

Sudden Cardiac Death in a 30-Year-Old Pregnant Woman

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Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with fibrofatty replacement (primarily of the right ventricular myocardium) and with ventricular arrhythmias including sudden cardiac death. Although ARVC is recognized with increasing frequency as a cause of arrhythmias in young individuals, very little information about this condition in the pregnant population is available. In this report, we describe a case of sudden cardiac death in a 30-year-old woman who was 18 weeks pregnant and was subsequently found to have ARVC on postmortem examination. We discuss the physiologic changes associated with pregnancy that may place a gravid woman with ARVC at increased risk for life-threatening arrhythmias and comment on options for pharmacotherapy in this population.

CASE PRESENTATION

A 30-year-old 18-week pregnant gravida 3, para 1 woman who appeared to be in her usual state of good health collapsed in the local medical clinic where she worked. Cardiopulmonary resuscitation was immediately instituted and cardiac monitoring revealed ventricular fibrillation. She was treated with 200 J of direct current energy delivered twice. After a brief period of pulseless electrical activity, her rhythm returned to ventricular fibrillation that was refractory to medical interventions, including intravenous (IV) fluids, repeat shocks, and multiple doses of IV medications per advanced cardiac life support protocol. She ultimately converted to sinus tachycardia after IV administration of norepinephrine and vasopressin as well as a repeat 360-J shock.

History

The patient had a past medical history of migraine headaches, a normal full-term pregnancy 2.5 years previously, and an ectopic pregnancy 6 years before her

cardiac arrest that required surgical intervention. She had used sumatriptan for headaches but had discontinued this medication after becoming pregnant. Her only current medication was acetaminophen as needed for headaches. There was no history of tobacco, alcohol, or illicit drug use. Her husband stated that she had a brief episode of palpitations 4 months prior to her cardiac arrest and slight shortness of breath with exertion 1 week before. There was no family history of cardiac disease or premature sudden cardiac death.

Physical Examination

On physical examination, her pupils were fixed and dilated. Additionally, there was no response to painful stimuli. There were no extra heart sounds or murmurs on cardiac auscultation. Her electrolytes were normal; the hemoglobin was low at 10.5 g/dL (normal, 12.0–16.0 g/dL), and total creatinine phosphokinase was elevated at 1246 U/L (normal, 20–200 U/L) with a normal troponin I. Electrocardiogram (ECG) showed sinus tachycardia at a rate of 105 bpm and QRS prolongation of 128 ms in the anterior precordial leads V1 to V3 (**Figure 1**). A chest radiograph taken on admission revealed mild pulmonary vascular congestion without cardiomegaly.

Clinical Course

Hemodynamic support was continued with IV norepinephrine and IV amiodarone was started. An

