

# Outcomes and management of arrhythmogenic right ventricular cardiomyopathy in pregnancy: a case report

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## Background

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited disease with an estimated prevalence of up to 1:5000 in the general population. Few cases of ARVC during pregnancy are described in literature.

## Case summary

A 32-year-old primigravida was referred to our clinic during the 32nd gestational week. Arrhythmogenic right ventricular cardiomyopathy diagnosis with biventricular involvement was made according to Task Force criteria. Beta-blocker therapy was started and an elective caesarean section was planned, during the 37th gestational week; no complications occurred. Thirteen months after delivery, the patient was readmitted in our hospital due to an episode of pre-syncope and after team discussion, an implantable cardioverter-defibrillator (ICD) was implanted.

## Discussion

This case suggests that the absence of signs and symptoms of heart failure (HF) at a first evaluation plays a major role to predict maternal and foetal outcome in ARVC. Our experience is consistent with the evidence that indicates a favourable outcome in asymptomatic patients treated with optimal medical therapy during pregnancy. In our case, despite no major HF or arrhythmic complications during pregnancy, delivery, and puerperium, we observed an arrhythmic disease progression more likely independent from pregnancy, leading to ICD implantation.

## Keywords

Arrhythmogenic right ventricular cardiomyopathy • Pregnancy • Sudden cardiac death • Heart failure • Implantable cardioverter-defibrillator • Case report

## Learning points

- We observed a favourable outcome during pregnancy, delivery, and puerperium in a pregnant arrhythmogenic right ventricular cardiomyopathy (ARVC) patient with biventricular dysfunction and ventricular arrhythmias, treated with optimal anti-arrhythmic medical therapy.
- To achieve this goal, a thorough follow-up programme in the last trimester and after delivery, due to an increased risk of further disease manifestations, is mandatory.
- Since the guidelines gap about the course of ARVC during pregnancy is evident, more effort is needed to improve our knowledge in this field. We would need a multicenter registry/prospective studies to evaluate the best management strategy.

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## Introduction

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited disease with an estimated prevalence of up to 1:5000 in the general population. Almost 50% of the cases are familial, showing autosomal dominant transmission with variable penetrance.<sup>1</sup> Few cases of ARVC during pregnancy are described in literature.<sup>2,3</sup>

## Timeline

32nd gestational week	Referral to our centre for a family history of arrhythmogenic right ventricular cardiomyopathy
33rd gestational week	Diagnostic tests performed; admission to our hospital ('pregnancy diseases' division) for monitoring
35th gestational week	Positive genetic test
37th gestational week	Caesarean delivery
Right after delivery	Monitoring in intensive care unit
Follow-up	Asymptomatic during the first 13 months
13 months after delivery	Readmission in our ward due to an episode of pre-syncope: implantable cardioverter-defibrillator implantation

## Case presentation

A 32-year-old primigravida was referred to our clinic during the 32nd gestational week after her gynaecologist found that she had irregular heartbeat during a routine visit and a family history for ARVC: her brother was a known case, with an implantable cardioverter-defibrillator (ICD) implanted in primary prevention and a positive genetic test for a homozygous mutation of Desmoglein-2 (DSG2) gene. Her past medical history was unremarkable, she was asymptomatic.

Her electrocardiogram (ECG) showed sinus rhythm, incomplete right bundle branch block, epsilon wave in V2, negative T waves in V1–V4, and premature ventricular contractions (PVCs) with negative concordance (Figure 1).

Echocardiogram revealed dilation of the right ventricle (RV), with RV outflow tract parasternal long axis (RVOT PLAX) 37 mm, RVOT parasternal short axis 38 mm; apical RV thinning/aneurism; reduced RV systolic function, tricuspid annular plane systolic excursion 15 mm, and S wave 7.7 cm/s. Global left ventricular (LV) function was preserved, despite septal dyskinesia.

A 24-h Holter ECG monitoring confirmed frequent PVCs (17 075), 769 couplets and a few runs of non-sustained ventricular tachycardia (NSVT) (Figure 2).

