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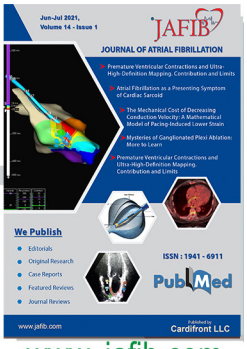

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Atrial Fibrillation as a Presenting Symptom of Cardiac Sarcoid

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Abstract

We submit an unusual presentation of spontaneous atrial fibrillation in a young, fit, active-duty U.S. military African-American male without evidence of structural heart disease. His atrial fibrillation was refractory to several ablation treatments over the course of 3 years. Subsequently he was diagnosed with extracardiac sarcoidosis and a fluorodeoxyglucose-positron emission tomography (FDG-PET) scan identified bi-atrial hypermetabolic lesions, concerning for cardiac sarcoidosis. Given the low incidence of atrial fibrillation in patients < 45 years-of-age, this case report aims to underscore consideration of cardiac sarcoidosis as a subclinical contributor towards developing atrial fibrillation in the appropriate patient population. Broadly more investigations are needed to explore the role of cardiac sarcoidosis with atrial involvement and the likelihood of developing atrial arrhythmias.

Learning objectives:

1) Atrial fibrillation (AF) in the absence of overt cardiac disease may be the first indication of another underlying disease. Therefore, AF in patients < 45y, which is refractory to catheter ablation should prompt further work-up for an underlying cause.

2) Cardiac sarcoid (CS) is known to cause congestive heart failure and a fatal complication, ventricular arrhythmias (VAs). Supraventricular arrhythmias (SVAs) in CS are infrequently described in literature, are less common than VAs, and include atrial tachycardia, atrial ectopy, atrial flutter, and AF.

Introduction

Sarcoidosis is a multi-organ chronic granulomatous disease of unknown etiology, characterized by non-caseating granulomas. Relatively uncommon, the annual incidence of sarcoidosis in the United States is estimated to be 0.011% among Caucasians and 0.036% among African-Americans, and is slightly more common in women than in men.[1] Clinical cardiac involvement in sarcoidosis has a prevalence of 5% and subclinical cardiac involvement is approximated to be 25%.[2] In the setting of cardiac sarcoidosis (CS), atrial arrhythmias are thought to be less common (19%) in comparison to ventricular arrhythmias (23%) and most commonly, complete heart block (30%).[3] The pathophysiology of atrial arrhythmias in CS remains unclear, but is thought to be less commonly either due to (1) sarcoid granulomatous deposition in the left atrium leading to inflammation and scarring or more commonly due to (2) elevated atrial pressures secondary to ventricular dysfunction and/or pulmonary hypertension.[4] Outside the setting of sarcoidosis, atrial fibrillation (AF) is the most common cardiac arrhythmia. In the United States, the 5 most common characteristics of patients with AF include female gender, age > 65years-of-age (y), hypertension, dyslipidemia, and obesity. However, the incidence of AF in patients < 45y, is only 3%.[5]

Key Words

Atrial Fibrillation, Atrial Arrhythmia, Cardiac Sarcoidosis, Cardiology, Internal Medicine

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Case report

A fit active-duty U.S. military African-American male with no significant past medical history initially presented with AF at age 40. His symptoms were a 3-day history of "racing heart," palpitations, and intermittent episodes of shortness of breath. He denied chest pain, diaphoresis, exercise intolerance, dyspnea on exertion, or any limitations in his activities of daily living. He maintained a vigorous physical fitness regimen, and was able to consistently score highly on his bi-annual military physical fitness test, which included running 2-miles within 13 minutes. Family history was negative for premature cardiovascular disease and AF.

