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CASE REPORT
Heart failure

Multi-modal treatment in a pregnant woman with untreated cardiac sarcoidosis complicated by cardiac dysfunction and ventricular arrhythmias: a case report and literature review

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Background The treatment of cardiac sarcoidosis during pregnancy is inherently challenging owing to its impact on the foetus.

Case summary We report a case of a 30-year-old pregnant woman with untreated cardiac sarcoidosis. One year prior to admission, she underwent permanent pacemaker implantation for complete atrioventricular block. Left ventricular ejection fraction (EF) showed a declining trend, and ventricular tachycardia (VT) was documented. Following an extensive evaluation, the patient was diagnosed with active cardiac sarcoidosis, and the pregnancy was detected at the same time. Considering the high risk of mortality and cardiovascular complications in pregnant patients with decreased EF and VT, we meticulously discussed the optimal timing of multi-modal treatment, including bisoprolol, eplerenone, sotalol, and prednisolone and cardiac resynchronization therapy with a defibrillator, and its effect on the foetus. These interventions improved the EF to 49%, and the baby was successfully delivered without adverse events or neonatal complications developing. At 8 months' post-partum, the mother and the baby were doing well, and the EF was 45%.

Discussion Cardiac sarcoidosis can lead to adverse outcomes for both the mother and the foetus. However, with multi-modal treatment individually optimized and implemented by a multi-disciplinary team of specialists in each field, even pregnant women with untreated cardiac sarcoidosis who present with reduced EF and VT can achieve safe childbirth.

Keywords Cardiac sarcoidosis • Pregnancy • Steroid • Cardiac resynchronization therapy • Case report

ESC curriculum 6.2 Heart failure with reduced ejection fraction • 9.8 Pregnancy with cardiac symptoms or disease • 5.11 Cardiac resynchronization therapy devices

Learning points

- Some pregnant women with cardiac sarcoidosis experience cardiovascular adverse events, including sudden death.
- In pregnant women, the potential impact of treatment on the foetus and the optimal timing for providing interventions must be discussed.
- Adequate risk assessment and timely interventions contribute to favourable maternal and foetal outcomes.

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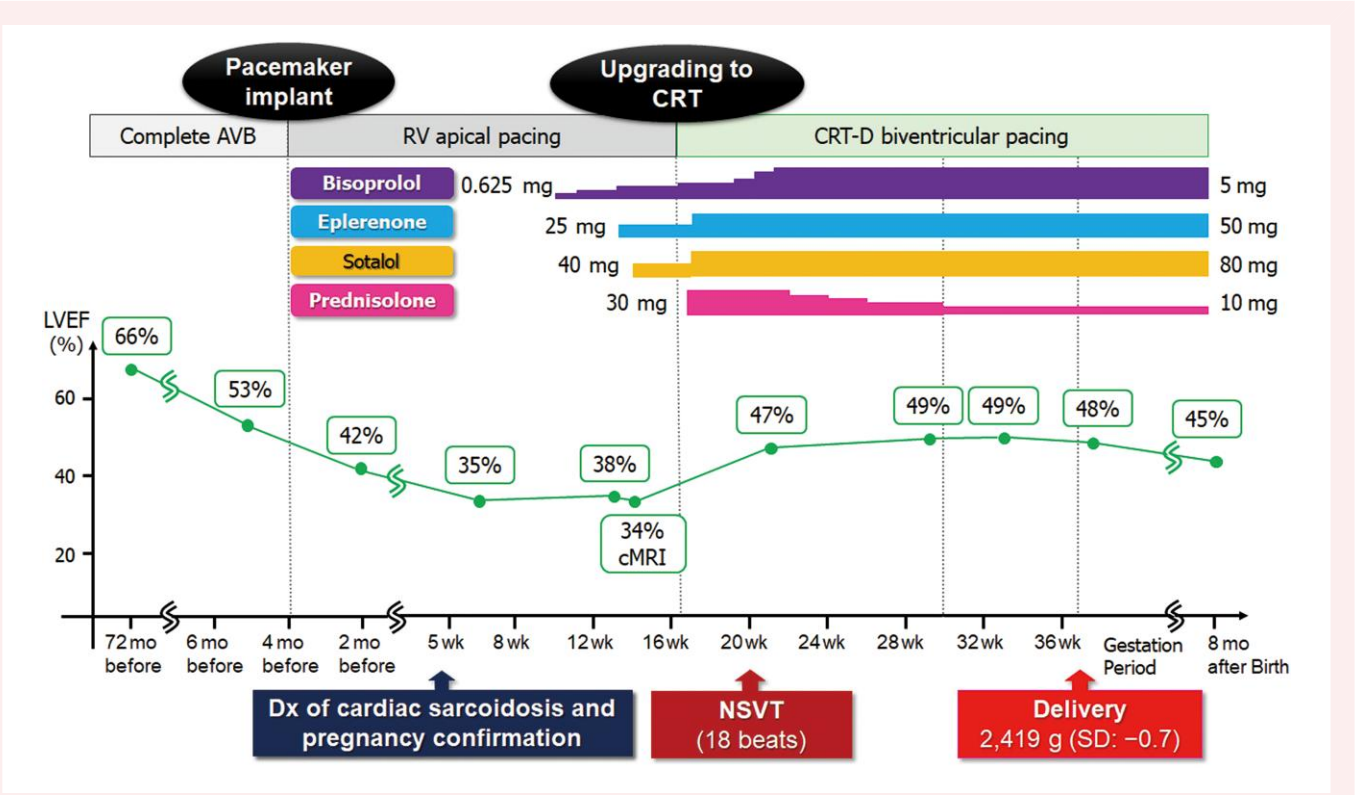
Introduction

