

Arrhythmogenic Right Ventricular Cardiomyopathy in Marathon Runners: Case Report

Cardiomiopatia Arritmogênica do Ventrículo Direito em Maratonista: Relato de Caso

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Introduction

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited disease of the cardiac muscle characterized by right ventricular dysfunction (global or regional) with or without left ventricular (LV) involvement in the presence of histological evidence of the disease and/or electrocardiographic abnormalities according to published criteria.¹

ARVC has age-dependent penetrance and is mainly characterized by episodes of ventricular arrhythmia that can progress to sudden cardiac death (SCD). The estimated prevalence ranges from 1:2,000 to 1:5,000, with a predominance in the Caucasian population and in people who practice strenuous exercise or competitive sports. Despite its low prevalence, ARVC represents approximately 5–20% of CSM cases in young people.²

Diagnosing ARVC is often difficult due to its heterogeneous clinical presentation, highly variable intra- and interfamilial expression, and incomplete penetrance.² Right ventricular (RV) hypertrophy also occurs in athletes, making the diagnosis more challenging in this population.^{3,4}

Case report

A 47-year-old female marathon runner with no family history of CSM was admitted to the emergency department reporting palpitations and presyncope. Admission electrocardiography (ECG) showed ventricular tachycardia (VT) with a left bundle branch and lower axis block morphology (Figure 1A) for which she was subjected to electrical cardioversion (ECV). Post-ECV ECG showed sinus rhythm with precordial T-wave inversion in V1-V4 (Figure 1B). Findings of laboratory tests, including myocardial necrosis markers, were normal. Echocardiography (ECHO) showed enlarged right cardiac chambers and RV systolic dysfunction (reduced tricuspid annular plane systolic excursion and strain) (Figures 2 and 3). Cardiac catheterization revealed no obstructive coronary disease. The patient was discharged

with instructions to suspend physical activity and undergo cardiac magnetic resonance (CMR). However, three months later she was readmitted with VT and hemodynamic instability and again underwent ECV. CMR showed RV with moderate dilation (RV end-diastolic volume index, 114 mL/m²; RV end-systolic volume index, 64 mL/m²), mild right ventricular systolic dysfunction (right ventricular ejection fraction, 43%; reference value, >45%), areas with dyskinesia and microaneurysm formation in the RV inferior wall, and dyskinesia in the RV outflow tract. The LV had preserved dimensions (LV end-diastolic volume index, 90 mL/m²; LV end-systolic volume index, 38 mL/m²) (Figure 4 and Table 1).

Considering these findings and using the Task Force Criteria (TFC-2010), the patient was diagnosed with ARVC, for which an implantable cardioverter defibrillator (ICD) and amiodarone and beta-blocker therapy were indicated. The patient is currently without complaint and followed on an outpatient basis.

Discussion

In 1994, the World Health Organization (WHO) classified ARVC as a non-ischemic cardiomyopathy. The condition generally manifests between the second and fourth decades of life.⁵ The most common clinical presentation is palpitations or exertional syncope. The clinical course of ARVC is characterized by arrhythmic events, which can lead to CSM and affect biventricular systolic function.³

RV hypertrophy is a common phenotypic expression and an essential component of the ARVC diagnosis. However, this finding is often seen in benign clinical conditions such as athlete's heart. RV hypertrophy has been described in imaging studies of a large proportion of athletes, with more accentuated remodeling in resistance exercises. In these cases, RV hypertrophy may overlap with pathological dilation in patients with ARVC, making the diagnosis even more challenging.³

The diagnosis of ARVC is based on the TFC-2010, which combines family history and electrophysiological, morphofunctional, and histological criteria. Patients with four points are diagnosed with ARVC, while those with three points are identified as probable ARVC carriers, knowing that the major criterion is worth two points and the minor criterion is worth one point.⁶

Structural and functional assessments are essential to the diagnosis of ARVC. The initial investigation consists of non-invasive tests (ECG, high-resolution ECG [HRECG], ECHO and/or CMR, and 24-hour Holter monitoring).²

Keywords

Arrhythmogenic right ventricular dysplasia; Echocardiography; Ventricular tachycardia.