Objectively, he was afebrile, normotensive with a blood pressure, 108/77 mmHg, heart rate, 89 beats-per-minute (BPM), respiratory rate, 20 breaths-per-minute, and had a normal body mass index, 24. Cardiovascular examination noted irregularly irregular rate and rhythm with normal first and second heart sounds. No murmurs, bruits, pulsating masses, or edema were observed. Jugular venous pressure was within normal limits. Peripheral pulses were normal in all extremities. Pulmonary examination was within normal limits. ECG (Figure 1) was notable for AF. Transthoracic and transesophageal echocardiogram (TEE) both demonstrated left ventricular ejection fraction (LVEF) 60-65% with normal sized ventricles, normal sized atria, no septal

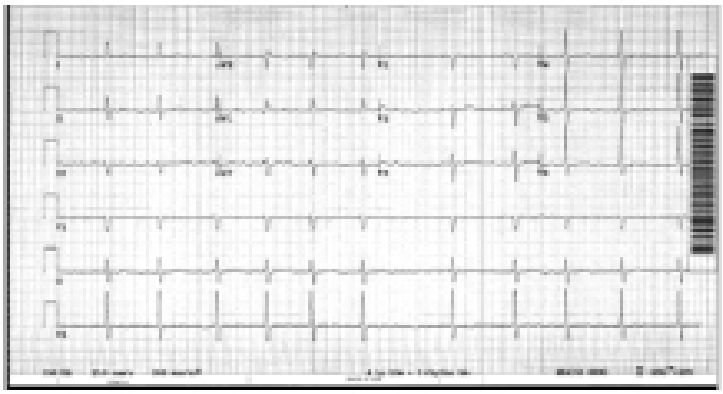

Figure 1: ECG demonstrating AF.

defects, trace mitral regurgitation, and otherwise normal valves. TEE was indicated to rule out left atrial thrombus prior to cardioversion. Left heart catheterization demonstrated no evidence of atherosclerotic cardiovascular disease. Polysomnography was obtained and was within normal limits. Patient underwent his first radio frequency ablation at age 40 and was successfully converted to normal sinus rhythm.

The following year, he developed symptomatic paroxysmal AF once again with heart rates up to 150 beats per minute. In the ensuing months, he failed beta-blocker rate control therapy and a rhythm control strategy with flecainide was chosen. Subsequently, he underwent 3 more ablations at ages 41, 42, and 43 over the course of 3 years respectively but his AF continued to be refractory. Fourteen-day ambulatory event monitoring was obtained after his latest ablation, which now confirmed persistent AF and identified rare episodes of non sustained ventricular tachycardia (NSVT) and ventricular ectopy (Figure 2). Ultimately, he was medically optimized on a combination of rate control (metoprolol succinate 25mg daily) and rhythm control (flecainide 100mg twice daily). Given that his CHA_2DS_2-VASc score was 0, he did not qualify for permanent anticoagulation. A defibrillator was not indicated at the time because NSVT burden was < 1% and the patient was still undergoing further work-up.

Shortly thereafter, patient (age 43) presented with right sided, non-exertional, non-dyspneic, non-radiating, non-traumatic chest pain localized to the ribs. Further work-up and imaging revealed bilateral hilar lymphadenopathy, small right sided pleural effusion, and several smaller bilateral pulmonary nodules. Right lower lobe endobronchial biopsy demonstrated chronic inflammation and noncaseating granulomas, confirming a diagnosis of sarcoidosis. FDG-PET scan noted hypermetabolic lesions within both atria, more prominent in the left atrium than in the right atrium (Figure 3) as well as a hypermetabolic lesion at the base of the cardiac septum (Figure 4). Maximum standardized uptake value (SUV) was 4.15, 3.8, and 4.21 in the left atrium, right atrium, and at the base of the cardiac septum respectively. Repeat echocardiogram noted diminished LVEF of 44%, left atrial dilation, left ventricular dilation, without wall motion abnormalities. Nuclear medicine myocardial perfusion scan demonstrated normal perfusion imaging of the heart without evidence of ischemia. Brain Natriuretic Peptide (BNP) was mildly elevated at 125 pg/mL, not consistent with heart failure (HF). Notably patient did not meet Framingham heart failure criteria and had no symptoms of HF. Steroid therapy was initiated with prednisone 20 mg daily and 3 months later, repeat FDG-PET scan noted resolution of hypermetabolic atrial lesions (Figure 3). Patient continued to be in AF, which had now progressed to permanent AF, CHA_2DS_2-VASc score stable at 0. Patient refused any further cardioversions and ablations. After extensive patient-physician discussion, rhythm control strategy with flecainide was abandoned and he was continued on rate control therapy with beta-blockade with good efficacy.