She was admitted to our tertiary referral hospital for monitoring. Metoprolol 150 mg/day was started. Genetic testing revealed the

same homozygous mutation of DSG2 (c.1496T>G, p.L499R, missense) described for her brother.

Arrhythmogenic right ventricular cardiomyopathy diagnosis was made according to three major Task Force criteria: ECG, echocardiogram, and family history.<sup>4</sup>

Antenatal corticosteroids were administered to prevent foetal lung immaturity and an elective caesarean section was planned, during the 37th gestational week.

No complications occurred: baby's Apgar score and birth weight were normal; mother's N-terminal prohormone of brain natriuretic peptide (NT-proBNP) was stable (peak 177 pg/mL).

After delivery, she was transferred to the intensive care unit (ICU) for monitoring. Metoprolol was stopped and sotalol was started (20 mg t.i.d., then titrated up to 80 mg t.i.d.). Cabergolin 0.25 mg b.i.d. for 2 days was administered to suppress lactation; ramipril 2.5 mg was started.

The subsequent Holter ECG monitoring showed a reduction of PVCs on sotalol.

Cardiac magnetic resonance (CMR) revealed biventricular dilatation (LV end-diastolic volume index 109 mL/m<sup>2</sup> - RV end-diastolic volume index 141 mL/m<sup>2</sup>) with diffuse late gadolinium enhancement showing areas of fibrofatty infiltration, mostly in the antero-lateral wall of the LV and in the RV (Figures 3–5). Multiple areas of dyskinesia were detected in both ventricles that showed reduced ejection fraction (EF): LVEF 44% - RVEF 32%.

At discharge the patient was asymptomatic and there were no signs of heart failure (HF).

A thorough follow-up programme was started; she has been stable and asymptomatic for 13 months after delivery. Then she started to have some episodes of palpitations and subsequently she was readmitted in our hospital due to an episode of pre-syncope.

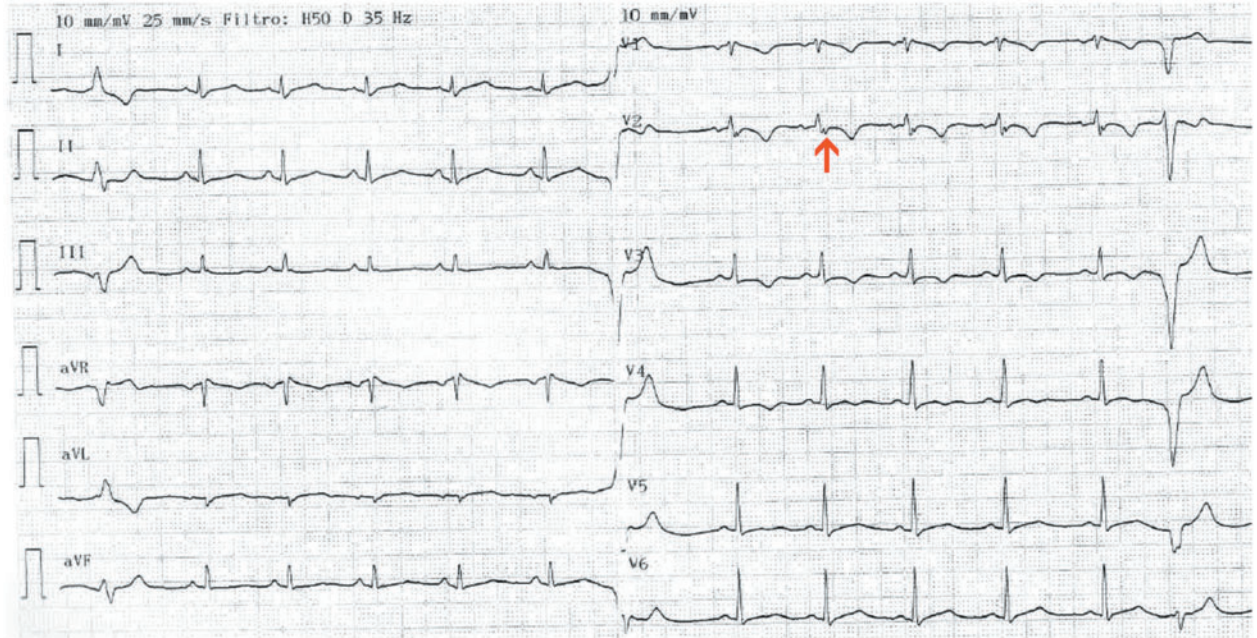
The ECG monitoring during the admission showed runs of NSVT (160/170 b.p.m.), monomorphic with left bundle branch block pattern; an exercise stress test did not elicit sustained ventricular arrhythmias (VA), but some couplets were seen. A new echocardiogram and CMR revealed a mild reduction of the LV volumes and a mild improvement of LV function (LVEF 55%), while the other features remained substantially unchanged.

