Two cases of cardiac sarcoidosis in pregnant women with supraventricular arrhythmia

Ebru Ertekin, Sulaiman Moosa, Jolien W Roos-Hesselink, Karen Sliwa

Abstract

We present two cases of cardiac sarcoidosis whose first presentation was in pregnancy. All findings confirmed the diagnosis of sarcoidosis with cardiac involvement in both patients.

The first patient, a 37-year-old, presented with dizziness and atrial fibrillation at 16 weeks’ gestation. Echocardiography revealed thickened interventricular septum with a speckled pattern. Cardiac MRI after delivery showed myocardial oedema/inflammation corresponding with the same regions with early enhancement and epicardial delayed enhancement in the basal to mid-inferoseptal and basal anterior left ventricular myocardial segments. Transbronchial biopsy revealed histology of scanty fragments of inflamed bronchial mucosa.

The second patient, a 31-year-old, was 17 weeks pregnant when she presented with daily palpitations and shortness of breath. She had prolonged episodes of supraventricular tachycardia. Echocardiography revealed a speckled septal and right ventricular wall pattern. Cardiac MRI after delivery showed basal and mid-ventricular mesocardial and epicardial enhancement, most compatible with sarcoidosis.

Keywords: cardiac sarcoidosis, pregnancy, arrhythmia

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Case 1: patient with atrial fibrillation

A 37-year-old primigravida presented to our cardiac clinic at 16 weeks’ gestation with a history of dizziness and atrial fibrillation (AF) without overt heart disease. She took no regular medication, did not smoke or drink alcohol, and had no diabetes mellitus or hypertension. Her medical history included AF diagnosed six years previously, and polycystic ovarian syndrome. There was no cardiac disease or sudden death in her family.

Physical examination revealed an irregular tachycardia of 130 beats per minute (bpm), blood pressure of 124/72 mmHg and no murmur. The electrocardiogram showed ventricular ectopics, intermittent AF and irregular P-wave morphology (Fig. 1). Echocardiography revealed a normal heart with an ejection fraction of 60%. She was prescribed atenolol 25 mg daily and aspirin 75 mg daily due to the risk of a cerebrovascular accident.

Echocardiography was repeated one month later and showed a thickened speckled septum and posterior wall with good left ventricular function (left ventricular ejection fraction 61%, left atrial diameter 34 mm, aortic diameter 28 mm, left ventricular end-diastolic diameter 53 mm). These findings were suspicious for an infiltrative disease, and cardiac sarcoidosis was considered to be the most probable diagnosis. The obstetric–cardiac team made a decision at that time to perform a full work-up for cardiac sarcoidosis post delivery.

She delivered under spinal and general anaesthesia at 38 weeks of gestation by caesarean section due to breech position. She gave birth to a healthy female baby of 2 780 g. On discharge she was prescribed aspirin 80 mg, eltroxin 100 μg and atenolol 50 mg. Three months post partum she had mild to moderate shortness of breath on effort, her blood pressure was 110/78 mmHg and her heart rate was 70–80 bpm while she was in AF.

MRI was performed four months after delivery and demonstrated the following findings: preserved biventricular systolic function and volumes, myocardial oedema or inflammation corresponding to the same regions with early enhancement and epicardial delayed enhancement in the basal to mid-inferoseptal and basal anterior left ventricular myocardial segments (Fig. 2). With these MRI findings, cardiac sarcoidosis was considered to be the most probable diagnosis. However, myocarditis was a less likely differential consideration.

CT chest demonstrated multiple bilateral pulmonary nodules predominantly in a perilymphatic distribution. Transbronchial biopsy confirmed the diagnosis of sarcoidosis. Microscopic examination showed scanty fragments of inflamed bronchial mucosa. Granulomas and viral inclusions were not seen. Additionally, serum angiotensin converting enzyme level was 23.8 U/l (normal range: 9–67 U/l).