Sarcoidosis is a systemic granulomatous disease that primarily affects adults aged <40 years, with a peak incidence in the 20s, and is more common in women.[1] Cases involving the heart can be severe and life-threatening. As cardiac sarcoidosis is rarely diagnosed during pregnancy, its course and prognosis remain unknown. According to several case reports of pregnant women with cardiac sarcoidosis,[2–7] all patients received corticosteroid therapy and underwent caesarean section, while some experienced cardiovascular adverse events, including sudden death. Hence, several factors, including the potential impact of treatment on the foetus as well as the patients themselves, should be considered in the management of pregnant patients with cardiac sarcoidosis.

Herein, we report a case of a 30-year-old pregnant woman with untreated cardiac sarcoidosis.

Summary figure



Case presentation

A review of the patient's medical history revealed that she experienced a complete atrioventricular block at the age of 24 years. Transthoracic echocardiography showed a left ventricular ejection fraction (EF) of 66% (see Supplementary material online, *Video S1*), and no significant abnormalities were found on ^{67}gallium scintigraphy, cardiac magnetic resonance imaging (MRI), or endomyocardial biopsy. Therefore, cardiac sarcoidosis was not diagnosed at that time.

The patient experienced worsening shortness of breath and then underwent permanent pacemaker implantation at the age of 29 to manage bradycardia caused by a persistent complete atrioventricular block. Subsequent evaluations revealed a gradual decrease in the EF to 42%. Additionally, ^{18}F-fluorodeoxyglucose positron emission tomography showed abnormal uptake, with a maximum standardized uptake value of 5.2 (*Figure 1A*), suggesting active cardiac sarcoidosis. When corticosteroid therapy was being considered, the patient was immediately referred to our hospital due to the discovery of her pregnancy.

Upon examination, she had a blood pressure of 122/62 mmHg, a pulse rate of 68/min, and an arterial oxygen saturation of 99% on room air. Heart murmurs or rales were not audible. Electrocardiography (ECG) revealed right ventricular apical pacing with a QRS duration of 146 ms (*Figure 2A*). The patient had no history of comorbidities and was 5 weeks' pregnant at the time of examination. Holter ECG monitoring revealed non-sustained ventricular tachycardia (VT) consisting of six consecutive ventricular beats accelerating from 150 to 190 b.p.m. The EF decreased to 35%, and a ventricular aneurysm was found at the apex of the right ventricle (*Figure 1B*; Supplementary material online, *Video S2*). Sarcoidosis was not observed in the skin, lungs, lymph nodes, or eyes. Based on these findings, isolated cardiac sarcoidosis was diagnosed.