Considering the clinical evolution with symptomatic arrhythmia and the biventricular extension of the disease, after team discussion, a single-chamber ICD was implanted. So far, there were no ICD interventions.

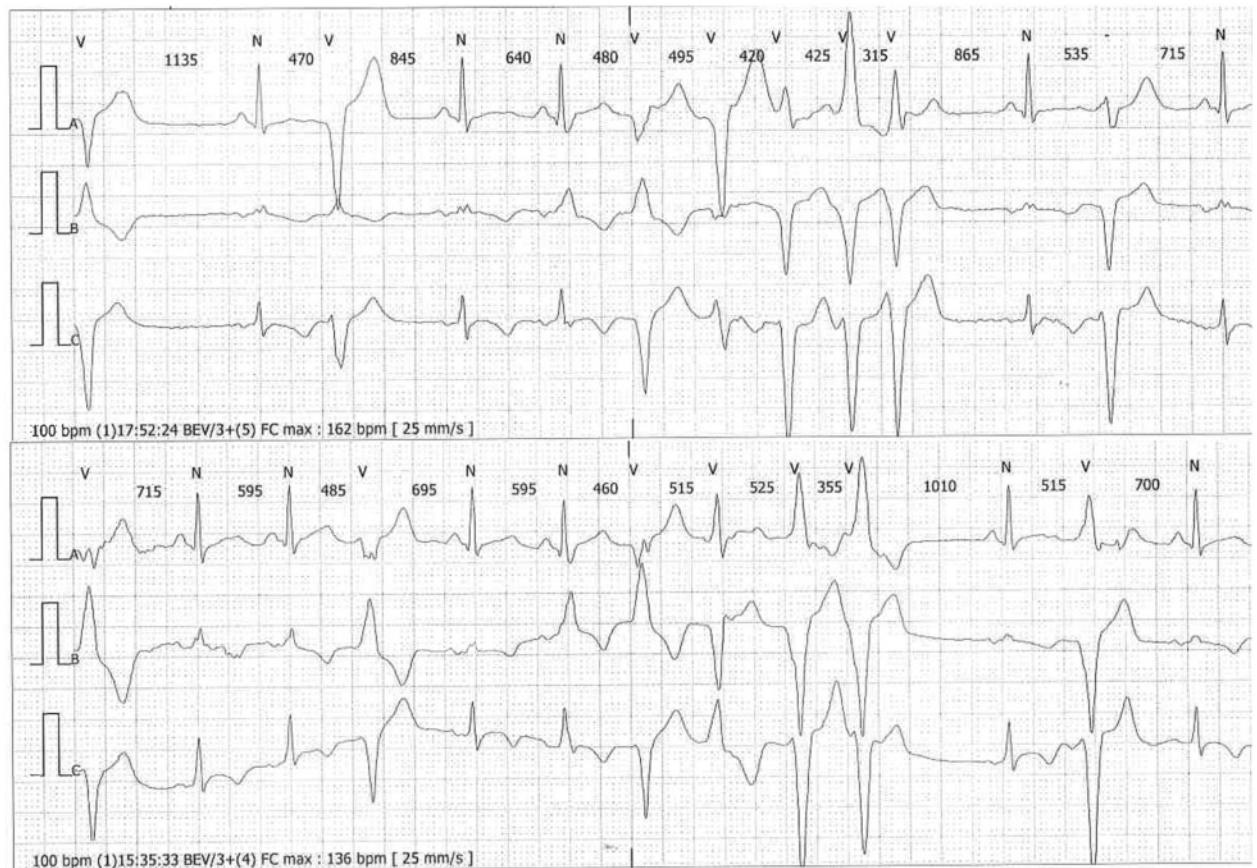
## Discussion

Arrhythmogenic right ventricular cardiomyopathy is an uncommon condition in which the main complications are arrhythmias, HF and high risk of sudden cardiac death (SCD). According to the expert consensus, patients with VA or right-sided HF are advised not to become pregnant.<sup>5</sup>

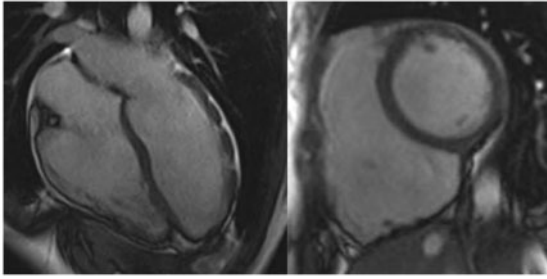
VT significantly increases risk of maternal mortality or severe morbidity and both reduced RV function and NT-proBNP >128 pg/mL are predictors of maternal cardiovascular events.<sup>6</sup> Therefore, for our patient, we decided to plan an elective caesarean section and to monitor the patient in ICU after delivery to deal with unexpected emergencies, considering that sympathetic overstimulation and fast



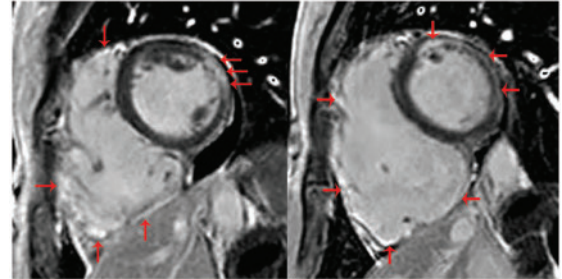
