Recurrent Syncope Due to Concurrent Cardiac Sarcoidosis and Large-Vessel Vasculitis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient:	**Male, 68-year-old**
Final Diagnosis:	**Sarcoidosis • vasculitis**
Symptoms:	**Syncope**
Medication:	**—**
Clinical Procedure:	**—**
Specialty:	**Rheumatology**

Objective: Rare co-existance of disease or pathology

Background: Cardiac sarcoidosis and large-vessel vasculitis are both rare diseases with a variety of presenting symptoms. Both can result in high morbidity and mortality if not diagnosed early. While they are each relatively uncommon on their own, there have been a few reports suggesting they may be more related than previously thought. This case report suggests that the 2 diseases can become symptomatic concurrently, complicating diagnosis.

Case Report: A 68-year-old male patient was diagnosed concurrently with cardiac sarcoidosis and vasculitis after several episodes of syncope thought to be due to arrhythmia. The patient was treated with high-dose corticosteroids, and repeat imaging showed decreased inflammatory changes in the cardiac tissue and large blood vessels.

Conclusions: Prior case reports have described vasculitis and sarcoidosis in the same patient; however, these patients usually had a long history of known sarcoidosis involving several organ systems. This case suggests that physicians should be alert to more limited forms of the disease in a patient with cardiac myopathy of unknown origin with new arrythmia. More research is also needed to determine how granulomatous disease and vasculitis are related to each other.

MeSH Keywords: Sarcoidosis • Syncope • Vasculitis

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Background

Sarcoidosis and vasculitis are both inflammatory diseases that can affect different organ systems. Sarcoidosis is defined by formation of non-caseating granulomas in the affected organs. Sarcoidosis is usually not fatal; however, when it is, cardiac involvement is often present [1]. Granulomatous disease in the cardiac tissue leads to numerous complications such as heart block and arrhythmias as well as dilated cardiomyopathy and pericardial effusions [2]. Morbidity related to large-vessel vasculitis relates primarily to complications from vessel stenosis and dissection [3,4], although some studies have also shown increased risk of atherosclerotic disease compared with the general public [5]. In this case report, we present a patient with repeated episodes of syncope who was found to have both cardiac sarcoidosis and inflammatory large-vessel disease.

Case Report

A 68-year-old man with a history of bladder cancer, idiopathic cardiomyopathy, and ventricular tachycardia presented to our hospital with an episode of tremors and unresponsiveness at home. He reported recurrent syncope over the previous few months. The patient denied fever, weight changes, arthralgias, myalgias, shortness of breath, cough, skin lesions or rashes, ophthalmologic complaints, and headaches. On physical exam, his vital signs were: blood pressure 116/63 mmHg, pulse 74 beats per minute, temperature 36.6°C, and respirations 18 breaths per minute. The remainder of his physical

exam was unremarkable. Laboratory tests showed a white blood cell count of 20.0 K/mL with 81% neutrophils, hemoglobin 8.2 g/dL, platelets 599 K/mL. Erythrocyte sedimentation rate (ESR) was >140 mm/hour, c-reactive protein 0.7 (normal <1.0 mg/dL). Blood chemistry was notable for creatinine 6.90 mg/dL, blood urea nitrogen 67 mg/dL, angiotensin converting enzyme 25 u/L, anti-neutrophil antibody detected by IgG with titer <1: 80, rheumatoid factor negative, cyclic citrullinated peptide negative, antineutrophil cytoplasmic antibody negative, serine protease 3 IgG negative, IgG 4 negative, myeloperoxidase antibody negative, C3 complement 73 at 88–165 mg/dL, and C4 complement normal. The infectious workup included a negative rapid plasma reagin test and negative hepatitis C antibody, and an HIV test from an outside hospital several months prior was nonreactive.