Considering the patient's pregnancy, a team consisting of obstetricians, arrhythmia specialists, and heart failure specialists carefully took into account the potential impact of treatment on the foetus and discussed the optimal timing for providing interventions. Our treatment plan included the administration of heart failure medications; upgrading an existing pacemaker to cardiac resynchronization therapy with defibrillator (CRT-D), which required the use of radiation and was not available until after 15 weeks' gestation; initiating corticosteroid therapy to prevent further progression of myocardial damage;[8] and reducing the corticosteroid dose to <15 mg/day of prednisolone at the time of delivery. We administered bisoprolol at an initial dose of 0.625 mg/day

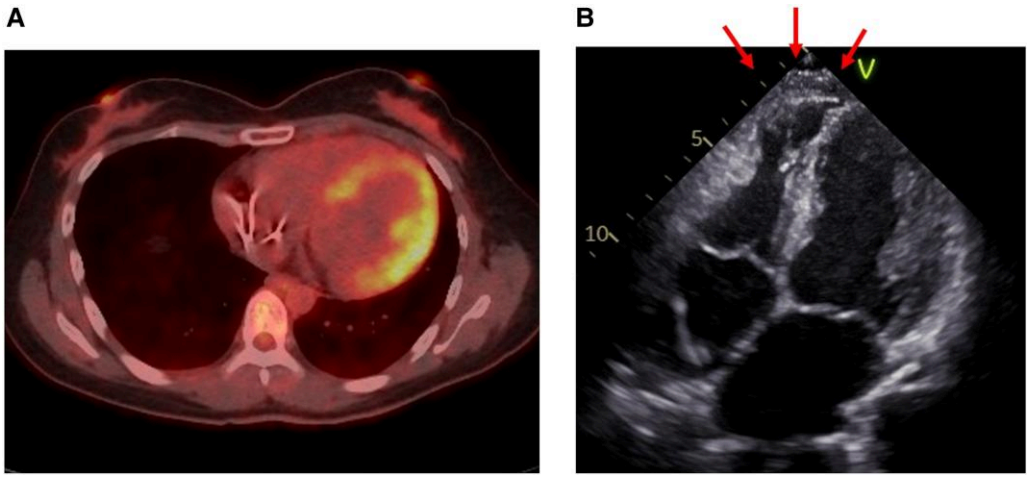


Figure 1 ^{18}F-fluorodeoxyglucose positron emission tomography and transthoracic echocardiography. (*A*) ^{18}F-fluorodeoxyglucose positron emission tomography showed abnormal uptake and (*B*) the right ventricular apex showed with the ventricular aneurysm.