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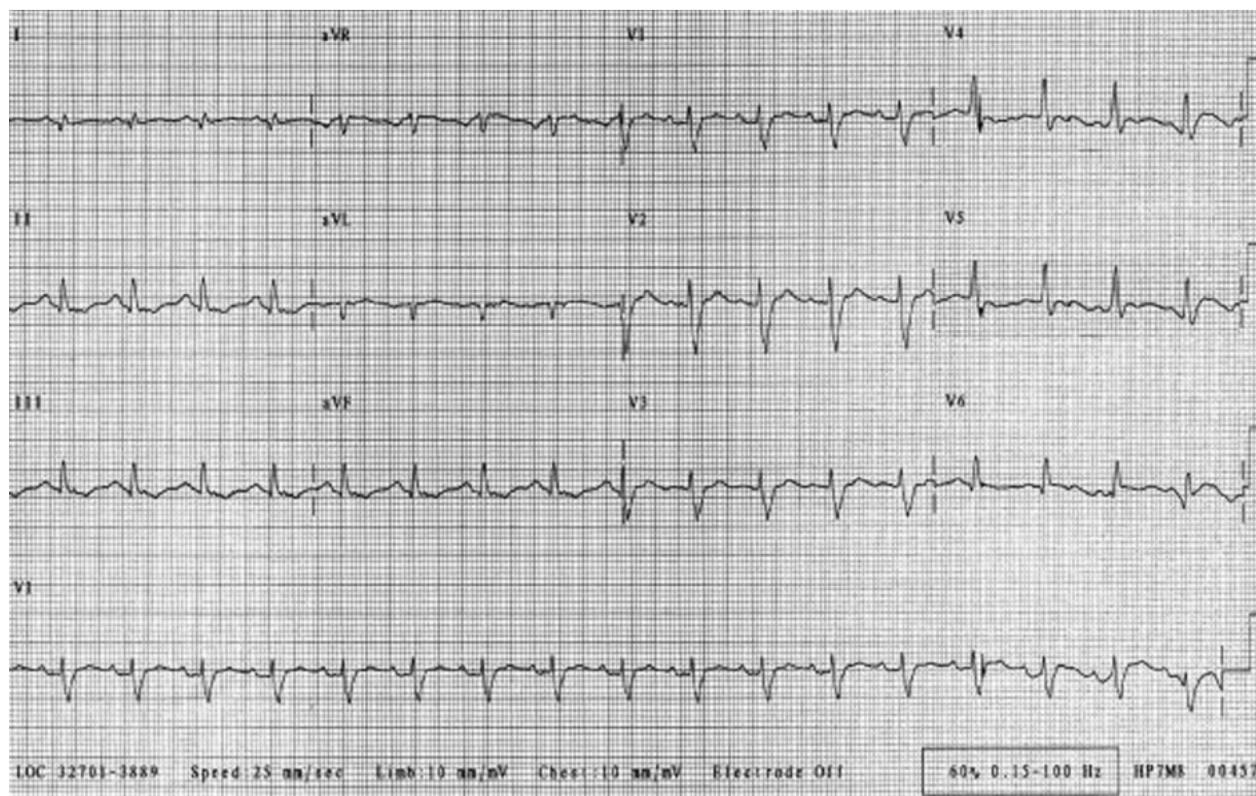


Figure 1. Electrocardiogram of the case patient demonstrating sinus tachycardia at 105 bpm with QRS prolongation of 128 ms in the anterior precordial leads.

echocardiogram revealed a dilated left ventricle with normal wall thickness and severe global hypokinesis with an estimated ejection fraction of 10%. Moderate to severe mitral regurgitation was noted with a normalized left atrium. The right ventricle demonstrated moderate global hypokinesis and the estimated peak pulmonary artery pressure was elevated at 37 mm Hg. Pulmonary embolus was initially considered as a possible etiology for her cardiac arrest and IV tissue plasminogen activator and IV heparin were empirically administered without significant change in hemodynamic status. Fetal demise was later confirmed by obstetrical ultrasound. Forty-eight hours after the patient was admitted, the decision to withdraw support was made because a computed tomography scan of her head showed diffuse cerebral edema consistent with anoxic injury and an electroencephalogram demonstrated no significant cortical activity.

Postmortem Examination

Postmortem examination revealed no evidence of cardiac or coronary artery congenital abnormality. On gross examination of the heart, a thin circumferential

zone of grayish-white to focally yellow tissue was present in the myocardium of both ventricles (**Figure 2**). Multiple histologic sections demonstrated varying degrees of myocardial cell loss with fibrofatty replacement in both the right and left ventricles, in some cases, extending the entire distance from the epicardial to the endocardial surface (**Figures 3 and 4**). The microscopic findings were compatible with ARVC in a biventricular distribution.

DISCUSSION

Arrhythmogenic Right Ventricular Cardiomyopathy

ARVC was first described by Dalla Volta¹ in 1964 and later termed arrhythmogenic right ventricular dysplasia by Fontaine in a 1977 report of stimulation and epicardial mapping studies in patients with sustained ventricular tachycardia.² The condition was formally categorized as a cardiomyopathy and termed ARVC in 1995 by the World Health Organization,³ which defines ARVC as a myocardial process “characterized by progressive fibrofatty replacement of right ventricular myocardium, initially with typical regional and later global right and some left ventricular involvement.”³

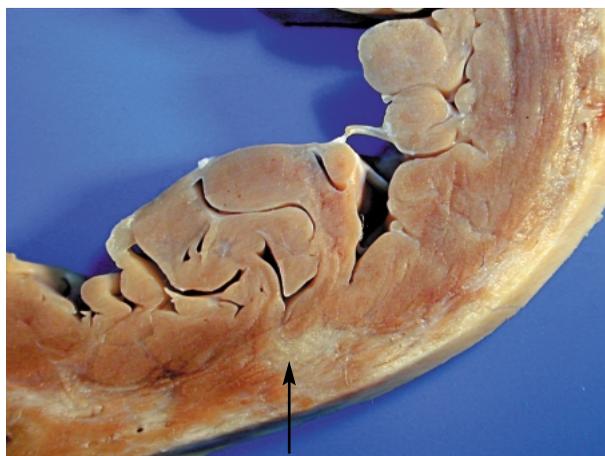


Figure 2. Gross section of the right ventricle demonstrating fibrofatty tissue (arrow) within the case patient's myocardium.

