PERIPARTUM CARDIOVASCULAR DISEASE MINI-FOCUS ISSUE

BEGINNER

CASE REPORT: CLINICAL CASE

Syncope in a Pregnant Woman

Infiltrative Cardiomyopathy and Presumed Cardiac Sarcoidosis

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ABSTRACT

Cardiac involvement in sarcoidosis is an uncommon manifestation of the disease process. Diagnosis and treatment during pregnancy can be challenging due to life-threatening ventricular arrhythmias. We describe a case of a 43-year-old, 21-week pregnant woman who presented after 2 episodes of syncope and was diagnosed with presumed cardiac sarcoidosis. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:101–6) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 43-year-old G3P0 21-week pregnant woman, with a history of hypertension and 2 first trimester pregnancy losses, presented to the emergency department after 2 episodes of syncope. The first episode occurred while the patient was driving, resulting in a

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LEARNING OBJECTIVES

- Cardiac sarcoidosis during pregnancy can have a life-threatening presentation.
- The use of cardiac magnetic resonance in early diagnosis of cardiac sarcoidosis enables early initiation of therapy and assists with risk stratification for primary prevention implantable cardioverter defibrillator placement.
- Cardiac involvement in patients with sarcoidosis (either clinical or subclinical) carries a worse prognosis compared with other manifestations of sarcoidosis.

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car accident. The second episode, which was witnessed, occurred at home and lasted for several minutes without tonic-clonic movements, incontinence, or post-ictal confusion. Each episode of syncope was preceded by dizziness but she did not complain of associated palpitations, chest pain, or shortness of breath. She denied any prior history of syncope, seizures, or cardiac abnormalities.

Her family history was significant for pacemaker implantation in her parents for unknown reasons. On initial examination, she was in no acute distress with skin abrasions on the right side of her face. She was afebrile, heart rate was 112 beats/min, regular rhythm, blood pressure 116/80 mm Hg, and respiratory rate 16 breaths/min. She was not orthostatic. Cardiovascular examination was unremarkable with no murmur, rubs, or gallops. No carotid bruits or elevated jugular venous pressure was noted. Respiratory examination was unremarkable, with normal breath sounds. Abdominal examination was significant for a gravid uterus. Her eye examination showed no evidence of

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conjunctivitis, uveitis, iris nodules, or scleral plaques. A thorough skin examination showed no evidence of erythema nodosum.

PAST MEDICAL HISTORY

Her past medical history included hypertension.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included vasovagal syncope, orthostatic syncope, syncope due to ventricular arrhythmias.

INVESTIGATIONS

Her hematological and basic metabolic profile were within normal limits. Her sodium level was 135 mEq/l, K 4.4 mEq/l, creatinine 0.8 mg/dl, hemoglobin 12.1 g/dl, platelet 257 K/µl, bilirubin test 0.4 mg/dl, alanine aminotransferase 30 U/l, aspartate aminotransferase 31 U/l, calcium 9.4 mg/dl, B-type natriuretic peptide 1226 pg/ml, and angiotensin-converting enzyme level 65 U/l (9 to 67 U/l). Troponin levels peaked at 0.11 ng/ml. Her initial electrocardiogram showed sinus tachycardia at a rate

