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Arrhythmogenic Right Ventricular Cardiomyopathy in an Endurance Athlete

Presenting with Ventricular Tachycardia and Normal Right Ventricular Function

Arrhythmogenic right ventricular cardiomyopathy, a genetically inherited disease that results in fibrofatty replacement of normal cardiac myocytes, has been associated with sudden cardiac death in athletes. Long-term participation in endurance exercise hastens the development of both the arrhythmic and structural arrhythmogenic right ventricular cardiomyopathy phenotypes. We describe the unusual case of a 34-year-old, symptomatic, female endurance athlete who had arrhythmogenic right ventricular cardiomyopathy in the presence of a structurally normal right ventricle. Clinicians should be aware of this infrequent presentation when evaluating athletic patients who have ventricular arrhythmias and normal findings on cardiac imaging studies. **(Tex Heart Inst J 2017;44(4):290-3)**

rrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically inherited disease that affects cardiac desmosomes and is characterized by fibrofatty replacement of normal cardiac myocytes.¹ Phenotypically, ARVC is usually characterized by right ventricular (RV) systolic dysfunction, RV structural deformation and resultant substrate for malignant ventricular tachycardia (VT), and risk of sudden cardiac death (SCD).¹

In athletes, specifically those participating in endurance sports, ARVC is a welldescribed cause of SCD.² From a pathophysiologic perspective, the hemodynamic volume challenge associated with chronic isotonic or endurance exercise leads to repetitive and sustained increases in RV afterload. In individuals with genotype-positive ARVC, increased RV afterload can directly facilitate the fibrofatty RV infiltrative process.³ Data strongly suggest that ongoing participation in endurance exercise, in a dosedependent manner, accelerates the progression of ARVC in patients with both the arrhythmic and structural phenotypes.³ Other controversial data suggest that chronic exposure to ultra-endurance exercise is associated with an ARVC-like exercise-induced RV cardiomyopathy.⁴

We present an unusual case of a marathon runner who had symptomatic VT and nonpathologic findings on cardiac imaging studies. Ultimately, genetic test results revealed a pathogenic frameshift mutation in the *PKP2* gene (which encodes the desmosomal plakophilin-2 protein), indicating the genetic form of ARVC.

Case Report

In June 2015, a 34-year-old female endurance runner presented for evaluation of new palpitations, presyncope, and premature ventricular contractions (PVCs) of RV outflow tract (RVOT) morphology (specifically, left bundle branch morphology with inferior axis). Previously, the patient had reported 2 unheralded syncopal events while nearing completion of 2 marathons, at 10 years and 5 years before the current presentation. Despite the absence of prodromal symptoms, those episodes had been attributed to dehydration. Her current symptoms were abrupt palpitations and lightheadedness while running. No chest discomfort, dyspnea on exertion, or syncope was associated with these symptoms, and she reported no recent illnesses. She was otherwise presumed healthy with no history of substance abuse. Her family history was

negative for SCD and for known genetically inherited cardiomyopathies or arrhythmias.

The patient had normal vital signs. A 12-lead electrocardiogram showed sinus rhythm with no epsilon waves, bundle branch block, or anterior repolarization abnormalities (Fig. 1). Results of 24-hour ambulatory Holter monitoring revealed a PVC burden of 12% (11,111 PVCs) at the RVOT. Transthoracic echocardiographic and cardiac magnetic resonance images revealed normal RV structure and systolic function (Fig. 2). Two-dimensional echocardiographic measurements of the RVOT were consistent and showed only mild dilation of 3.1 cm (16.7 mm/m²) in the long- and short-axis views. Tissue-Doppler systolic velocities at the basal RV free wall were normal (11 cm/s), as was RV global longitudinal strain (-18.4%) (Fig. 3). Of note, there were no RV aneurysms, sacculations, or regions of dyskinesia, and cardiac magnetic resonance revealed no myocardial regions with delayed gadolinium enhancement uptake.