The patient was suspected to have cardiogenic syncope. He underwent positron emission tomography (PET) with regadenoson pharmacologic stress testing. This revealed 2 focal areas of hypoperfusion in the mid-inferior and mid-lateral regions of the left ventricular myocardium, which did not conform to a coronary artery vascular territory (**Figure 1**). Lesions were concerning for non-caseating granulomas. There were no reversible perfusion defects during the stress portion of the PET to suggest ischemic disease. This study was followed with 18F-fluorodeoxyglucose (FDG) PET with computed tomography, which showed increased metabolic activity in the mid-inferior and mid-lateral regions of the left ventricle myocardium, corresponding to the areas of poor perfusion on the stress PET (**Figure 2**). There was an additional area of increased metabolic activity in the basal septal
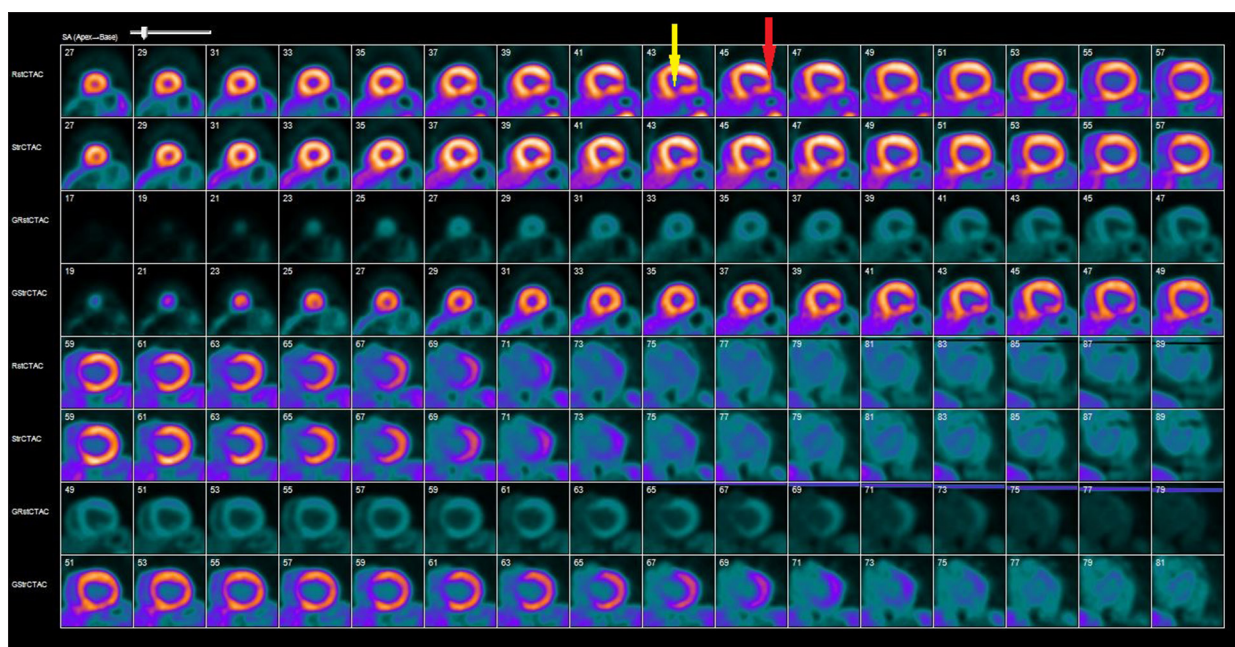

Figure 1. Pharmacologic stress/rest rubidium PET myocardium perfusion image showed 2 focal areas of round hypoperfusion in the mid-inferior (yellow arrow) and mid-lateral (red arrow) regions of the left ventricular myocardium.
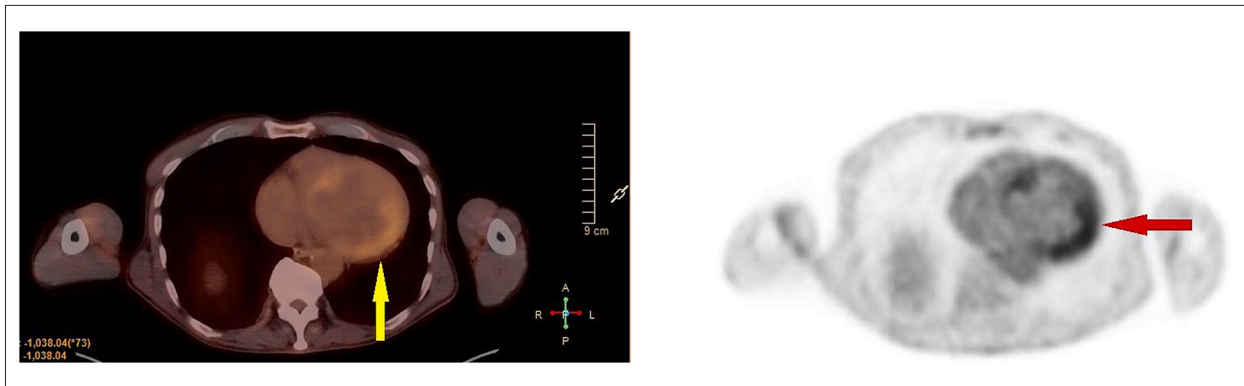
Figure 2. The 18F-fluorodeoxyglucose PET/CT scan showed a focal area of increased metabolic activity in the mid-inferior (yellow arrow) and mid-lateral (red arrow) regions of the left ventricular myocardium, corresponding to the areas of decreased perfusion noted on the rubidium perfusion study.

region without abnormal perfusion defect on the stress PET. The FDG PET/CT also revealed a 1.8×1.5 cm area of increased metabolic activity in the anterior pericardial region suggestive of a lymph node. There was no unusual metabolic activity in the lungs, hilar, or axillary regions. There was diffusely increased metabolic activity in the ascending aorta, arch, bilateral common carotid arteries, and subclavian and brachial arteries, which was suggestive of vasculitis.

