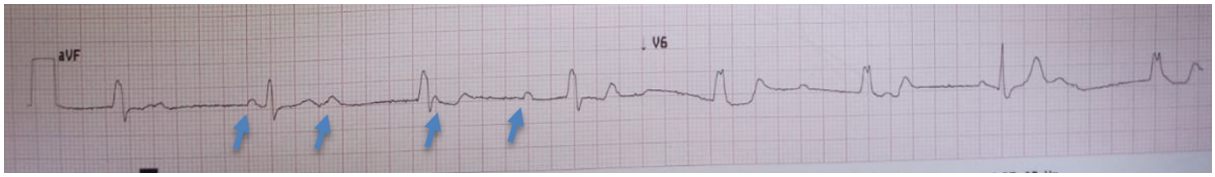

Figure 1a: ECG at admission showing complete AV block.

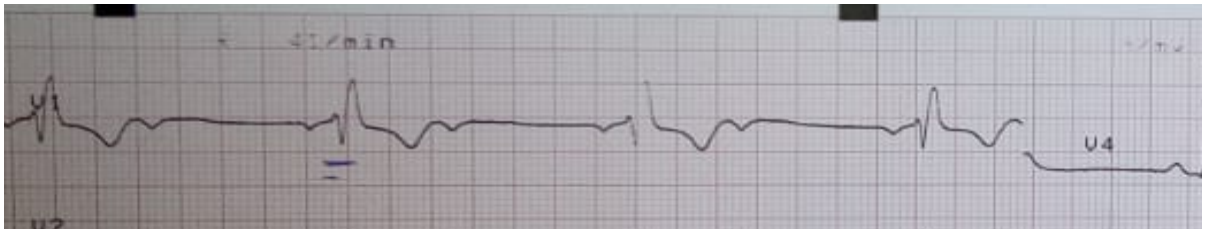

Figure 1b: ECG at admission showing Right Bundle Branch Block (RBBB) pattern.

the complete AV block, we opted for the placement of a temporary right internal jugular transvenous pacemaker in the right ventricle.

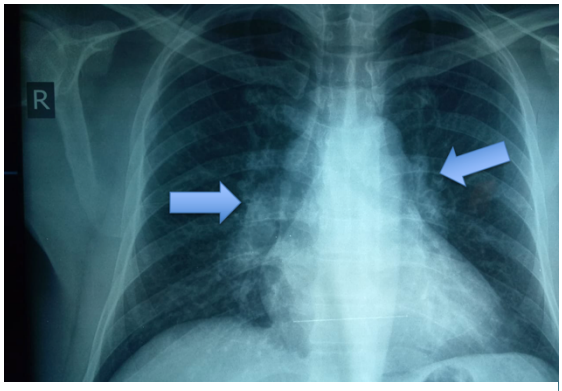

Figure 2: Chest radiography showing bilateral hilar lymphadenopathy.

At this point, there was a high level of suspicion of sarcoidosis. A bronchoscopy was done and showed an incidental aberrant right bronchus intermedius segment. Biopsies were taken from the right and left transbronchial regions. Empiric high dose pulse steroid therapy with intravenous prednisone 1 g/day was initiated.

Within 24 hours of administering steroids, AV node conduction resumed with an atypical RBBB as well as a left anterior fascicular block. Three doses of prednisone were administered. This led to a gradual improvement of the conduction from an intermittent complete AV block to Mobitz II AV block and then to sinus bradycardia. The patient underwent a fluorodeoxyglucose-positron emission tomography (FDG-PET) scan that showed curvilinear FDG uptake throughout the left ventricular (LV) myocardium including the free wall and interventricular septum, and a slightly more intense focal uptake at the interventricular septum (Figure 3).