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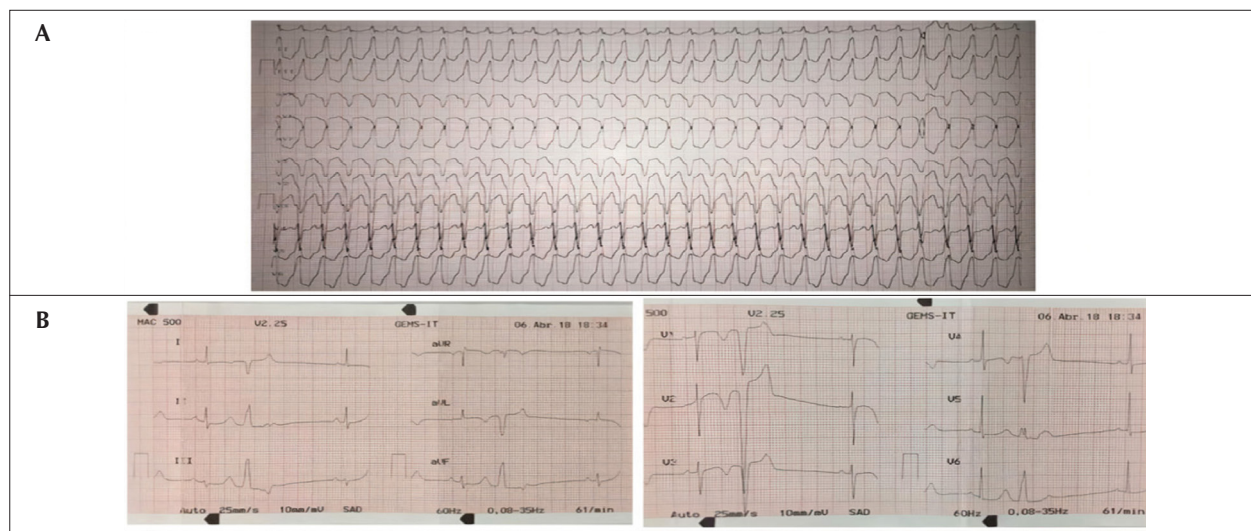


Figure 1 – Twelve-lead electrocardiogram. (A) Ventricular tachycardia with left bundle branch block morphology. (B) Sinus rhythm with extrasystole and T-wave reversal in V1-V4.