Endomyocardial biopsy was not done because of the location of the metabolically active lesions in the left ventricle. Cardiac magnetic resonance imaging was not performed because of the patient's acute kidney injury and chronic kidney disease. Because the patient's symptoms improved and no arrhythmia was detected during his hospital stay, he was not started on glucocorticoids. He was prescribed a wearable defibrillator. In the outpatient setting, his ESR was still elevated at 65 mm/h. A repeat FDG PET/CT showed persistence of the metabolically active lesions in the same areas of the myocardium as well as the aorta and smaller branches. He was started on prednisone 60 mg (1 mg/kg/day) by mouth daily for 4 weeks and then tapered by 10 mg every 2 weeks. He continued to be asymptomatic. He was not a candidate for methotrexate, leflunomide, or azathioprine because of severe renal dysfunction. After 4 weeks of treatment, his ESR decreased to 22 mm/h. Later, he was transitioned to hospice care due to the poor prognosis of his bladder cancer.

Discussion

In this case report, we describe a patient who was diagnosed with concurrent sarcoidosis and large-vessel vasculitis detected with PET imaging after an episode of syncope. Because of the patient's serious comorbidities, histologic confirmation was not possible. Treatment with high-dose steroids was started and the patient remained asymptomatic.

Few reports have described sarcoidosis with inflammatory large-vessel disease [6–8], and it remains unclear if these 2 diseases are related. Although they have been considered 2 separate diseases [9], there is also histopathologic evidence more recently that they may be a continuum of a single disease state rather than separate entities, especially in the case of giant cell myocarditis [10]. Previously, it was noted in these patients that the diagnosis of sarcoidosis preceded the vasculitis, often by several years [8].

Large-vessel vasculitis is mainly divided into Takayasu arteritis (TAK) and giant cell arteritis (GCA). Presentations that do not fit into the Chapel Hill Consensus Conference guidelines often share features of both diseases or are associated with another systemic disease. Given that the patient's age was too advanced to fit the criteria for TAK and the vessels involved are not commonly seen in GCA [11], this presentation was deemed to be an otherwise undefined vasculitis. While there are reported cases of sarcoid-associated vasculitis, the sarcoidosis is generally systemic and known prior to the diagnosis of vasculitis.

Cardiac granulomas are found during autopsy in 20-30% of patients with known sarcoidosis, although these patients frequently do not have clinical manifestations while alive [12]. Patients who do have cardiac symptoms generally experience arrhythmias and cardiomyopathies. Those patients with sarcoid-associated vasculitis have a range of presentations depending on the vessels involved. According to Fernandes et al., there is no single clinically significant presentation observed in these patients. The presence of vasculitis did not seem to impact the extent of cardiomyopathy experienced by the patients [7]. More recently, there has been some discussion as to whether patients with sarcoidosis-induced vasculitis actually had TAK with concurrent sarcoid, a more common phenomenon. This same group also suggests that it may cause granulomatous disease resembling sarcoid [13]. In these cases,

differentiating which symptoms appeared first chronologically is important for diagnosis.

Treatment of cardiac sarcoidosis and sarcoidosis-associated vasculitis is with glucocorticoids and other immunosuppressive agents, as their benefits are established in noncardiac sarcoidosis. Glucocorticoids result in resolution of conduction abnormalities [14] and recovery of left ventricular function or reduction in further loss of function [15]. There is some evidence that this benefit may not be as long-lasting as initially suspected [16]. Most studies show some benefit to starting steroid therapy at the time of diagnosis in patients who are symptomatic or show signs of organ damage, rather than starting therapy after monitoring for further disease progression. The treatment course commonly includes several weeks of high-dose steroids followed by several months of taper [2,16].

Conclusions

This case is notable because it represents previously undiagnosed cardiac sarcoidosis with large-vessel vasculitis in a relatively asymptomatic patient. The only presenting symptom was syncope, likely due to ventricular arrythmias. More studies are needed to elucidate the possible etiologic links between these 2 inflammatory diseases.

Conflicts of interest

None.

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