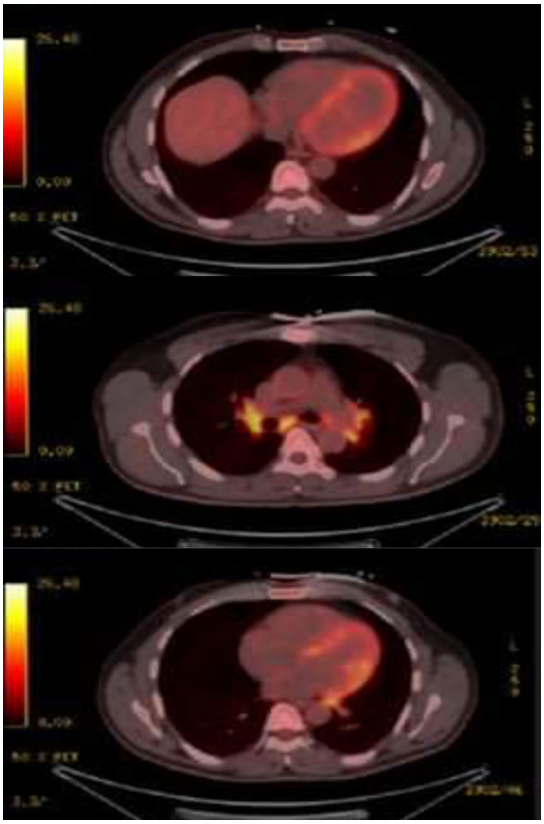

Figure 3: FDG-PET scan of the heart, showing curvilinear FDG uptake throughout the left ventricular (LV) myocardium including the free wall and interventricular septum, and a slightly more intense focal uptake at the interventricular septum.

The results of transbronchial biopsies subsequently showed numerous scattered granulomas in the lung parenchyma with no caseous necrosis (Figure 4), thereby confirming the diagnosis of sarcoidosis with cardiac involvement.

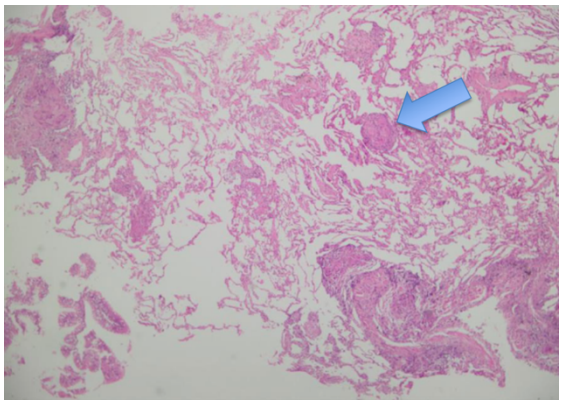

Figure 4: Histopathological evaluation of the tranbronchial tissue showing non-caseating granuloma typical of sarcoidosis.

The dilemma we encountered was choosing the appropriate cardiac device for this patient. Although the patient demonstrated a partial response to steroids with some improvement in conduction, it was clear that he needed a permanent pacemaker. The LVEF was normal, thus there was no strict indication for an ICD based on heart function. However, the involvement of the infra-His conduction system indicates cardiac sarcoidosis affecting the ventricular myocardium, which places the patient at higher risk of ventricular arrhythmias and sudden cardiac death. As such, a dual-chamber defibrillator would be indicated. The patient was expected to require 100% right ventricular (RV) pacing which might be associated with the development of pacing-induced cardiomyopathy. Thus, a strong argument could be made for a biventricular cardiac resynchronization defibrillator to be placed to avoid RV pacing and prevent the development of cardiomyopathy. A dual-chamber ICD was implanted and the patient was discharged on oral prednisone 1 g/day. A follow-up plan consisted of serial echocardiography and consideration of a new coronary sinus lead in the event of left ventricular dysfunction in the future. However, the patient was lost to follow-up.

Discussion

In the context of its varying clinical presentation, diagnosing CS can be quite challenging. One of the accepted guidelines used is the one proposed by the Japan Society of Sarcoidosis and Other Granulomatous Disorders (JSSOG) [10]. Imaging modalities such as CMR and FDG-PET scans are considered of great importance in terms of diagnosis and management of CS [11]. In addition, it is important to note that an endomyocardial biopsy can be done [5]. However, it yields a low sensitivity [5].

CS management ranges from medical therapy (corticosteroids and immunotherapy) to device implantation [5]. Corticosteroid therapy is a known drug of choice when it comes to the treatment of systemic sarcoidosis. However, no sufficient data is proving its benefits on CS. Kandolin et *al.* reported the long-term effects of corticosteroids in patients with CS; Survival rates were 97%, 90%, and 83% during a 1-year, 5-year, and 10-year follow-up respectively [12]. An adequate dose of corticosteroid has not been established yet. Yazaki et *al.* reported that doses as low as 30mg or as high as 60mg can improve long-term prognosis [13].