Discussion

Organs commonly involved in sarcoidosis include lungs, lymph nodes, skin, eye and central nervous system. Clinical cardiac involvement occurs in as few as 5% of sarcoid patients, although autopsy studies have demonstrated subclinical cardiac involvement in up to 25% of sarcoid patients. Notably in Japan, the leading cause of death in sarcoid patients is CS (up to 85%).[6] CS is known to cause congestive heart failure and a fatal complication, ventricular arrhythmias (VAs). Supraventricular arrhythmias (SVAs) in CS are infrequently described in literature, are less common than VAs, and include atrial tachycardia, atrial ectopy, atrial flutter, and AF.[3,7] Rarely, atrial arrhythmias (AAs) are caused by direct granulomatous involvement of the atria. Typically AAs are due to LV dysfunction or cor pulmonale.[7]

Our patient was clinically diagnosed with cardiac sarcoidosis based on the Heart Rhythm Society Consensus Statement for the Diagnosis of CS and the Japanese Ministry of Health and Welfare Criteria for Diagnosis of CS.[6] Specifically, he had (A) biopsy proven extracardiac sarcoidosis, (B) abnormal FDG-PET scan with notable bi-atrial and cardiac septal hypermetabolic lesions, (C) abnormal ECG (NSVT), and (D) abnormal echocardiogram demonstrating reduced LVEF< 50% without evidence of ischemia. The wide complex tachycardia noted on ambulatory monitor (Figure 2A) was thought more likely to be NSVT rather than supraventricular tachycardia with aberrancy (Ashman phenomenon) due to presence of an additional example of NSVT without the long-short sequence (Figure 2B), ventricular ectopy (Figure 2C), and presence of hypermetabolic lesion within the cardiac septum (Figure 4). Taken together, these findings were fundamentally diagnostic of CS.

In the setting of CS, LV dysfunction was thought to be secondary to infiltrative granulomatous myocardial disease. CHA_2DS_2-VASc score was utilized for anticoagulation, which was 0, therefore patient did not qualify for long-term anticoagulation. Beta-blockade for AF without treating the underlying cause (CS) was insufficient but beta-blocker

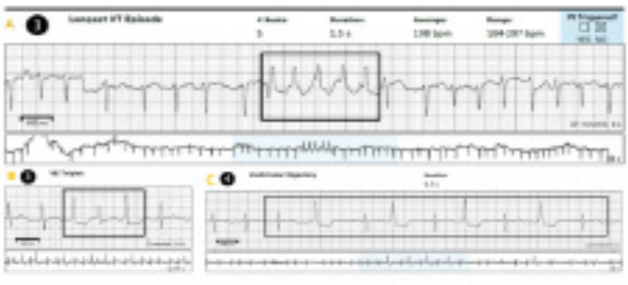

Figure 2: Ambulatory event monitor demonstrating asymptomatic NSVT lasting 5 beats (A), asymptomatic NSVT lasting 3 beats (B), and ventricular bigeminy (C).

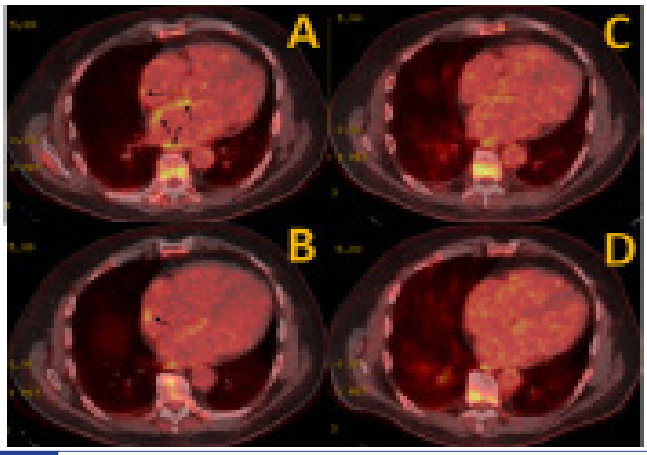

Figure 3: FDG-PET scan demonstrating bi-atrial hypermetabolic lesions (A and B), which resolved with steroid therapy (C and D). Hypermetabolic lesions are more prominent in the left atrium than in the right atrium (A and B). Left atrial maximum SUV was 4.15 and right atrial maximum SUV was 3.8 (A and B).