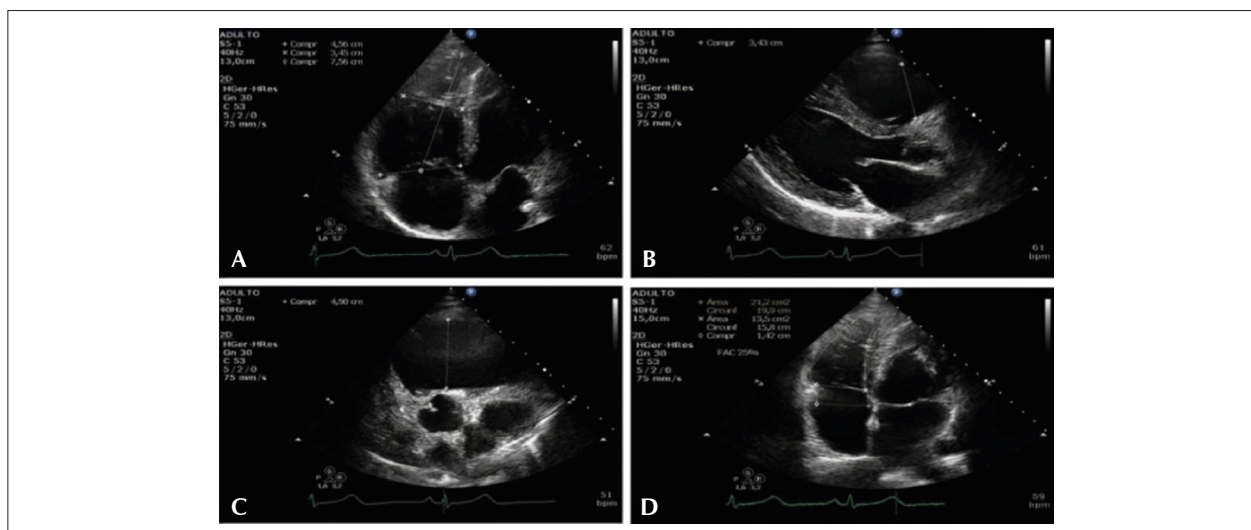


Figure 2 – Transthoracic echocardiogram. (A) Diameters of the right ventricle in the apical four-chamber view. (B) Right ventricular outflow tract measurement in the longitudinal parasternal cut. (C) Right ventricular outflow tract measurement in the transverse parasternal cut. (D) Calculation of right ventricular area variation in the apical four-chamber view.

T-wave inversion in V1-V3 is the most common ECG finding in ARVC (up to 83% of patients) and a major criterion for its diagnosis.^{2,7} Although ECG analysis is essential in the initial stratification, about 12% of patients with ARVC may have normal ECG findings, reinforcing the need for a diagnostic evaluation based on the TFC-2010.²

ECHO is the initial test in ARVC investigations. Findings suggestive of ARVC include global or segmental ventricular wall abnormalities associated with cavity dilation (mostly right) and RV hypertrophy with systolic dysfunction.² Systolic

function assessments must be based on several parameters, as decreased fractional area change has been described in athletes, showing the importance of strain use.⁸

CMR assesses morphofunctional abnormalities and tissue characterization using late gadolinium enhancement, providing information on the presence and amount of fibrofatty replacement in the myocardium.^{4,6} In addition to the parameters included in the TFC-2010, other characteristic ARVC abnormalities can be visualized, such as RV microaneurysms. Better accuracy (98%) is evidenced