of 113 beats/min, with no ST or T-wave changes and normal QT interval (Figure 1). Telemetry monitoring showed multiple short runs of nonsustained ventricular tachycardia (NSVT) (Figure 2) and 1 run of 30-s sustained ventricular tachycardia (VT). Chest radiograph was not performed because of pregnancy. A subsequent radiograph postpartum showed right paratracheal opacity suggestive of adenopathy. Transthoracic echocardiogram showed moderate to severe inferior wall hypokinesis and moderate mitral regurgitation with a left ventricular ejection fraction (LVEF) of 40%. On the basis of these findings, differential diagnosis included coronary artery disease versus coronary artery dissection. Coronary angiography was not performed at that time because of concerns for fetal radiation exposure. A submaximal exercise stress echocardiogram was performed that showed hypokinesis of the inferior-lateral and posterior wall extending from the base to the mid left ventricle at rest, with minimal improvement in regional contractility with stress, suggestive of myocardial scar. Subsequently, cardiovascular magnetic resonance (CMR) demonstrated a severely dilated left ventricle with LVEF of 41% and patchy intramyocardial and epicardial delayed enhancement suggestive of myocardial fibrosis or scar
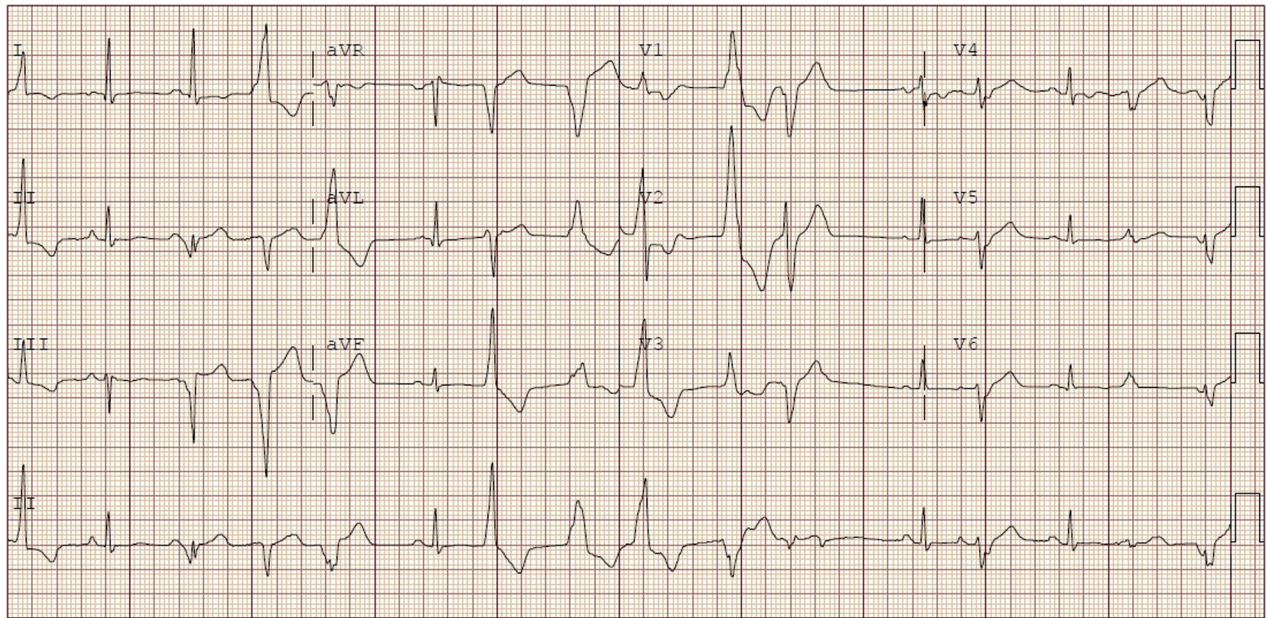
FIGURE 1 Initial Electrocardiogram
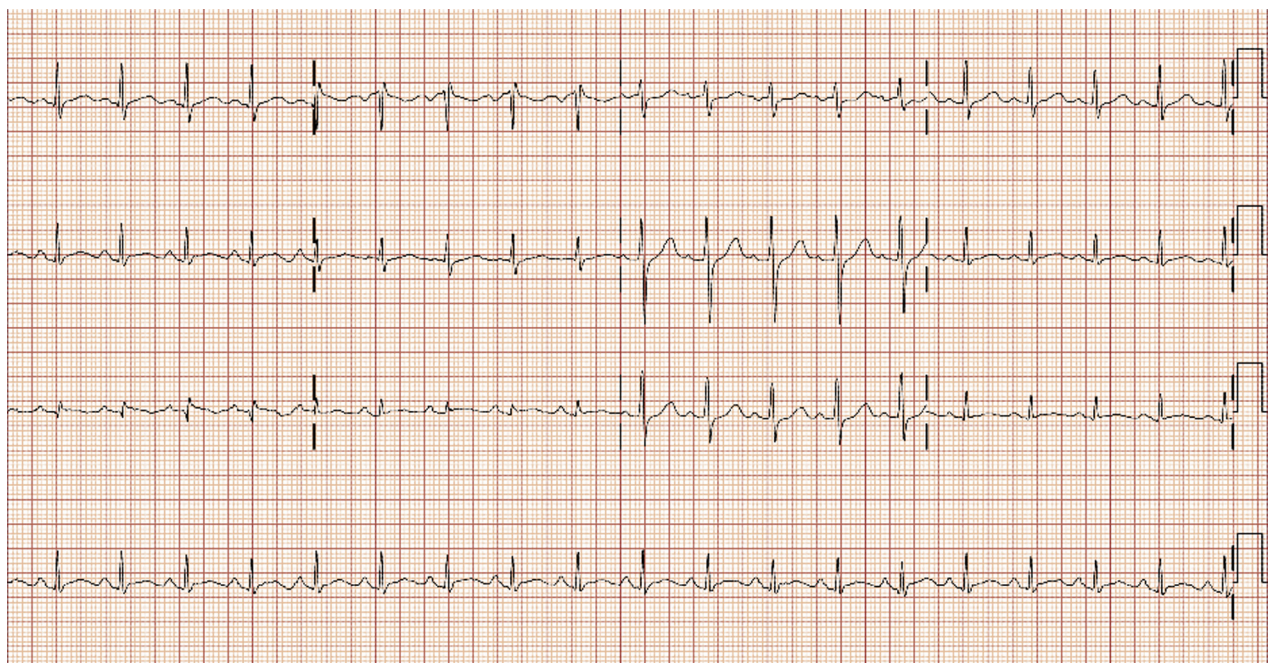
Initial electrocardiogram of the patient showing sinus tachycardia and no significant ST-T-wave changes.

