

Incidental Finding of Arrhythmogenic Right Ventricular Cardiomyopathy in a 72-Year-Old Man Admitted With Acute Coronary Syndrome

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Introduction

Arrhythmogenic right ventricular cardiomyopathy (ARVC) – also known as arrhythmogenic right ventricular (RV) dysplasia – is a genetic disorder characterized by progressive loss of RV cardiomyocytes, which are replaced with fibrofatty tissue. This replacement may delay intraventricular conduction and contribute to ventricular arrhythmias through a fibrosis-related macro-reentry mechanism. Thus, ARVC is one of the main causes of arrhythmic cardiac arrest in young people and athletes.¹

Although initially designated as dysplasia, ARVC is not a congenital defect in the myocardium development. It is caused by mutations in the genes that encode desmosomal proteins, which are responsible for cell-to-cell adhesion. This discovery led to the disease being recognized as cardiomyopathy and included in the classification of cardiomyopathies by the American Heart Association.^{1,2}

Diagnosis is complex due to the diverse clinical presentations, intra and interfamilial variations of expressiveness and incomplete penetration. Since the original report by Fontaine and Marcus in 1982, there have been substantial advances in understanding its pathogenesis, clinical manifestations, and long-term prognosis. However, this condition is still understudied and becomes a challenge when outside the most prevalent aspect.¹ A case report and literature review are presented, focusing on the current understanding of its pathogenesis, diagnostic evaluation with new imaging methods, and approach to risk stratification and therapy.

Case Report

A 72-year-old male was admitted to the emergency room with antacid-resistant epigastric pain. During the interview,

he denied having chest pain, dyspnea or palpitations. Furthermore, he revealed a history of chest pain on exertion, unspecified arrhythmia, hypertension and dyslipidemia. He denied any previous infarction episodes and/or alterations in previous cardiological exams. Upon physical examination, no relevant alterations were found. The diagnosis of non-ST-elevation myocardial infarction (NSTEMI) was established based on the electrocardiogram, which showed inverted T waves in inferior and anterior leads (Figure 1A), in addition to changes in ultrasensitive troponin, with typical infarction behavior. No electrocardiographic changes suggestive of RV infarction were observed.

An early invasive stratification was performed, where a subocclusive lesion was found in the middle third of the right coronary artery (Figure 1B), requiring percutaneous angioplasty and successful drug-eluting stent implantation. A transthoracic echocardiogram (TTE) was performed, showing preserved left ventricular ejection fraction and no changes in contractility, but severe RV involvement (akinesia and segmental dyskinesia, increased trabeculations, reduced strain, lateral wall microaneurysms and a significant ejection fraction reduction by 3D echocardiography; see Figure 2). Given these RV alterations and their disagreement with the angiographic (obstruction of the right coronary artery in the middle third, after the acute marginal branch origin) and clinical findings, primary RV disease was considered. Cardiac magnetic resonance imaging was performed, which corroborated the echocardiogram findings and showed alterations suggestive of ARVC, in addition to RV diffuse transmural enhancement that suggested it was secondary to fibrofatty infiltration (Figure 3). Upon gathering the findings of the evaluation with multimodality of cardiovascular imaging, the diagnosis of ARVC was established based on the Task Force criteria (Table 1).³

The 24-hour Holter identified frequent ventricular extrasystoles without complex arrhythmias. After discussion with the Heart Team and genetic disease specialists, the patient was classified at low risk for sudden death, therefore, without indication for implantable cardioverter defibrillator (ICD) at that time. Family members were instructed to perform additional screening. The patient was discharged from the hospital on dual antiplatelet therapy, statins, beta-blockers and angiotensin-converting enzyme inhibitors. He is currently under outpatient follow-up with no evidence of arrhythmic events.