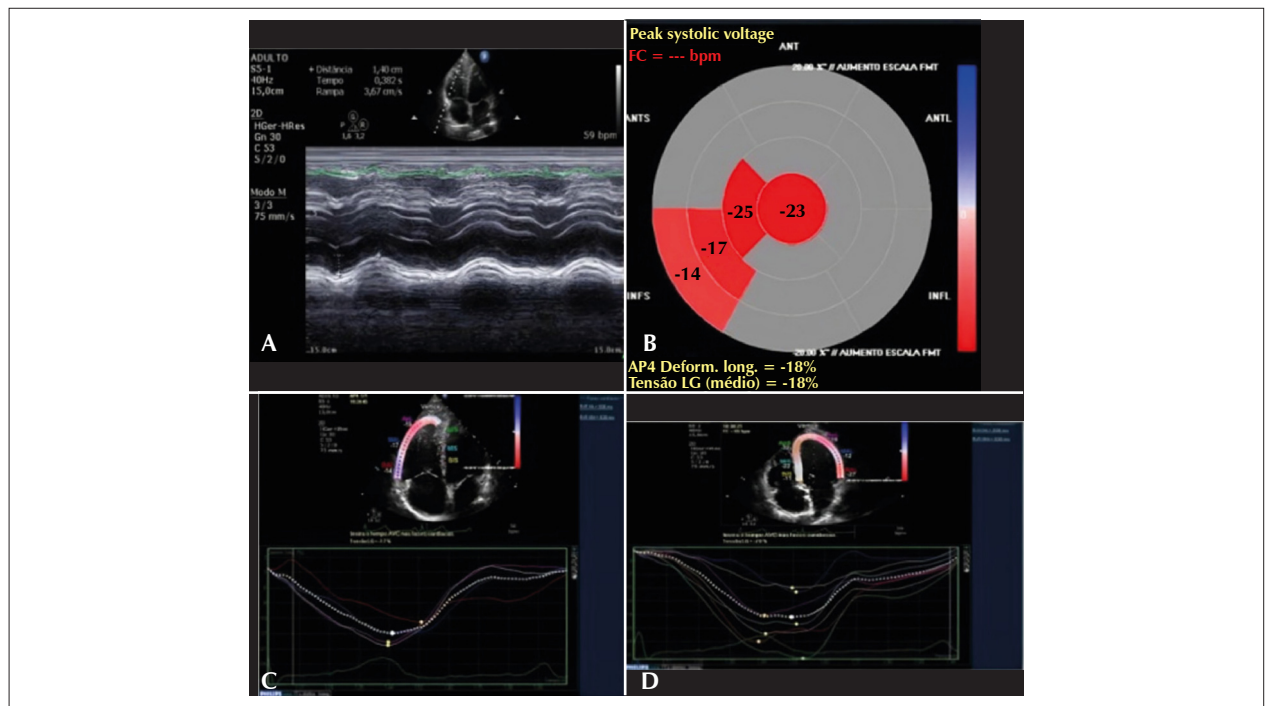


Figure 3 – Transthoracic echocardiogram. (A) Measurement of the tricuspid annular plane systolic excursion. (B and C) Right ventricular strain. (D) Left ventricular strain.

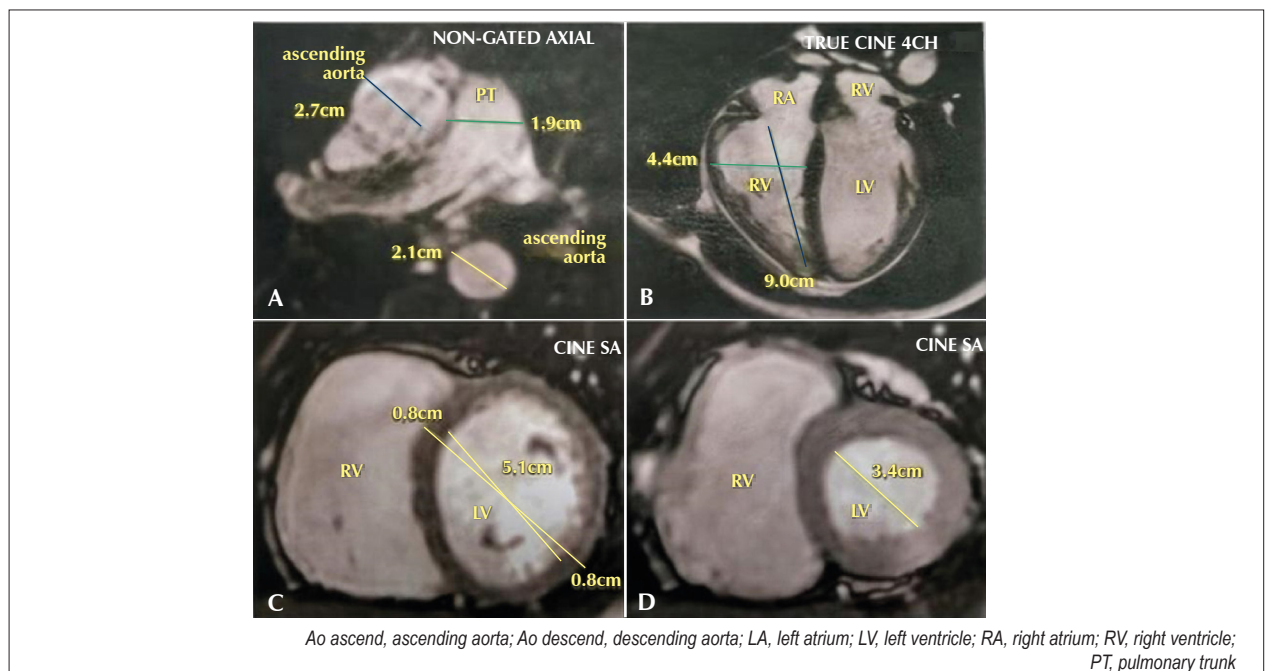


Figure 4 – Magnetic resonance image showing moderate right ventricular dilation.