Steroid therapy was started after the diagnosis of sarcoidosis by transbronchial biopsy. At the follow-up visit 10 months after delivery, her symptoms had improved and she was on atenolol 25 mg daily, prednisone 40 mg daily, with calcium supplementation, vitamin D, isoniazid 200 mg daily, with calcium supplementation, vitamin D, isoniazid 200 mg daily, with calcium supplementation, vitamin D, isoniazid 200 mg daily (antibiotics) and eltroxin 100 mcg daily.

All findings confirmed the diagnosis of sarcoidosis. As there was cardiac involvement, steroid therapy was prescribed. Steroid therapy was successful and improved her symptoms.

Case 2: patient with supraventricular tachycardia

The second patient we saw was a 31-year-old woman who was 17 weeks pregnant with her third pregnancy. She had prolonged...
episodes of supraventricular tachycardia of unknown origin with almost daily palpitations on minimal effort. At that time she was diagnosed with NYHA functional class II failure off medication (she was not on any medication at presentation). Her mother had sarcoidosis. Her obstetric history included two threatened miscarriages and two viable births, both vaginal delivery.

Physical examination was normal and her heart rate was 78 bpm. Holter monitoring did not identify ventricular tachycardia. Echocardiography revealed a speckled pattern at the basal segment of the septum and right ventricular wall, suspicious for an infiltrative disease. Left ventricular function was good (LVEF 53%) and no valve dysfunction was observed. In view of the clinical history, those features were highly suggestive of sarcoidosis with cardiac involvement. Verapamil 40 mg daily was started and MRI investigation was booked after pregnancy for further investigation.

One month later she presented with increased palpitations on verapamil. She had previously responded to verapamil but did not respond to atenolol or propanolol. The palpitations started without any obvious trigger and lasted one hour. Haemoglobin was 11.7 g/dl (normal range, non-pregnant woman: 12.0–15.5 g/dl) and thyroid stimulating hormone was 1.29 mU/l (normal range: 0.34–4.25 mU/l). She had normal electrocardiography. Verapamil dosage was increased to 80 mg because of the increased complaints of palpitations.

At 30 weeks of pregnancy, she presented at the clinic with daily palpitations and shortness of breath. The palpitations did not improve on verapamil. Her blood pressure was 108/58 mmHg, she had a regular heart rate of 104 bpm (sinus rhythm) and was not in congestive heart failure. At that time verapamil was stopped due to its possible side effects on the foetus.

She delivered at 36 weeks of gestation by emergency caesarean section due to foetal distress. She gave birth to a healthy male baby of 2.760 g. Echocardiography was repeated three months postpartum and demonstrated a speckled pattern, diastolic left ventricular dysfunction with right ventricular function of 50% and left ventricular function of 68%.

MRI was performed four months after delivery and showed a mildly enlarged left ventricle, reduced LVEF (< 50%) but no regional wall motion abnormality. The delayed gadolinium sequences showed basal and mid-ventricular mesocardial and epicardial enhancement (Fig. 3). The radiologist concluded that these features could be consistent with sarcoid-related myocardial scarring. The patient declined to have a transbronchial biopsy.

After starting steroid therapy, there was a marked improvement in her symptoms, including shortness of breath. The cardiac MRI was repeated and showed a marked increase in LVEF (from < 50% before starting steroid therapy to 70% after starting the therapy).

Discussion

Our cases demonstrate that cardiac sarcoidosis may manifest for the first time during pregnancy. Reports on cardiac sarcoidosis related to pregnancy are rare. Cardiac sarcoidosis, a potentially
life-threatening condition, is probably an underdiagnosed disease, as cardiac involvement is clinically apparent in only about 5% of all patients, while cardiac granulomas are found in about 25% of patients with sarcoidosis who are examined at autopsy. Cardiac sarcoidosis may occur without apparent disease in other organs. It has been reported to occur most frequently in middle-aged or older women in Japan, although its incidence in Western countries was shown to have no gender difference and to be higher in the younger generation.

