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Case Report

Pleural and pericardial effusions with cardiac conduction system and myocardial involvement: A rare presentation of sarcoidosis [☆]

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ABSTRACT

Sarcoidosis is a granulomatous immune disorder that can infiltrate many organ systems. When the cardiac system is involved, the myocardium and conduction system are frequently affected. We report the case of a patient presenting with complete heart block following cardioversion from atrial flutter accompanied by pleural and pericardial involvement whose diagnosis of sarcoidosis was subsequently made on pathological examination. Pericardial effusion and pleural effusion are rare manifestations of sarcoid, and the both of them happening simultaneously (less than 10 case reports) in conjunction with cardiac conduction system and myocardial involvement are almost nonexistent in the literature (one case report). As cardiac involvement in sarcoid can drastically increase the mortality, it is important to be vigilant for the diverse manifestations of cardiac involvement in all patients for which there is clinical suspicion of sarcoid.

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Introduction

Sarcoidosis is an immune disorder caused by noncaseating granulomas that form in almost any organ system, most frequently the lungs. About 5%-7% of sarcoid patients have clinically significant cardiac involvement throughout their course, though autopsy studies suggest a much more substantial percentage of subclinical involvement [1,2]. Additionally, it has been shown that up to 30% of sarcoidosis deaths in the United States are due to cardiac involvement [3,4]. Curiously, cardiac involvement is higher in Japanese cohorts, with 85% of patient mortality resulting from cardiac complications [5]. Diagnosis

of cardiac sarcoidosis remains challenging, as involvement can take on vastly differing phenotypes. Pathologically, the myocardium and conduction system are commonly involved. Endocardial and pericardial disease are much less common, but still reported [1,6].

Case

A 55-year-old male was admitted to the hospital for symptomatic bradycardia and episodes of complete heart block in the setting of multiple cardioversions for atrial fibrillation.

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Fig. 1 – MRI cardiac morphology w/ and w/o contrast, T1/T2 parametric mapping with STIR and flow quantification sequences, demonstrating biatrial enlargement and pericardial effusion.

He initially presented with worsening episodes of dizziness, shortness of breath, and chest discomfort happening for 2 months and lasting for about 15-20 minutes, 3×/day. He had a history of long-standing atrial flutter for 3 years. Workup prior to hospitalization had included an echo showing LVH and biatrial enlargement, as well as a cardiac catheterization with no evidence of ischemia. In 2019, the patient had potential pulmonary sarcoidosis as noted on CT scan with mediastinal adenopathy. However, he did not obtain a follow-up bronchoscopy due to a combination of COVID-related resource strains on healthcare and patient nonadherence. This patient also had a history of persistent pericardial effusion initially noted in November 2021 w/o evidence of cardiac tamponade, for which he was previously on colchicine, but discontinued due to diarrhea. He had undergone his third attempt at cardioversion for atrial flutter 5 days prior to admission.

In the hospital, he was persistently bradycardic to the 40s. Rales could be heard bilaterally on pulmonary auscultation, and there was 1+ pitting edema present bilaterally. BNP was high at 635, and chest X-ray showed marked cardiomegaly with findings suggestive of mild pulmonary edema / heart failure. EKG showed complete heart block and echo showed ejection fraction 40%. High-sensitivity troponins were low.

In the hospital, the patient underwent placement of a BIV ICD in the setting of complete heart block. He received a cardiac MRI (Fig. 1) showing impaired RVEF, LVEF, and biatrial enlargement, suggestive of an infiltrative process. A persistent pericardial effusion without tamponade physiology was noted and the patient underwent pericardiocentesis with pericardial drain placement with 1.5 L drained. Chest CT (Fig. 2) showed hilar and mediastinal lymphadenopathy, multiple nodular airspace opacities in both upper lobes, and a large right pleural

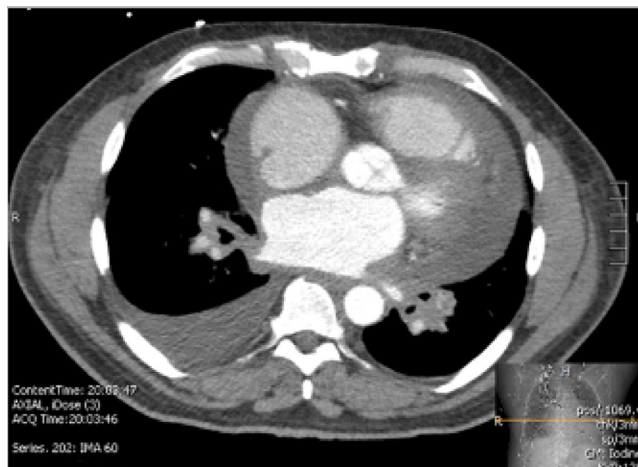


Fig. 2 – Chest CT w/ contrast demonstrating hilar and mediastinal lymphadenopathy.