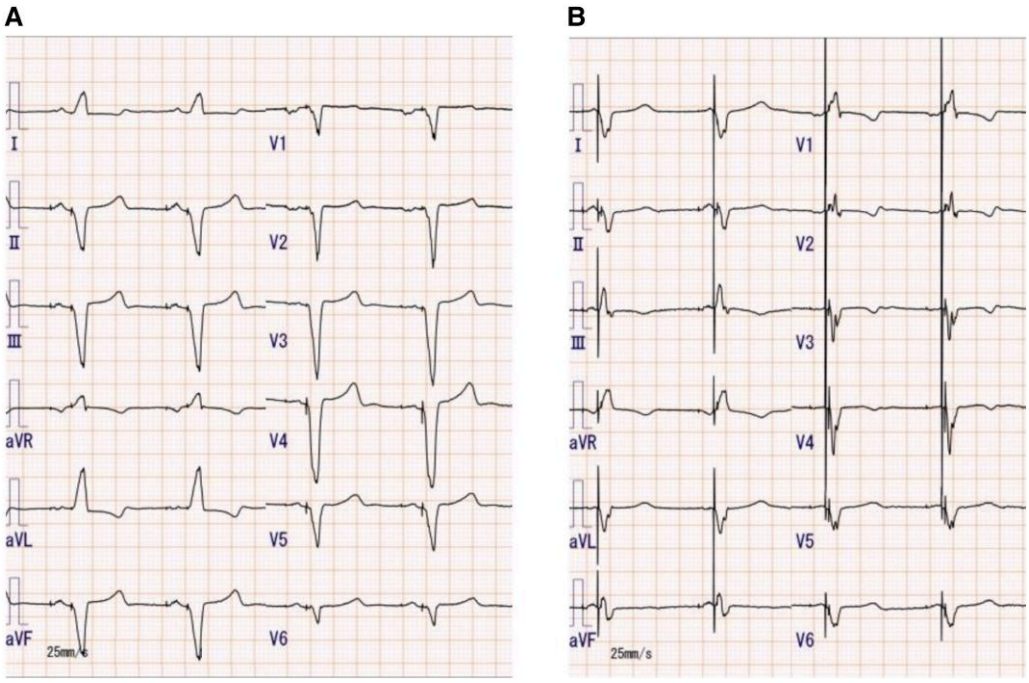


Figure 2 Electrocardiography before and after the upgrade to cardiac resynchronization therapy with defibrillator. (*A*) The electrocardiography showed right ventricular apical pacing with a QRS duration of 146 ms. (*B*) After initiating cardiac resynchronization therapy biventricular pacing, the electrocardiography showed a QRS of 137 ms.

and gradually increased the dose. Eplerenone 25 mg/day and sotalol 40 mg/day were then added. The EF evaluated by MRI was 34%. Gadolinium contrast media contraindicated during pregnancy was not administered. At 16 weeks of gestation, the implantation of a CRT device was performed. The radiation dose delivered during this procedure was 75 mGy with an estimated foetal exposure dose of 3 mGy. On the ECG, the QRS duration was shortened to 137 ms (*Figure 2B*). Following the initiation of CRT with biventricular pacing, bisoprolol was up-titrated to 2.5 mg/day, eplerenone was increased to 50 mg/day, and sotalol was increased to 80 mg/day. After confirming wound healing, corticosteroid therapy was started with an initial dose of 30 mg/day of prednisolone at 18 weeks of gestation. During the early phase of this treatment initiation, one episode of non-sustained VT occurred in 18 consecutive beats. Bisoprolol was further up-titrated to 5 mg/day.

Table 1 Case reports on cardiac sarcoidosis and pregnancy

Case	References	Age	Initial symptoms	EF	Timing of diagnosis	Treatment	Delivery (gestation period)	Maternal outcome	Fatal outcome
#1	Euliano *et al.*[2]	33	Heart failure	30%	Pre-pregnancy	Corticosteroid	Caesarean (36 weeks)	Good	Good
#2	Wallmuller *et al.*[3]	35	Cardiac arrest	N/A	Pre-pregnancy	CPR	Caesarean (32 weeks)	Death	Death
#3	Seballos *et al.*[4]	27	Heart failure	32%	Post-partum	Corticosteroid and ACEI	Caesarean (36 weeks)	Death	Good
#4	Ertekin *et al.*[5]	37	AF	60%	Post-partum	Corticosteroid and β-blocker	Caesarean (34 weeks)	Good	Good
#5	Ertekin *et al.*[5]	31	SVT	53%	Post-partum	Corticosteroid	Caesarean (32 weeks)	Good	Good
#6	Sugishita *et al.*[6]	30	CAVB	Normal	Post-partum	Corticosteroid and temporary PM	Caesarean (36 weeks)	Good	Good
#7	Agrawal *et al.*[7]	43	VT	40%	During pregnancy	Corticosteroid, β-blocker, ICD, and sotalol	Caesarean (33 weeks)	Good	Good

ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; CAVB, complete atrioventricular block; CPR, cardiopulmonary resuscitation; EF, left ventricular ejection fraction; ICD, implantable cardioverter-defibrillator; PM, pacemaker; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