Keywords

Echocardiography, Three-Dimensional; Global Longitudinal Strain; Arrhythmogenic Right Ventricular Dysplasia

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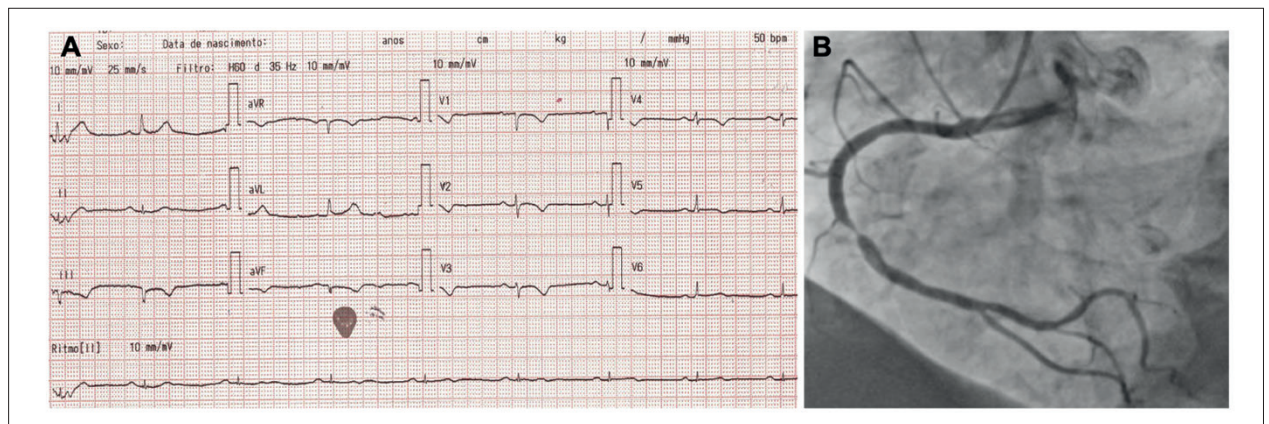


Figure 1 – A) Admission electrocardiogram with negative T waves in leads V1 to V5 and DIII and aVF; B) Cardiac catheterization showing a subocclusive lesion in the middle third of the right coronary artery.