**Sarcoidosis in pregnancy**

The incidence of sarcoidosis in pregnancy is estimated to be 0.02 to 0.05%. Maternal sarcoid symptoms may improve during pregnancy but may be more severe after delivery. The changes in the severity of sarcoidosis during pregnancy are possibly due to increased serum steroid levels, which rapidly decrease after delivery. On the other hand, sarcoidosis can progress during pregnancy, or as our two cases show, manifest for the first time during pregnancy. Sudden death secondary to ventricular
tachyarrhythmias or conduction abnormalities accounts for 25–65% of cardiac sarcoidosis-related deaths. Complicated sarcoidosis has been associated with postpartum maternal death. Our two patients delivered by caesarean section and had no further complications.

Diagnostic tools

There are no currently accepted international guidelines for the diagnosis of cardiac sarcoidosis. The diagnosis of cardiac sarcoidosis can be difficult, as it can be asymptomatic or non-specific. Cardiac sarcoidosis is manifested clinically as a cardiomyopathy with loss of ventricular function, or tachyarrhythmias and bradyarrhythmias (palpitations, syncope and sudden death).

Both our patients presented with atrial arrhythmias. The first patient (case 1) had atrial fibrillation (more frequent and faster heart rate than before pregnancy) and the second patient (case 2) had supraventricular tachycardia. The most common location for granulomas and scars is the left ventricular free wall, followed by the interventricular septum, often with involvement of the conducting system.

Endomyocardial biopsy sample for pathological research that is positive is hard to obtain and has a low diagnostic yield (<20%) because cardiac involvement tends to be patchy, and granulomas are more likely to be located in the left ventricle and basal part of the ventricular septum. A pathological diagnosis of cardiac sarcoidosis was not performed in our two patients for these reasons. Instead, we chose to perform a less-invasive cardiac MRI. Cardiac MRI with gadolinium enhancement and a 18F-FDG PET scan are valuable aids in the diagnosis of cardiac sarcoidosis.

Since sudden death may be the first sign of cardiac sarcoidosis, electrophysiological studies to detect any conduction delays or increased risk of sustained arrhythmias should be strongly considered in all patients with suspected cardiac sarcoidosis. Most authorities recommend placement of an electronic pacemaker for complete heart block, and an automatic implantable cardioverter–defibrillator for ventricular fibrillation or tachycardia and markedly reduced left ventricular ejection fraction.

Sarcoidal granulomas produce angiotensin converting enzyme (ACE), and ACE levels are elevated in 60% of patients with sarcoidosis. However, a serum ACE level is an insensitive and non-specific diagnostic test and a poor therapeutic guide. A recently published expert consensus statement provides guidance for clinicians on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. Unfortunately they do not have recommendations for pregnant patients as there is limited evidence for this specific patient population.

Treatment

The initial treatment of sarcoidosis is often prednisone 20–40 mg daily for six to 12 weeks, with dose reduction thereafter. As cardiac sarcoidosis is a potentially life-threatening situation, the initial dose is 1 mg/kg daily. Although a minimum of 12 months of maintenance therapy is often advised to prevent relapse, several investigators believe that treatment should be stopped as early as six months after initiation.

Oral steroid therapy is usually performed to treat atrioventricular block due to cardiac sarcoidosis. However, its efficacy against cardiac sarcoidosis in general is only about 50%. Although cardiac sarcoidosis is a known inflammatory disease and despite more than 50 years of the use of corticosteroids for treatment, there is no proof of survival benefit from this treatment.

As specific guidelines on cardiac sarcoidosis in pregnant women do not exist, in case of occurring relevant bradycardia or tachycardia, pacemakers and ICDs may be considered. Since there is no evidence of giving immunosuppressive therapy for pregnant women, we suggest that efforts should be made to

Fig. 3. Cardiac MRI images of case 2. Basal short-axis left ventricular magnitude (A), and PSIR (B) delayed enhancement images, demonstrating mesocardial (white arrow in A) and epicardial enhancement (white arrow in B).
prevent (further) pregnancy in women with proven or suspected cardiac sarcoidosis.

Conclusion
Our two cases demonstrate that cardiac sarcoidosis may manifest for the first time during pregnancy. Even though it is rare, especially during pregnancy, it should be considered when patients present with shortness of breath (on minimal effort) and palpitations or arrhythmias. Early institution of steroid therapy is warranted when this diagnosis is suspected due to the increased risk for rhythm or conduction system disorders and sudden death.

References