therapy following steroid therapy for systemic sarcoid was an effective rate-control strategy. Evident by improvement in conduction disease following steroid initiation as reported by Mehta et al.[1]

Initially, the patient presented with AF at age 40 without any evidence of structural heart disease or ischemia. His AF was refractory to 4 radiofrequency ablation treatments. Probable atrial sarcoid involvement was not identified till 3 years later via FDG-PET scan. The role of infiltrative cardiomyopathies like CS and the probability of developing SVAs in patients < 45y remains unclear. This case raises 2 questions, which require further investigation. (1) Predicting which young patients are at risk for developing SVAs with evidence of structural heart disease on echocardiography (left atrial enlargement and/or diastolic dysfunction). (2) More elusive and arguably more interesting is predicting which young patients are at risk for developing SVAs with no evidence of structural heart disease on echocardiography. Our case exemplifies the latter.

AF is primarily a disease of the elderly. The prevalence of AF in patients < 40y is as low as 0.5% and data on patients < 35y are scant. The pathophysiology of AF in young patients is broad and includes genetic factors, cardiomyopathies, and ion-channelopathies, and life-style factors (e.g. alcohol).[8] AF in the absence of overt cardiac disease may be the first indication of another underlying disease, or more rarely termed lone AF if no extracardiac cause can be identified.[9] Therefore AF in patients < 45y, which is refractory to catheter ablation should prompt further work-up for an underlying cause.

In patients with CS, development of AF is thought to be due to remodeling of the tricuspid annulus from elevated ventricular diastolic pressure. Uncommonly, however AF can be from inflammation, myocardial granulomatous involvement, and scarring. Deposition of sarcoid granuloma may occur more commonly and with greater density in the left atrium than in the right.[4] Due to these hypothesized structural changes, atrial ablation can offer a high, short, and intermediate post-procedural AF abortion rate. Saguner et al. estimated the efficacy of AF catheter ablation in young adults (mean age: 31) to be 84%.[10] Even after successful ablation, patients should be anticoagulated with warfarin or novel oral anticoagulant for at least 2 months, with continuation based on patient's current stroke risk profile rather than the clinical outcome of the procedure.[11]

In patients with AF with concomitant CS, the underlying granulomatous disease should be treated. However, there is limited data to guide therapeutic management in CS alone.[12] In our patient, with both cardiac and systemic sarcoid disease, the mainstay of treatment are corticosteroids to suppress granuloma formation and inflammation, as it has been shown to improve clinical and radiological findings. The survival benefit of steroids is unknown. Although there is some data to suggest improvement in cardiac magnetic resonance imaging findings at 12 months with steroid doses greater than 20 mg per day, more data are needed to determine the ideal dose for treatment. Steroid sparing agents such as methotrexate and azathioprine may also be used for refractory cases, although there is no consensus regarding ideal treatment regimen among non-steroidal options.[13] CS should be considered in the appropriate patient population presenting with AF. These include patients without a readily identifiable cause for AF who remain at an elevated risk for developing Sarcoidosis. Individuals at higher risk include those who are modestly female predominant, have age < 55y, are African-American, lack a history of hypertension, dyslipidemia, obesity, diabetes, tobacco use, and evidence of structural heart disease to include coronary artery disease and valvular disease.[14,15,16] CS should always be on the differential for patients presenting with new complete AV block, heart failure, and/or ventricular tachycardia without an apparent cause. Similarly, all patients with extracardiac sarcoidosis should be evaluated for CS.[17]

Acknowledgments

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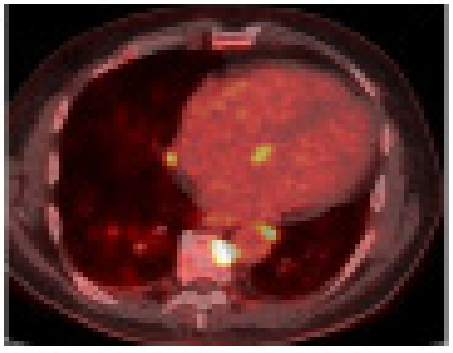

Figure 4: FDG-PET scan demonstrating hypermetabolic lesion within the base of the cardiac septum with maximal SUV 4.21.

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