Left ventricular involvement has been increasingly recognized as a feature of ARVC and the development of left ventricular failure in the later stages of the disease has been described.⁴ Our patient demonstrated marked left ventricular dysfunction in the setting of only modest right ventricular hypokinesia. While this may represent an unusual presentation of ARVC primarily involving the left ventricle, these findings may also have been the result of global ischemic changes secondary to the patient's prolonged cardiac arrest.

The prevalence of ARVC has been estimated to be 1 in 5000; however, it is increasingly recognized as a cause of life-threatening arrhythmias in young adults, accounting for up to 20% of sudden deaths in individuals younger than 35 years.^{5,6} Familial forms of the disease were first reported in 1982, and up to 50% of cases are inherited in an autosomal dominant pattern with incomplete penetrance and variable expression.^{7,8} The gold standard for diagnosis of ARVC is the histologic demonstration of fibrofatty replacement of right ventricular myocardium. As with our patient, the diagnosis is often made at postmortem examination; however, clinical criteria based on cardiac structural alterations, repolarization/conduction abnormalities, arrhythmias, and family history allow for the diagnosis to be made antemortem.⁹

ARVC and Pregnancy

Arrhythmias during pregnancy have been described,¹⁰ however, little has been written in the medical literature regarding pregnancy and ARVC. To the best of our knowledge, the first and only reported case of ARVC and pregnancy was by Villanova et al¹¹ in 1998. In this report, a 30-year-old woman who had been

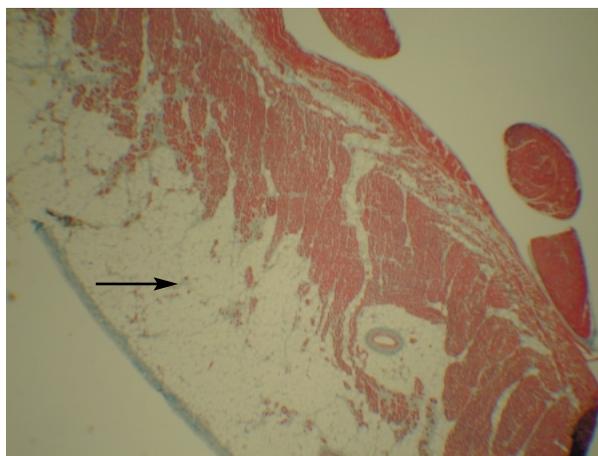


Figure 3. Histologic section of the free wall of the case patient's right ventricle (hematoxylin and eosin stain) demonstrating marked replacement of the subepicardial layers (arrow) by fibrofatty tissue.

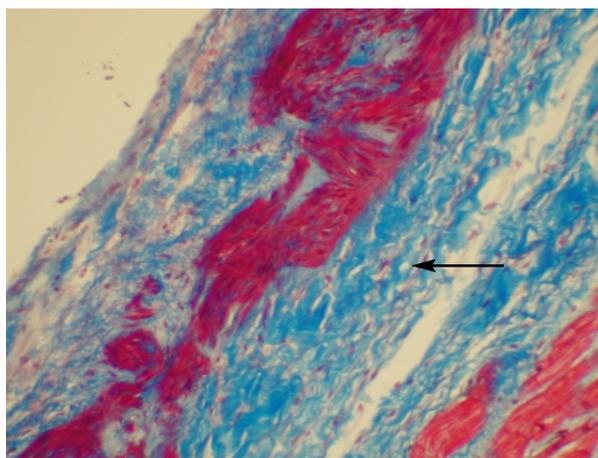


Figure 4. Histologic section of the free wall of the right ventricle (trichrome stain) demonstrating fibrous tissue (arrow) within the case patient's myocardium.

diagnosed with ARVC at age 22 years and treated with flecainide became pregnant. Flecainide was continued, and the patient was monitored every 3 months with 12-lead ECG, signaled averaged ECG, 24-hour ECG, and echocardiogram. No significant abnormalities were appreciated, and she delivered a healthy full-term baby via cesarean section.