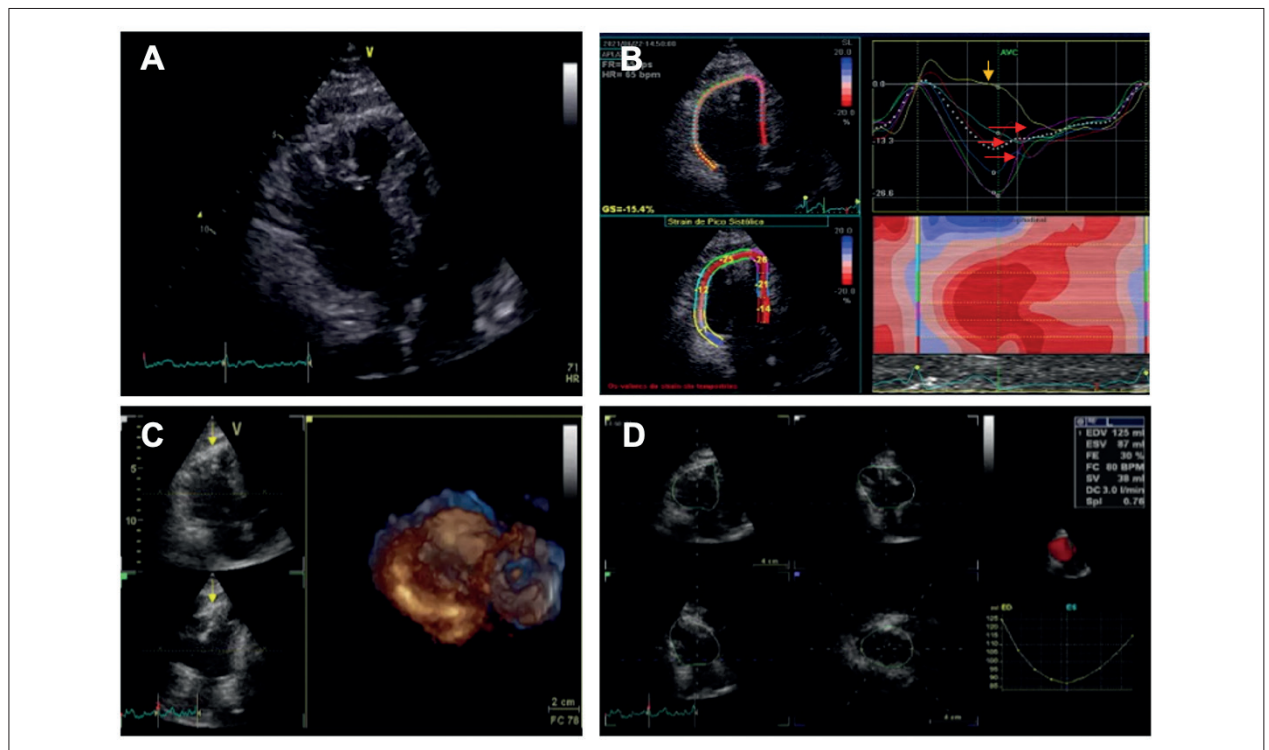


Figure 2 – TTE showing A) Significant dilation of the right ventricle (RV), associated with increased trabeculations and images suggestive of microaneurysm in the RV lateral wall; B) Reduced RV longitudinal strain, segmental dyskinesia (yellow arrow) and high mechanical dispersion (red arrow); and C, D) three-dimensional full volume method that identified an RV ejection fraction of 30%, corresponding to significant systolic dysfunction.

Discussion

Current literature discusses clinical indicators that raise the diagnostic suspicion of ARVC, such as (1) frequent ventricular ectopy; (2) ventricular tachycardia with superior axis LBBB morphology/multiple QRS morphologies; and (3) arrhythmogenic sudden death.⁴ However, the definitive diagnosis is hindered by the disease's low prevalence and lack of specific tests, becoming even more complex when affecting elderly patients.^{1,4} In this context, ARVC diagnosis

is performed using the Task Force criteria (2010),³ first listed in 1994 and revised in 2010 (Table 1), which, despite having limitations in their sensitivity, provides an efficient tool to direct diagnostic reasoning.¹ When applying the criteria, patients are submitted to structural, tissue and electrocardiographic investigation in search of major (two points) and minor (one point) findings. Patients who score four or more are diagnosed with ARVC, while those who score three are likely carriers of the disease.^{1,3,4}

Case Report

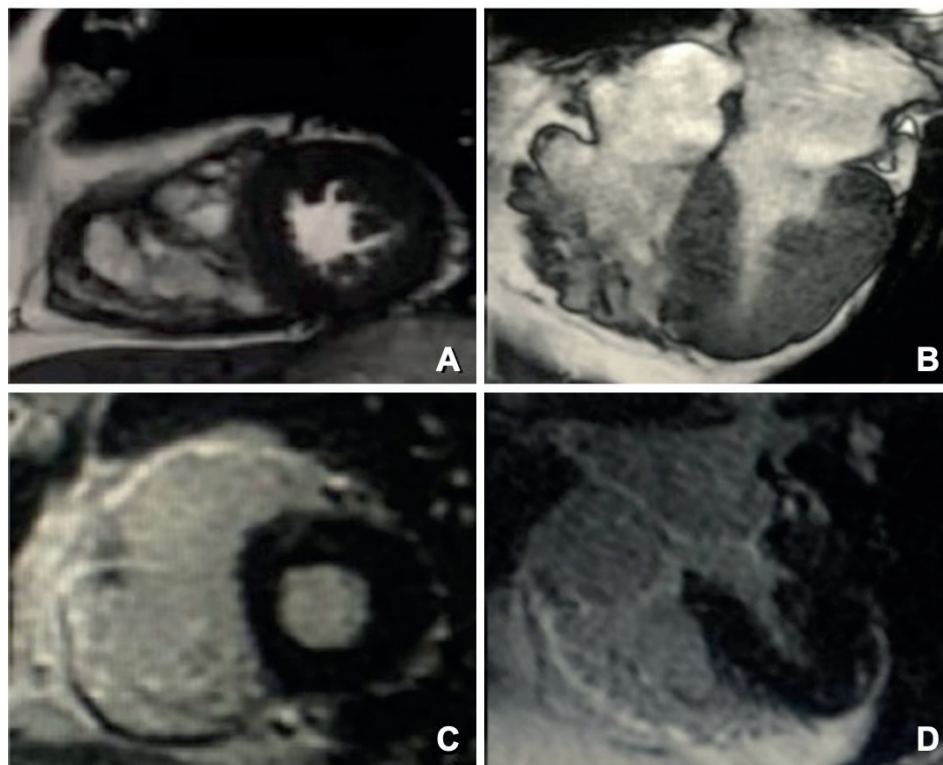


Figure 3 – A) Short-axis systolic view; and B) four-chamber view showing RV dilation and lateral wall alterations (microaneurysms). (C and D) RV diffuse transmurular delayed enhancement.