FIGURE 2 Electrocardiogram From Second Admission

Electrocardiogram from second admission showing ventricular ectopy.

(**Figure 3**). In addition, there was increased T2-weighted signal in the basal inferolateral and apical lateral segment, consistent with myocardial edema. Significant perihilar adenopathy was also noted (**Figure 4**). Endomyocardial biopsy was deferred because of the risk of radiation exposure to the fetus with fluoroscopy and patient preference (denied having biopsy). Overall, these findings were highly suspicious of cardiac sarcoidosis manifesting as recurrent syncope from ventricular arrhythmias.

MANAGEMENT

The patient was started on prednisone 60 mg daily with slow taper and metoprolol tartrate 50 mg 3 times a day with no further episodes of sustained ventricular tachycardia noted during the hospitalization. In addition, a single-chamber implantable cardioverter defibrillator (ICD) was implanted before hospital discharge.

FOLLOW-UP

Six weeks after the index admission, she was admitted with shortness of breath. She was diuresed with intravenous furosemide for acute decompensated heart failure, noticed significant improvement, and was discharged on day 3. Four weeks thereafter, she was admitted to the obstetrics intensive care unit for recurrent heart failure symptoms and treated with diuretics. Repeat echocardiogram showed LVEF was 35%. Her ICD interrogation demonstrated episodes of VT treated with antitachycardia pacing. Four days later, she experienced her first appropriate ICD shock, and was started on sotalol. She was diagnosed with oligohydramnios. Because of obstetric complications, a cesarean delivery was performed at 33 weeks+1 day gestational age (day 11 of admission). Her infant was initially admitted to the neonatal intensive care unit, but was discharged after 8 days (day 19 of admission). Her post-operative course was complicated by episodes of NSVT and VT with 3 ICD shocks occurring within a 90-min period and worsening heart failure. Sotalol was discontinued and amiodarone infusion was started, with no further episodes of VT or NSVT. She was treated with intravenous diuretics. She remained clinically stable and was discharged home 8 days postpartum. Her discharge medications included prednisone taper, sotalol 80 mg twice a day, furosemide 40 mg daily, and metoprolol succinate 50 mg daily. Lisinopril was started as an outpatient. She has not had any further episodes of VT in almost 2 years. Subsequent coronary angiogram demonstrated normal coronaries. A fluorodeoxyglucose positron