Pathogenesis of ARVC in pregnancy. Although there is no known direct correlation between pregnancy and ARVC, some of the same arrhythmogenic triggers for ARVC are affected by pregnancy and may place the gravid female with this condition at higher

risk for arrhythmias. Studies suggest that abnormalities of myocardial sympathetic function are present in ARVC and adrenergically-mediated ventricular arrhythmias have been strongly implicated.¹² In a study of 44 individuals with ARVC, isoproterenol infusion resulted in 1 or more episodes of ventricular tachycardia in 88% of patients compared with only 2% in 50 matched controls without structural heart disease.¹³ This aggravation of ventricular arrhythmias by catecholamine exposure in ARVC may have direct implications on the pregnant female. It has been demonstrated in animal models that sympathetic nervous system activity increases throughout pregnancy with catecholamine turnover in the heart increasing by 92% and urinary norepinephrine excretion increasing 2.6-fold compared with nonpregnant controls.¹⁴ Along with increased circulating levels of catecholamines, it is postulated that elevated levels of estrogen and progesterone during pregnancy may amplify adrenergic responses,¹⁰ possibly further increasing the risk of arrhythmia in this population.

Cardiac chamber dynamics have also been implicated in the arrhythmogenicity of ARVC. Two-dimensional echocardiographic studies of athletes reveal that right ventricular size increases with physical exertion.¹⁵ It is this increased stretch of fibrofatty right heart tissue in individuals with ARVC that is thought to contribute to ventricular arrhythmias during exercise. In fact, ARVC has been implicated in up to 3% of deaths associated with physical activity.¹⁶ Like exercise, pregnancy influences cardiac chamber dimensions. In normal pregnancy, maternal plasma blood volume begins to increase by 6 weeks gestation and continues to increase up to 50% by 30 weeks.¹⁷ While the majority of this extra volume remains in the peripheral vascular system as a result of hormone-mediated vasodilation, significant increases in cardiac chamber dimensions during the 15th to 35th week of pregnancy have been confirmed by serial echocardiographic analysis.^{18,19} Hypervolemia and associated right ventricular dilation during pregnancy, therefore, may promote ventricular irritability in the gravid female with ARVC.

Treatment of ARVC in pregnancy. No precise guidelines exist for the treatment of ARVC and even less information is available regarding pregnant patients with this disease. Therapeutic options include antiarrhythmic pharmacotherapy, catheter ablation, implantable cardioverter defibrillator, surgical resection of arrhythmogenic foci, and heart transplant. Sotalol has been shown to be the most effective antiarrhythmic agent at suppressing ventricular arrhythmias in individuals with ARVC. In a study of 81 patients with ARVC,

sotalol prevented ventricular tachycardia during programmed ventricular stimulation in 68% of patients compared with only 12% with class Ic antiarrhythmics and only 6% with class Ia and Ib agents.²⁰ In the only report of pharmacologic treatment of ARVC during pregnancy, flecainide (a class Ic antiarrhythmic) resulted in an uneventful pregnancy and delivery.¹¹ Flecainide is listed as a pregnancy class C drug by the US Food and Drug Administration (FDA). Sotalol is a FDA pregnancy class B drug. Given its superior efficacy and decreased risk of fetal harm compared with other antiarrhythmics, sotalol may be the pharmacotherapy of choice in the pregnant individual with ARVC.

CONCLUSION

Although rare, ARVC is increasingly being recognized as a cause of life-threatening arrhythmias in young individuals and athletes. Enhanced adrenergic activity and increases in cardiac chamber dimensions during pregnancy may augment the risk of ventricular arrhythmia in a gravid female with ARVC. Very little experience in treating pregnant individuals with ARVC is available; however, sotalol, given its superior efficacy at suppressing ventricular arrhythmia in ARVC and its favorable profile with regard to fetal risk, may be the drug of choice when initiating pharmacotherapy in this group of individuals. **HP**

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