effusion. Since cardiac MRI and CT findings were concerning for sarcoidosis, the patient had an EBUS with transbronchial biopsy. The pathology report showed non-necrotizing granulomas with Astroid bodies, consistent with sarcoidosis (Figs. 3 and 4). Patient tissue was negative for both the Acid-Fast Bacteria (AFB) stain (Figs. 5 and 6) and the Grocott Methenamine Silver (GMS) stain (Figs. 7 and 8). Of note, paratracheal lymph nodes, pre-carinal lymph node, and pericardial and pleural cavity fluid did not show granulomas.

Once sarcoidosis was confirmed pathologically, the patient was placed on prednisone (60 mg, decreasing by 5 mg every 2 weeks until 40 mg daily, which he will need for at least 3 months) and methotrexate (2.5 mg weekly, increasing by 2.5 mg weekly until he achieves target dose 15 mg weekly), with goals to prevent disease progression and worsening ventricular dysfunction. He was also placed on folic acid supplementation, Bactrim for PJP prophylaxis, and pantoprazole for GI prophylaxis. He was placed back on colchicine for 6 weeks.

Discussion

Sarcoidosis can impact essentially any organ system, with a heterogeneous array of manifestations within each particular one. Cardiac sarcoidosis, by extension, encompasses a wide spectrum of clinical presentations, ranging from asymptomatic to sudden cardiac death [7]. Our case emphasizes this point, as our patient's sarcoid involved the cardiac conduction system, myocardium, pericardium, lung parenchyma, and pleura leading to heart block, dilated cardiomyopathy, and pleural and pericardial effusions. Cardiac involvement most commonly occurs in conjunction with other organ system involvement, but may occur in isolation [1]. It may be prudent to evaluate all patients with systemic sarcoidosis for cardiac involvement, due to the possibility of sudden cardiac death [7]. In our patient's case, it would have been reasonable to suggest workup for cardiac involvement when potential pulmonary sarcoidosis was noted on his CT scan 4 years prior.

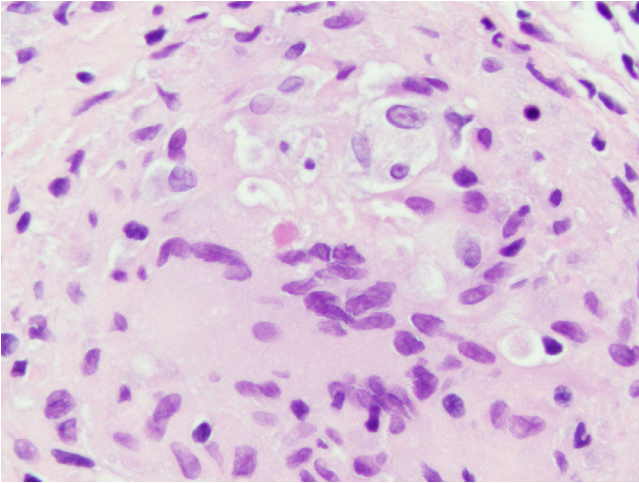


Fig. 3 - High power patient tissue with astroid body, hematoxylin and eosinophil stain (H&E), x441 magnification.

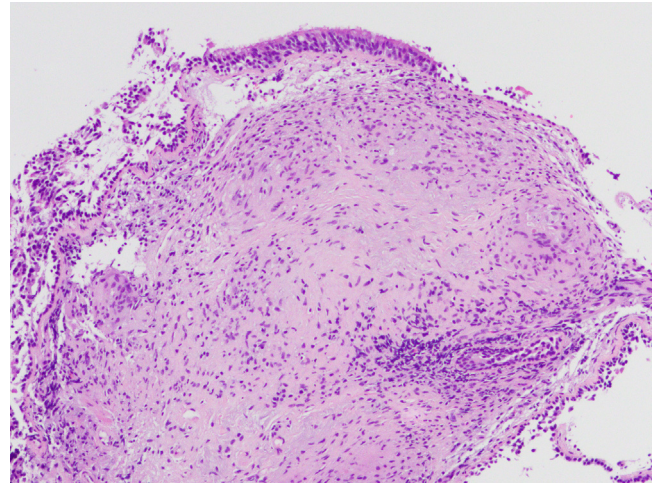


Fig. 4 - Medium power patient tissue with granuloma, H&E stain, x140 magnification.