**Figure 1** Basal 12-lead electrocardiogram: sinus rhythm, incomplete right bundle branch block, epsilon wave in V2 (see red arrow), negative T waves in V1–V4, and premature ventricular contractions with negative concordance.



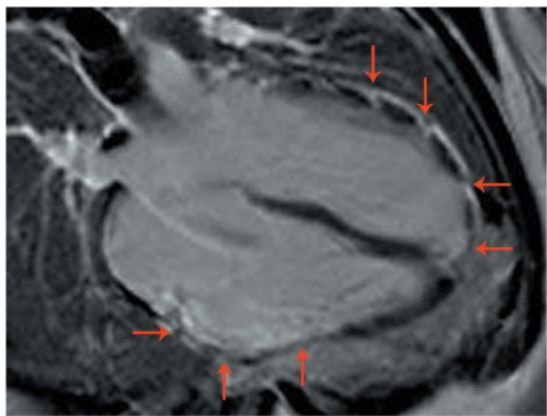
**Figure 2** Holter electrocardiogram strip: frequent premature ventricular contractions, couplets, and triplets.



**Figure 3** Cardiac magnetic resonance static cine images (short-axis and four-chamber views) showing right ventricular dilatation.



**Figure 5** Cardiac magnetic resonance late gadolinium enhancement phase sensitive inversion recovery sequences (short-axis views) marking areas of fibrofatty infiltration in the right ventricular (diffusely) and in the antero-lateral wall of the left ventricular (see red arrows).



**Figure 4** Cardiac magnetic resonance late gadolinium enhancement phase sensitive inversion recovery sequences (four-chamber views) marking areas of diffuse fibrofatty infiltration in the basal sub-tricuspid segment and mid right ventricular walls and in the lateral wall of the left ventricular (see red arrows).

hemodynamic changes may be regarded as an arrhythmogenic trigger in ARVC.