when segmental contractility changes and signs of pre- and postcontrast abnormalities (including LV fatty infiltration and late enhancement) are considered together.⁹

Twenty-four-hour Holter monitoring quantifies the number of ventricular extrasystole episodes and accesses the

morphology of the arrhythmia, which may suggest its site of origin. The presence of ≥ 500 ventricular extrasystole episodes is considered a minor criterion.⁷

Endomyocardial biopsy is not routinely indicated for all patients with suspected ARVC; rather, it should be used

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only for probands with the sporadic form of ARVC and predominant LV involvement when the final diagnosis depends on the histological exclusion of phenocopies such as chronic myocarditis, sarcoidosis, or other myocardial disorders.⁴

Although the presence of mutation is part of the TFC-2010, the test results should be analyzed carefully, as a negative test does not exclude the possibility of disease and a positive

result should lead to differentiation between causal mutations and non-pathogenic variants. Therefore, genotyping is used to identify the mutation considered causal in probands with phenotypic diagnostic criteria.⁹

The clinical management of ARVC aims to reduce the risk of SCD and improve quality of life by alleviating arrhythmic and heart failure symptoms.⁴ Sports activity increases the risk

Table 1 - Revised Task Force Criteria 2010.

1. Structural changes and global or regional dysfunction
Major criteria - Two-dimensional echocardiography - Regional RV akinesia, dyskinesia, or aneurysm associated with one of the following diastolic measurements: - LPC RVOT ≥ 32 mm (LPC/BSA ≥ 19 mm/m²) or - TPC RVOT ≥ 36 mm (TPC/BSA ≥ 21 mm/m²) or - FAC $\leq 33\%$ - CMR - Regional RV akinesia or dyskinesia or RV contraction dyssynchrony associated with one of the following measurements: - RV EDV BSA ≥ 110 mL/m² (in males) or ≥ 100 mL (in females) - RV ejection fraction $\leq 40\%$ - Right ventriculography - Akinesia, RV dyskinesia Minor criteria - Two-dimensional echocardiography - Akinesia, RV dyskinesia, or RV contraction dyssynchrony and one of the following measurements of diastolic function: - LPC RVOT ≥ 29 to < 32 mm (LPC/BSA ≥ 16 to < 19 mm/m²) or - TPC RVOT ≥ 32 to < 36 mm (TPC/BSA ≥ 18 to < 21 mm/m²) or - FAC $> 33\% \leq 40\%$ - CMR - Regional RV akinesia or dyskinesia or RV contraction dyssynchrony and one of the following measurements: - RV EDV BSA ≥ 100–110 mL/m² (in males) or ≥ 90–100 mL/m² (in females) - RV ejection fraction $> 40\%$ but $\leq 45\%$
2. Tissue aspects
Major criteria - Residual myocyte count $< 50\%$ by morphometric analysis (or $< 50\%$, if estimated), with RV free wall fibrous replacement in ≥ 1 specimen with or without fatty tissue replacement on an endomyocardial biopsy Minor criteria - Residual myocyte count of 60–75% by morphometric analysis (or 50–65%, if estimated) with RV free wall fibrous replacement in ≥ 1 specimen with or without fatty tissue replacement on endomyocardial biopsy
3. Repolarization abnormalities
Major criteria - Inverted T-waves in right precordials (V1, V2, and V3) or extending beyond V3 in patients aged > 14 years (in the absence of an RBCD-QRS ≥ 120 ms) Minor criteria - Inverted T-waves in V1 and V2 in patients aged > 14 years in the absence of CRBB - Inverted T-waves in V1, V2, V3, and V4 in patients aged > 14 years in the presence of CRBB
4. Depolarization/conduction abnormalities
Major criteria - Late potentials on HRECG in ≥ 1 of 3 parameters in the absence of a QRS wave ≥ 110 ms on 12-lead ECG: - Filtered QRS duration (fQRS) ≥ 114 ms - QRS terminal duration < 40 microV and ≥ 36 ms - Root mean square voltage 40 ms and ≤ 20 microV - QRS end portion duration ≥ 55 ms (measured from S-wave nadir to end of ventricular depolarization - including R') in V1, V2, or V3 Source: Adapted from Elias et al.² BSA, body surface area; CMR, cardiac magnetic resonance; CRBB, complete right bundle branch block; EDV, end-diastolic volume; HRECG, high-resolution electrocardiography; LPC, longitudinal parasternal cut; RV, right ventricle; RBCD, right bundle branch conduction disorder; RVOT, right ventricular outflow tract; TPC, transverse parasternal cut.