ARVC suspicion was only listed for the patient under investigation after the disagreement between the angiographic findings and the subsequent echocardiographic evaluation. In order to explain the RV alterations, such as those found, a proximal occlusion of the right coronary artery, reaching the acute marginal branch, with RV infarction characteristics, would be necessary, which was not revealed by the patient's exams or symptoms.

Moreover, changes in the electrocardiogram on admission disagree with the coronary disease found, with inverted T waves in V1-V3 leads being the most common finding in ARVC.⁴

The RV structural and functional findings on this case's echocardiogram and cardiac magnetic resonance are typical of ARVC, with segmental alteration being a compulsory factor.

Once the diagnosis of ARVC is established, it is important to decide how to manage the patient in order to reduce the risk of sudden death. Although ICD acts positively in reducing mortality from arrhythmic causes, its implantation has been related to short- and long-term complications. In relation to this, there is a lack of prospective and randomized studies that support the routine use of the ICD prophylactically.⁵ The estimation of the risk of sustained ventricular arrhythmia based on inherent characteristics of the patient and their history is an ally in management decisions.^{5,6} Some situations are considered high risk, such as patients with recovered cardiac

arrest or patients with previous events of sustained ventricular arrhythmia, history of arrhythmogenic syncope, significant RV and/or left ventricular systolic dysfunction. Shared decision-making between patient and physician should always be considered regarding risks, benefits and longevity itself.⁶

An American cohort with 312 patients with ARVC showed that ventricular tachycardia at presentation or its induction by electrophysiological study, male patients, inverted T waves in ≥ 3 precordial leads, and premature ventricular contraction count $\geq 1000/24h$, were predictors of appropriate therapy in patients with ICD.⁷ However, further studies are needed to better individualize the risk of sudden death in these situations.

The combination of pharmacological therapy through beta-blockers and antiarrhythmics are measures that minimize the use of appropriate therapy by the ICD. Also, part of the recommendation is neurohormonal blockades with angiotensin-converting enzyme inhibitors and beta-adrenergic receptor antagonists. Another recommended therapy is catheter ablation, although it has been shown not to be able to reduce the risk of sudden death and increase survival rates, being categorized as an adjuvant therapy.^{5,8}

Conclusion

ARVC is a hard-to-diagnose genetic disorder often associated with adverse clinical outcomes. With advances