The reasons for a usually favourable outcome of pregnancy in ARVC are still uncertain: the gradual nature of hemodynamic overload during pregnancy could limit the severity of the disease manifestations and positively affect maternal outcomes.<sup>2</sup> The importance of haemodynamic overload during pregnancy is reflected by the reduction of LV volumes after pregnancy detected with CMR in this patient.

We observed a reduction of VA after delivery, suggesting that both the effects of hormonal changes and the anti-arrhythmic efficacy of sotalol may be extremely relevant.

Considering that indications on treatment of VA in ARVC in pregnancy are lacking, we relied on Guidelines on idiopathic VA in pregnancy.<sup>6</sup> Beta-blockers are in Class I level of evidence C, while sotalol or flecainide are in Class IIa/C and should be considered for prevention if other drugs fail. We started metoprolol because it is the most familiar drug in the heart-pregnancy team of our Institution, being

used to its foetal, neonatal and maternal effects. After delivery, we switched to sotalol because we did not observe a reduction of arrhythmias on metoprolol and in our experience sotalol it is a good option for patients with biventricular ARVC, allowing to avoid long-term adverse extracardiac effects of amiodarone.<sup>7</sup>

Stopping lactation reduces the high metabolic demand and enables early optimal medical treatment.<sup>6</sup> We thought that in our case cabergoline may be beneficial for the same purposes.

The decision whether to implant an ICD and the timing of the implantation in ARVC is controversial and should be individually based. We considered pre-syncope a warning of disease progression which, together with the biventricular involvement, the significant RV dysfunction, the evidence of rapid NSVT, and the homozygous pathogenic mutation should be regarded as carriers of increased risk of SCD.<sup>8,9</sup> On this basis, we decided to proceed with ICD implantation.

In biventricular ARVC, the most common areas of fibrofatty infiltration are LV postero-basal and antero-lateral walls in a subepicardial/mid-wall distribution.<sup>10,11</sup> Our patient exhibited some of these features (*Figures 4 and 5*): biventricular involvement in ARVC during pregnancy is a rare finding and specific studies are lacking, moreover, a homozygous mutation of DSG2 is a rare finding with few cases reported in the literature.<sup>12</sup>

It is remarkable that in our case, despite no major HF or arrhythmic complications during pregnancy, delivery, and puerperium, we observed an arrhythmic disease progression more likely independent from pregnancy, leading to ICD implantation. This highlights the importance of continued follow-up in order to determine the optimal time to intervene in these patients, in order to detect the changes that may suggest the right timing to intervene.

## Conclusion

This case suggests that the absence of signs and symptoms of HF at a first evaluation plays a major role to predict maternal and foetal outcome, as other case series suggest. Neither HF nor other major cardiac complications occurred during this lady's pregnancy, delivery,

and puerperium, although both ventricles were involved by the disease.

Our experience is consistent with the evidence that indicates a favourable outcome in asymptomatic ARVC patients treated with optimal anti-arrhythmic medical therapy during pregnancy and with the need for a thorough follow-up programme in the last trimester and after delivery, due to an increased risk of further disease manifestations.

Given the gap in guidelines regarding the optimal management of ARVC during pregnancy, further registry and/or prospective studies could help evaluate the best management strategy.

## Lead author biography



Dr Margherita Calcagnino graduated with 110/110 cum laude in 2004 at the University of Pavia. She attended the 4-year Residency of Cardiology at the University of Pavia and she subsequently attended and completed a PhD on Internal Medicine at the same University. She contributed to a number of research projects on cardiovascular field and she

worked from January 2009 to June 2011 at The Heart Hospital, University College of London: her mentor was Prof. WJ McKenna, very well known internationally for his knowledge and experience in cardiomyopathies. She now works in Milan in the field of cardiomyopathy, imaging, and pregnancy.

## Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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