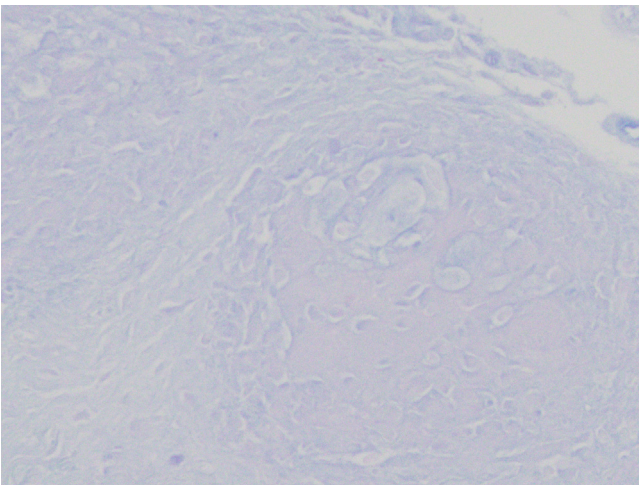


Fig. 5 - Patient neg. AFB stain tissue, x441 magnification.

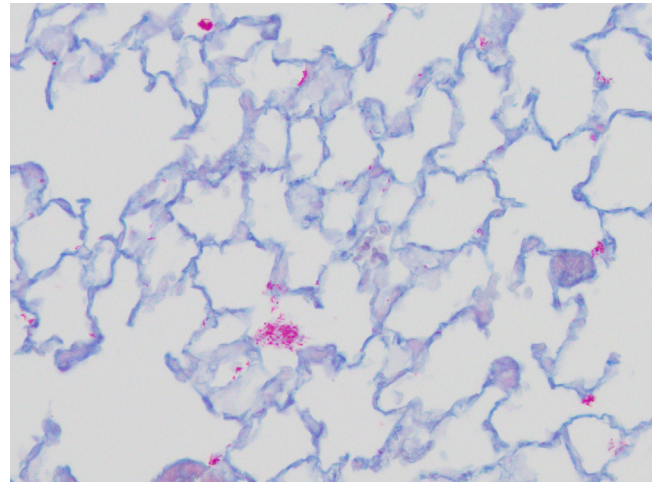


Fig. 6 - AFB stain pos. control, x441 magnification.

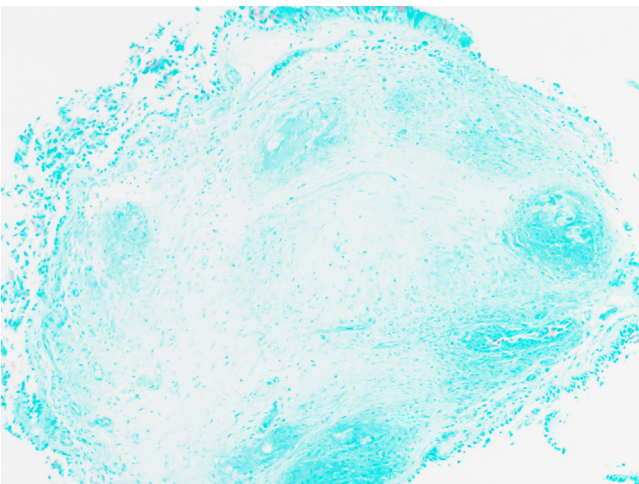


Fig. 7 - Patient neg. GMS stain tissue, x140 magnification.

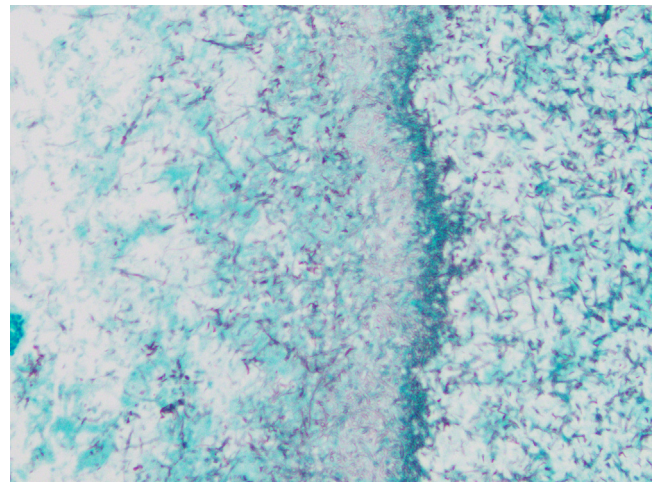


Fig. 8 - GMS stain pos. control, x441 magnification.