The patient underwent a treadmill electrocardiographic stress test. Initial tracings showed infrequent PVCs of the RVOT that disappeared after 2 minutes of exercise (Fig. 4A). At 5 minutes, however, sustained and symptomatic VT of RVOT morphology developed (Fig. 4B), and the test was aborted. The patient reported lightheadedness. No episodes of VT were recorded after exercise cessation, and the symptoms resolved.

Given the exercise-induced VT, we recommended that the patient undergo an invasive electrophysiologic study in consideration of RVOT foci ablation. Although results on RV voltage mapping were normal, stimulation with isoproterenol induced several PVC morphologies, nonsustained VT, and an episode of polymorphic VT. Accordingly, no ablation was attempted. Because of concern about the patient's exercise-induced symptoms, reproducible malignant VT, and lack of a clear RVOT focus, genetic testing was performed, and it revealed a mutation in PKP2. The diagnosis of ARVC is based on the 2010 revised Task Force criteria, which include major and minor criteria in 6 categories: 1) global or regional dysfunction and structural alterations, 2) tissue characterization of the wall, 3) repolarization abnormalities, 4) depolarization or conduction abnormalities, 5) arrhythmias, and 6) family history.⁵ The diagnosis



Fig. 1 Baseline 12-lead electrocardiogram shows sinus rhythm.

of definite ARVC was made because of the presence of one major diagnostic criterion (identification of a pathogenic ARVC mutation) and 2 minor diagnostic criteria (>500 PVCs in 24 hr and VT of RVOT configuration).⁵

The patient underwent implantation of a subcutaneous intracardiac defibrillator. She was started on antiarrhythmic therapy with flecainide, which reduced her symptomatic palpitations. Substantial exercise limitations were recommended, including discontinuing endurance running.

Discussion

As in other genetically inherited cardiomyopathies, the phenotypic expression of genotype-positive ARVC is unpredictable and dynamic. The current case illustrates that, although rare, ARVC can be characterized by substantially discordant RV structural and arrhythmic phenotypic patterns. As reported in ARVC registry data,



Fig. 2 A) Two-dimensional transthoracic echocardiogram (short-axis linear view) shows the right ventricular outflow tract dimension. **B**) Cardiac magnetic resonance image (4-chamber view) shows a structurally intact right ventricle (RV) and the calculated end-diastolic volume (EDV).

Supplemental motion image is available for Figure 2B.



Fig. 3 A) Tissue-Doppler echocardiogram (4-chamber view) shows systolic velocity (S') at the basal right ventricular (RV) free wall. B) Speckle-tracking echocardiogram (4-chamber view) shows RV global longitudinal strain (GLS).

the overwhelming majority of patients have RV structural pathologic conditions in conjunction with symptomatic ventricular arrhythmias.¹ Although our patient's preserved RV architecture was notable, it remains likely that the expression of the primary arrhythmic phenotype was accelerated by long-term endurance exercise. Of note, *PKP2* mutations are responsible for most genetically inherited cases of ARVC⁶ and have been associated with a primary arrhythmic phenotype.⁷⁹ Thus, in addition to underlying genetic characteristics, various mechanisms related to host factors and possibly environmental factors most likely account for the differential manifestations of phenotypic ARVC, as illustrated in our case.

Arrhythmogenic RV cardiomyopathy must be excluded in symptomatic endurance athletes. Clinically, practitioners who care for athletes face the challenge of differentiating "gray-zone" exercise-induced RV structural adaptations from pathologic RV remodeling.¹⁰ Given that exercise limitations are essential in the treatment of ARVC, clinicians should be aware of unusual manifestations of the disease.³ Our case illustrates that genetic forms of ARVC should be considered in the differential diagnosis, particularly in athletes who present with symptomatic ventricular arrhythmias despite reassuring cardiac imaging findings. Focused genetic testing is not routinely performed in patients with



exercise protocol shows the disappearance of premature right ventricular contractions. **B**) Rhythm strip 5 minutes into exercise protocol shows ventricular tachycardia of right ventricular outflow tract morphology.

ARVC; however, testing was diagnostic in our case. Sports cardiologists and sports-medicine practitioners should be aware of this rare and unusual presentation in symptomatic endurance athletes.

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