of SCD in adolescents and young adults with ARVC. Thus, it is important to highlight that these patients should not participate in competitive or endurance sports (class I); rather, they should practice only low-intensity recreational sports (class IIa).²

Current therapeutic options for ARVD include lifestyle changes, beta-blockers, antiarrhythmics, catheter ablation, ICD, and heart transplantation. Beta-blocker therapy should be instituted empirically in all patients with a clinical diagnosis of ARVC due to its ability to reduce the risk of ventricular arrhythmia and prevent myocardial disease progression.^{2,7}

Antiarrhythmic therapy should be considered adjunctive therapy to ICD in patients with multiple appropriate therapies (class I) and may be considered in patients with frequent ectopic activity and/or non-sustained VT (NSVT; class IIa).^{2,6}

The natural history of ARVC is characterized by the risk of CSD, hence the importance of stratifying patients by need for an ICD, which should be recommended in ventricular fibrillation and sustained VT (class I) and considered in the

presence of unexplained syncope, NSVT, and severe RV or LV dysfunction (class IIa).^{2,7}

Cases such as this of ARVC in a marathon runner are difficult to diagnose, highlighting the importance of the integrated analysis of clinical, electrocardiographic, and morphofunctional factors. It is essential to be aware of physiological responses in athletes, paying attention to the reference values for this group (Table 2), to minimize diagnostic errors.

Authors' contributions

Research conception and design, data collection: DVC and IABL; data analysis and interpretation, statistical analysis, manuscript writing, and critical review of the manuscript for important intellectual content: AKBS, EPM, and IABL.

Conflict of interest

The authors have declared that they have no conflict of interest.

Table 2 - Comparison of athlete's heart and arrhythmogenic right ventricular cardiomyopathy.

	Athlete's heart	ARVC
Family history	Negative	Positive in 50% of cases
Symptoms	Absent	Palpitations, syncope, and sudden death
Electrocardiographic changes	Incomplete right bundle branch disorder, increased QRS voltage, early repolarization pattern in right precordials with inverted T-waves preceded by J point/ST segment elevation	T-wave inversion in right precordials, presence of epsilon waves, time from S-wave nadir to QRS end ≤ 55 ms, low QRS voltage
RV dilation	Global dilation	More pronounced dilation in the inflow tract than in the outflow tract
RV/LV	< 1 (balanced enlargement of both ventricles)	> 1
Global RV dysfunction	Absent or mild dysfunction (FAC reference value $< 32\%$)	Present
RV segment change	Absent	Present
RV longitudinal strain	Preserved	Reduced
Regression after winding down	Present	Absent
Late enhancement CMR	Preserved	Reduced
Ventricular arrhythmia	Present	Absent

ARVC, arrhythmogenic right ventricular cardiomyopathy; CMR, cardiac magnetic resonance; FAC, fractional area change; LV, left ventricle; RV, right ventricle.

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