Prednisolone was then gradually tapered down to 15 mg/day by 26 weeks of gestation. At 29 weeks, the EF improved to 49%. Prednisolone was then further reduced to 10 mg/day at 30 weeks of gestation. The patient delivered a baby through vaginal birth following labour induction at 37 weeks + 1 day gestation, without signs of worsening heart failure or life-threatening arrhythmias. The newborn's birth weight was 2419 g (SD: −0.7), and the Apgar scores at 1, 5, and 10 min were 8, 9, and 10, respectively. No congenital anomalies of concern were identified, both mother and infant were doing well at 8 months' post-partum, and the EF was 45% (see Supplementary material online, *Video S3*).

Discussion

Pregnancies complicated by cardiac dysfunction resulting from sarcoidosis are presumed to be at an increased risk of mortality and severe cardiovascular complications;[9,10] however, only a small number of related case reports have been published so far. *Table 1* summarizes the cases of seven patients whose pregnancies were complicated by cardiac sarcoidosis reported to date. Sarcoidosis was diagnosed before pregnancy in two patients, during pregnancy in one patient, and after delivery in four patients. All patients gave birth via caesarean section at 32–36 weeks of gestation. The EF reported in these studies varied from 30% to the normal range. Patient #3 was a 27-year-old woman[4] with an EF of 32% who developed congestive heart failure 5 days' post-partum, experienced cardiac arrest, and died 16 months later. Patient #2 was a 35-year-old pregnant woman (32 weeks of gestation)[3] who experienced cardiac arrest at home, and the foetus died. Patient #7, a 43-year-old woman[7] with an EF of 40% and VT, was treated with sotalol and underwent implantable cardioverter-defibrillator placement. The mother and baby had good prognoses, highlighting the importance of anti-arrhythmic therapy.

Pregnant patients with an EF of <45% are generally considered to have a higher risk for complications.[10] The incidence of congestive heart failure is reportedly the highest in 23–30 weeks of gestation when the circulating blood volume increases.[11] Considering this aspect, we started the medical treatment for heart failure immediately. The recurrence rate of tachyarrhythmia during pregnancy is ∼44%.[12] In addition, the incidence of ventricular arrhythmia is known to increase temporarily when corticosteroid administration is initiated.[13] In fact, 18 consecutive ventricular beats were recorded in the fourth week of prednisolone treatment (30 mg/day). Hence, sotalol was used for treating VT, as in Patient #7. Beta-blockers, mineralocorticoid receptor antagonists, and sotalol are safe for use during pregnancy. The use of corticosteroids increases the risk of cleft lip and palate during the first trimester of pregnancy[14] as well as the risk of infection and delayed wound healing.[15] We thought that CRT-D device implantation is preferred after 16 weeks of gestation, because the use of radiation may cause congenital malformations at 2–8 weeks of gestation and mental retardation at 8–15 weeks of gestation.[16] Considering all these factors, the CRT-D device implantation date and prednisolone start date were planned so that the prednisolone could be tapered to 15 mg/day according to the standard protocol by 30 weeks of gestation, when emergency delivery was possible. These multi-modal treatments restored the cardiac function in a short period, thereby enabling normal delivery without complications. Future studies should perform careful follow-ups and assess for the recurrence of cardiac sarcoidosis associated with post-partum endogenous cortisol depletion.

Conclusion

This case report describes the successful application of a multi-modal treatment approach in a pregnant woman with untreated cardiac sarcoidosis. With the treatment individually optimized and implemented by a multi-disciplinary team of specialists in each field, adequate risk

assessment and timely interventions contribute to favourable maternal and foetal outcomes.

Lead author biography

Tomohiro Yoshii graduated from the Yokohama City University Medical School, Japan, in 2015. After 2 years of medical training in the Saitama Red Cross Hospital, he is currently practising as a clinical fellow in the Department of Cardiovascular Medicine of the National Cerebral and Cardiovascular Center. His main research interest cardiomyopathy and echocardiography.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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