For the prevention of sudden cardiac death, ICD implantation may be considered in patients with CS [14]. According to the 2017 AHA/ACC/HRS guideline, Class I recommendations for ICD implantation in CS include: sustained ventricular tachycardia (VT) or cardiac arrest, and LVEF less than or equal to 35%. Class IIa recommendations include LVEF of more than 35% plus one of the following: syncope, cardiac scarring evident by CMR or PET scan, indication for permanent pacing, or inducible ventricular arrhythmia [14]. In our case, the LVEF was normal. However, the presence of a complete AV block was a clear indication of a permanent ICD implantation. The Heart Rhythm consensus states that pacemaker implantation can be done even if the AV

block reverses with the help of corticosteroids [7].

Possible future LV dysfunction is a major issue to deal with in patients with implanted ICDs. The depression in LV systolic function can become manifested at an early stage and may persist after the cessation of pacing [15]. Currently, there is no consensus on an increased risk of LV dysfunction caused by ventricular pacing [16]. However, a wider QRS in a patient with pre-existing heart disease may serve as a predictor for LV dysfunction in the future [16].

In our case, the dilemma was about choosing which type of ICD is the best for our patient. We opted for the biventricular pacing although current data do not support its use in patients with preserved LVEF. According to the literature, biventricular pacing is the preferred option in those with LV dysfunction and AV block [16]. Furthermore, Once the patient with pacing develops an LV dysfunction (decrease in LVEF), an upgrade to biventricular pacing is still possible [16]. Based on some studies, it is reasonable to consider choosing the biventricular pacing over the routine RV pacing; Biventricular pacing showed to be superior to RV pacing in terms of avoiding the risk of developing LV dysfunction [15]. This hypothesis was tested in the Pacing to Avoid Cardiac Enlargement (PACE) trial, which compared biventricular pacing to RV pacing in bradycardic patients with normal LVEF [15]. At 1-year follow-up, RV pacing resulted in a significant reduction in LVEF and enlargement in left ventricle end systolic volume (LVESV) which were prevented by biventricular pacing [15]. This benefit was shown in the subgroup of patients with AV block [15]. Extended 2-year follow-up demonstrated further deterioration of LVEF and LVESV in the RV pacing group, but no deterioration in the biventricular pacing group [15]. Further analysis showed that the development of pacing-induced systolic dyssynchrony was associated with LVEF reduction and LV adverse remodeling [15]. Despite these encouraging studies, the evidence is not yet sufficiently strong to support the widespread adoption of biventricular pacing in patients with normal LVEF because of conflicting results from other trials [17]. According to the PREVENT-HF study, there was no difference between RV and biventricular pacing in terms of LVEF and LV remodeling in patients with heart block [17]. Furthermore, RV pacing showed worsening in patients with HF with reduced LVEF; The Dual Chamber and VVI Implantable Defibrillator (DAVID) trial found that dual-chamber (right atrial and right ventricular) pacing was detrimental in patients with HF with reduced LVEF (≤ 40%). Likely, the RV component of dual-chamber pacing and the frequency of pacing were primarily responsible for the detrimental effect [18]. However, according to the biventricular pacing for an atrioventricular block to prevent cardiac desynchronization (BIOPACE) study, the frequency of HF hospitalization in both RV and biventricular pacing groups was equal (P = 0.8); this may be related to the high incidence of biventricular pacing implantation failure (14.1%) [19].

Other than ICD, cardiac resynchronization therapy (CRT) upgrade is another possible strategy. CRT is a technique used to manage atrial and ventricular asynchrony, producing an anti-arrhythmic effect through pacing in more than one location, and consequently providing a more adequate pattern of depolarization [20]. However, this carries a higher risk of acute complications versus a de novo implant because of venous access issues, the risk of damage or extraction of old leads, the higher risk of infection, and the additional time that may be required [21].

Conclusion

Biventricular pacing reverses LV remodeling and reduces HF hospitalization and mortality in patients with established HF, low LVEF, and wide QRS or who require frequent ventricular pacing, in whom biventricular pacing could be remarkably more beneficial than routine RV pacing. A preventive role of biventricular pacing in avoiding HF in

subjects with normal LVEF remains controversial. Although guidelines do not currently recommend routine biventricular pacing for all patients with heart block due to a lack of studies favoring the biventricular pacing over the RV pacing, the increasingly recognized potential for harmful effects of RV pacing and accumulating evidence of the benefits of biventricular pacing, the "one move, double the gains" strategy deserves more attention and discussion.

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