The most common clinical manifestations of cardiac sarcoidosis include cardiomyopathy and subsequent heart failure due to involvement of the myocardium, and arrhythmias due to involvement of the conduction system [1]. Granuloma invasion of the myocardium most commonly targets the interventricular septum and the left ventricular free wall [3,5]. Granuloma invasion of the conducting system may lead to dangerous tachy- or brady-arrhythmias, of which right bundle branch block and AV block are most prevalent. Supraventricular arrhythmias can occur as well, with atrial flutter, as in our patient, demonstrated in 18% of patients with cardiac sarcoidosis [1,6]. Endocardial and pericardial disease are much less common than myocardial disease, but have been reported [1,6]. The most common manifestation of pericardial sarcoidosis is pericardial effusion, with most of these occurring asymptotically and without tamponade physiology [8]. Although the lung is the most commonly involved organ (90%), pleural involvement in sarcoidosis is infrequent, mirroring the rarity of pericardial involvement. Further, pleural effusion secondary to pleural sarcoidosis only has a prevalence of 1.1%–1.5% [8].

On review of the literature, less than ten case reports have described concurrent pleural and pericardial effusions secondary to sarcoidosis. Only one of these cases additionally included both cardiac conduction system and myocardial involvement [9]. The remaining cases most often presented as massive pericardial and pleural effusion of unknown etiology [9–14]. It is important to closely follow cases of combined pulmonary and cardiac involvement in sarcoid patients. This combination of organ system involvement accounts for most of the morbidity and mortality associated with sarcoid [5].

Initial diagnostic tests for cardiac sarcoidosis include but are not limited to ECG, 24-h Holter monitoring, echocardiography, PET scan, and cardiac MRI. The definitive diagnosis of cardiac sarcoidosis is made with biopsy. However, endomyocardial biopsy is an invasive procedure that lacks sensitivity, presumably due to the patchiness of endomyocardial involvement [1,4]. Thus, only 25% of patients' endomyocardial biopsies reveal noncaseating granulomas. Additionally, a positive biopsy alludes to a potential worse outcome, as it demonstrates more extensive disease [4]. Therefore, according to the World Association of Sarcoidosis and other Granulomatous Disorders organ assessment instrument, cardiac sarcoidosis can be assumed with biopsy of lung or lymph node showing noncaseating granulomas if other alternative causes for cardiac symptoms have been reasonably excluded [15].

Steroid therapy and pacemaker implantation are the 2 main therapeutic approaches in cardiac sarcoidosis patients. Corticosteroid sparing agents may be considered if a patient does not respond to corticosteroids or cannot tolerate the side effects [7]. Implantation of an implantable cardioverter-defibrillator (ICD) should be evaluated in all patients with sarcoidosis with cardiac involvement, after a careful estimation of the risk of arrhythmias and sudden cardiac death [16]. Other specific treatments depend on the specific clinical manifestations of cardiac sarcoidosis, for example pericardiocentesis or pericardial window for single or recurrent pericardial effusions, respectively. Heart failure medications such as ACEIs, ARBs, BBs, and diuretics may be used [17]. Heart transplantation is considered in advanced, drug resistant heart failure or

dangerous ventricular arrhythmias that have been resistant to implantable devices [17]. Unfortunately, even with treatment, cardiac sarcoidosis has a worse prognosis than sarcoidosis involving any other organ system [7].

Conclusion

Manifestations of sarcoidosis may be manifold, and the literature includes reports of both pleural and pericardial effusions. The pericardium is the least frequently involved in cardiac sarcoidosis, and the pleura is similarly rarely involved in pulmonary sarcoidosis. Thus, the constellation of both these manifestations along with heart block and dilated cardiomyopathy in our patient was a particularly interesting combination. Treatment for cardiac sarcoid patients is multidisciplinary, and includes implantable devices, pericardial window, and immunosuppressive medications. Cardiac involvement increases the morbidity and mortality for sarcoid patients, even more drastically when other organ systems such as the lungs are involved in the disease pathology. Therefore, it is important to preemptively pursue screening for cardiac involvement in sarcoidosis patients.

Patient consent

Informed consent for the publication of this case was obtained from the patient during their inpatient stay.

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