FIGURE 3   Cardiovascular Magnetic Resonance Images
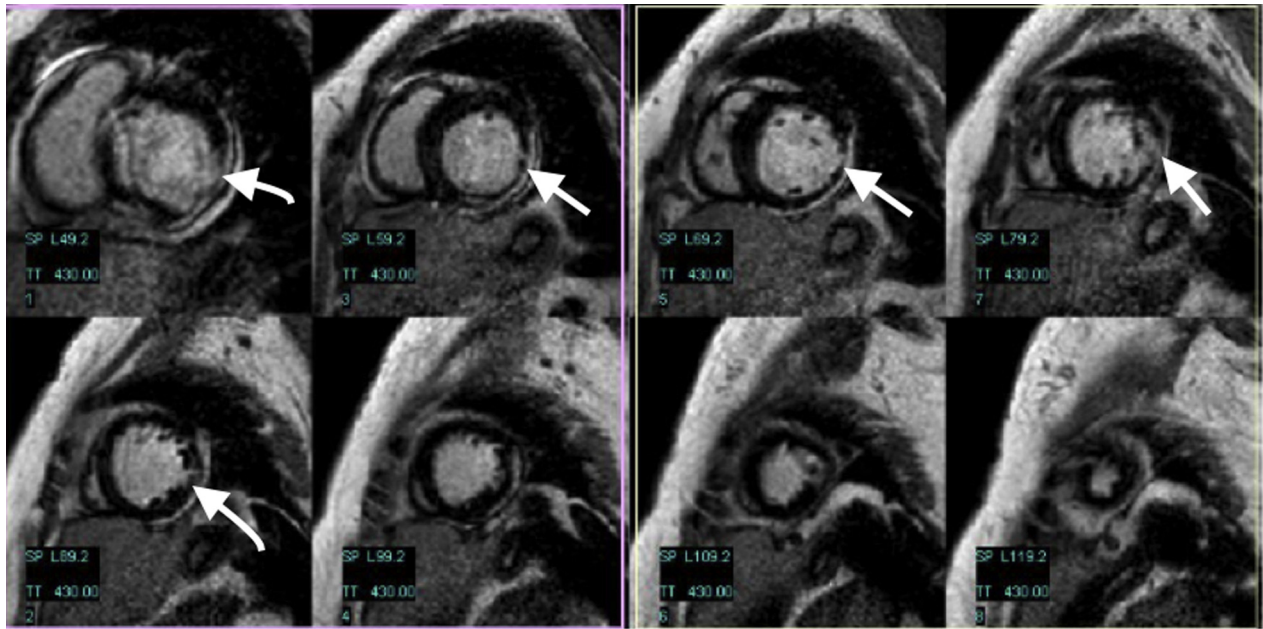
Cardiovascular magnetic resonance images depicting patchy intramyocardial and epicardial delayed enhancement suggestive of myocardial fibrosis or scar. **Arrows** indicate the hyperenhancing myocardium and epicardium in a patchy distribution.

emission tomography (FDG PET) was not performed because of its nonavailability at our center at the time of her admission. Although this test is now available, the patient had relocated to a different hospital.
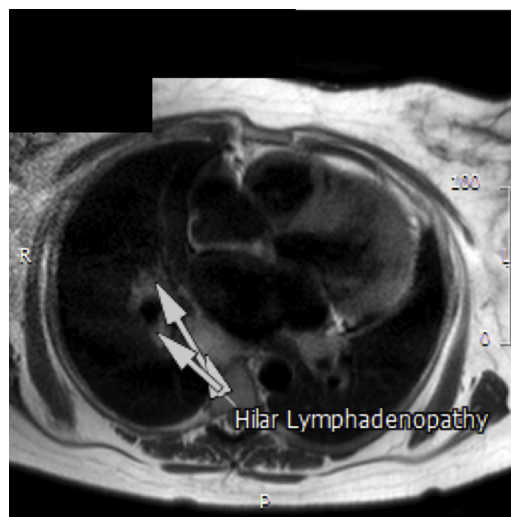
FIGURE 4   Cardiovascular Magnetic Resonance Images

Cardiovascular magnetic resonance images depicting hilar lymphadenopathy.

Presently, she remains clinically stable with New York Heart Association functional class II symptoms, with most recent LVEF of 35%.

DISCUSSION

Sarcoidosis is a systemic granulomatous disease that has a wide variety of manifestations ranging from an asymptomatic abnormal chest radiograph to progressive multiorgan failure. Cardiac sarcoidosis is an uncommon manifestation of the disease process and is clinically apparent in only approximately 2% to 7% of patients [1], but found in 20% to 25% of patients with known sarcoidosis on postmortem examination [2]. Cardiac involvement portends a much worse prognosis than other manifestations of sarcoidosis because of the associated arrhythmias, sudden cardiac death, and cardiomyopathy. It can also manifest as a myocardial infarction due to coronary artery infiltration with sarcoid tissue, granulomatous valvular involvement, clinical pericarditis, and intracardiac masses resembling atrial myxoma.

Cardiac sarcoidosis during pregnancy carries a high risk of potentially lethal outcome for both the mother and infant. There have been only a handful of cases reporting clinical manifestations of cardiac

sarcoidosis during pregnancy. This case highlights the importance of evaluation of syncope in young women with no prior cardiac risk factors, as it could represent a life-threatening ventricular arrhythmia due to an infiltrative myocardial disease.

A case series from 1957 following 10 cardiac patients with sarcoidosis through 16 pregnancies suggested an ameliorating effect on sarcoidosis during the prenatal period. It was hypothesized that an increased production of corticoids by the adrenal glands during gestation was responsible for this effect (3). Two case reports suggested postnatal cardiac acceleration of sarcoidosis (4,5). On the contrary, 2 other case reports suggested a considerable risk of a lethal cardiac event during the final trimester among patients with cardiac sarcoidosis (6,7). Our patient presented with her first syncopal episode during mid pregnancy.

Various imaging modalities are available for the evaluation of cardiac sarcoidosis. Echocardiographic findings are often nonspecific; however, the ventricular septum or the left ventricular free wall may appear hyperechogenic because of granulomatous involvement and scar formation. CMR is an excellent imaging modality in the evaluation of patients with suspected cardiac sarcoidosis. It enables fast, accurate, high-resolution, and noninvasive diagnosis of subclinical or clinical cardiac sarcoidosis. CMR detects edema from inflammation using T2-weighted imaging; tissue characterization with T1-weighted imaging; and late gadolinium enhancement for the evaluation of scar, edema, and fibrosis. The late gadolinium enhancement pattern often seen in cardiac sarcoidosis is a patchy, multifocal distribution similar to that seen in our patient. The use of gadolinium-based contrast enhancement during pregnancy is controversial. Gadolinium is water-soluble and can cross the placenta into the fetal circulation and amniotic fluid. Hence, gadolinium use is recommended to be limited to situations in which the benefits clearly outweigh the possible risks (8).

^{18}F-FDG PET has a high sensitivity for detection of active cardiac sarcoidosis. As per a meta-analysis of 164 patients with systemic sarcoidosis, FDG PET had a sensitivity and specificity of 89% and 78%, respectively, as an initial diagnostic tool for cardiac sarcoidosis (9). However, endomyocardial biopsy has a sensitivity of <25%, because of the patchy distribution of granulomas (10). When endomyocardial biopsy cannot be performed, the Japanese Society of Nuclear Cardiology 2017 (11) recommends isolated cardiac sarcoidosis to be diagnosed clinically only when FDG PET reveals abnormally high tracer accumulation in the heart and at least 3 other

criteria of the following major criteria (a) to (e) are satisfied.

a. High-grade atrioventricular block (including complete atrioventricular block) or fatal ventricular arrhythmia (e.g., sustained ventricular tachycardia and ventricular fibrillation)
b. Basal thinning of the ventricular septum or abnormal ventricular wall anatomy (ventricular aneurysm, thinning of the middle or upper ventricular septum, regional ventricular wall thickening)
c. Left ventricular contractile dysfunction (left ventricular ejection fraction <50%)
d. 67Ga citrate scintigraphy or ^{18}F-FDG PET reveals abnormally high tracer accumulation in the heart
e. Gadolinium-enhanced magnetic resonance image reveals delayed contrast enhancement of the myocardium

Because of the nonavailability of FDG PET scan at our center, this test could not be performed at the time of presentation. Our case satisfies 3 major criteria (sustained VT, nonischemic scar on magnetic resonance imaging, and reduced LV function) with no extra cardiac findings of sarcoidosis, thereby making it highly suspicious of cardiac sarcoidosis.

Certain considerations must be taken into account during the evaluation and treatment of pregnant women, including minimizing fetal radiation exposure, selection of medications with the least teratogenic risk, and advising against breastfeeding if medications with high breastmilk excretion, such as sotalol, are used. In addition, there can be concerns with ICD during pregnancy. A study by Natale et al. (12) suggested that pregnancy does not increase the risk of major ICD-related complications or result in high number of ICD discharges. A smaller study reported similar findings, but described 1 miscarriage that may have been induced by an ICD shock (13). Despite the use of steroids for more than 5 decades, there remains no proof of mortality benefit from corticosteroids in patients with cardiac sarcoidosis (14). A systematic review of 10 papers showed limitation of data to draw conclusions about LV function recovery, ventricular arrhythmia burden, and mortality with corticosteroids. The most convincing data were related to AV conduction recovery, pointing toward benefits of corticosteroids (15).

The diagnosis of cardiac sarcoidosis is often delayed or missed altogether (12). Hence, it is important for clinicians to maintain a high index of clinical suspicion in the appropriate clinical scenario. There remains much to be understood about this disease and its specific management in childbearing women.

CONCLUSIONS

Cardiac sarcoidosis has a lethal risk of ventricular arrhythmias, which can affect the mother and fetus. Diagnosis and management of cardiac sarcoidosis in a pregnant patient, and understanding the risks of various diagnostic tests and medications to the fetus, is of high importance to a cardiologist. Coordination of care between the cardiologist and high-risk obstetrician is necessary for the best outcome for the mother and fetus.

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