Table 1 – Task Force Criteria for the Diagnosis of ARVC (2010)³

1 – Structural changes and global or regional dysfunction
Major criteria – Two-dimensional echocardiogram: Regional RV aneurysm, akinesia, or dyskinesia associated with one of the following diastolic measures: RVOT PLAX ≥ 32 mm (PLAX/BS ≥ 19 mm/m²) or RVOT PSAX ≥ 36 mm (PSAX/BS ≥ 21 mm/m²) or Change in fractional area $\leq 33\%$ – Cardiac Magnetic Resonance Regional RV dyskinesia or akinesia, or RV contraction dyssynchrony associated with one of the following: RV EDV BS ≥ 110 mL/m² (male) or ≥ 100 mL/m² (female) RV ejection fraction $\leq 40\%$ Right ventriculography RV aneurysm, akinesia, or dyskinesia
Minor criteria – Two-dimensional echocardiogram: RV dyskinesia, akinesia, or RV contraction dyssynchrony, and one of the following diastolic function measures: RVOT PLAX ≥ 29 to < 32 mm (PLAX/BS ≥ 16 to < 19 mm/m²) or RVOT PSAX ≥ 32 to < 36 mm (PSAX/BS ≥ 18 a < 21 mm/m²) or Change in fractional area $> 33\%$ to $\leq 40\%$ – Cardiac Magnetic Resonance Regional RV dyskinesia or akinesia, or RV contraction dyssynchrony, and one of the following: RV EDV/BS ≥ 100 to 110 mL/m² (male) or ≥ 90 to 100 mL/m² (female) RV ejection fraction > 40 to $\leq 45\%$
2 – Tissue aspects
Major criteria Residual myocyte count $< 60\%$ by morphometric analysis (or $< 50\%$ if estimated), with RV free wall fibrous replacement in ≥ 1 sample, with or without fatty replacement tissue on endomyocardial biopsy.
Minor criteria Residual myocyte count from 60% to 70% by morphometric analysis (or 50% to 65% if estimated), with RV free wall fibrous replacement in ≥ 1 sample, with or without fatty replacement tissue on endomyocardial biopsy.
3 – Repolarization abnormalities
Major criteria Inverted T waves in right precordial leads (V1, V2, and V3) or extending beyond V3 in individuals > 14 years old (in the absence of RBBB-QRS ≥ 120 ms)
Minor criteria Inverted T waves in V1 and V2 in individuals > 14 years old (in the absence of RBBB) Inverted T waves in V1, V2, V3, and V4 in individuals > 14 years old (in the presence of RBBB)
4 – Depolarization/conduction abnormalities
Major criteria Epsilon wave (reproducible low amplitude signals between the end of QRS and the beginning of the T wave) in the right precordial leads (V1 - V3)
Minor criteria Late potentials on HR-ECG in ≥ 1 of 3 parameters in the absence of QRS ≥ 110 msec on 12-lead ECG: Filtered QRS (fQRS) duration ≥ 114 msec QRS terminal duration < 40 microV ≥ 38 ms Terminal mean square voltage 40 ms ≤ 20 microV Duration of the final portion of the QRS ≥ 55 ms (measured from the nadir of the S wave to the end of ventricular depolarization - including R') in V1, V2 or V3

Case Report

5 – Arrhythmias

Major criteria

Unsustained or sustained VT with RBBB-like morphology and superior axis

Minor criteria

Non-sustained or sustained VT with morphology suggestive of RVOT (LBBB-type morphology and inferior or indeterminate axis) or > 500 ventricular extrasystoles/24h on 24h Holter

6 – Family history

Major criteria

ARVD/D in a first-degree relative who meets this task force 2010 criteria

Pathologically confirmed ARVD/D in a first-degree relative (autopsy or biopsy)

Identification of pathogenic mutation classified as associated or probably associated with ARVD/D in the patient under evaluation

Minor criteria

History of ARVD/D in first-degree relatives

History of ARVD/D in a first-degree relative for whom it was not possible to determine if criteria are met

Premature sudden death (< 35 years old) with suspected ARVD/D in a first-degree relative

ARVD/D confirmed pathologically or according to the criteria in a second-degree relative

ARVD/D: arrhythmogenic right ventricular heart disease/dysplasia; BSA: body surface area; CMR: cardiac magnetic resonance; ECG: electrocardiogram; EDV: end-diastolic volume; RBBB: right bundle branch block; LBBB: left bundle branch block; PLAX: long-axis parasternal window; PSAX: short-axis parasternal window; RV: right ventricular; RVOT: right ventricular outflow tract; HR-ECG: high-resolution electrocardiogram; VT: ventricular tachycardia; BS: body surface.

in complementary exams and greater knowledge about the patients' profiles, more and more cases of the disease have been discovered. Diagnosis in elderly patients makes management even more complex, requiring careful evaluation by the multidisciplinary team. Although ICD implantation is considered the most accepted therapeutic strategy in individuals with ARVC, adequate stratification of the patient's risk, as well as additional data about their clinical history, is required to analyze its indication.

Author Contributions

Conception and design of the research: Fernandes RM, Souza VQC; acquisition of data and analysis and interpretation of the data: Fernandes RM, Weber LC, Souza VQC, Guedes MB, Azevedo DFC; writing of the manuscript: Fernandes RM, Weber LC, Souza VQC, Guedes MB; critical revision of the manuscript for intellectual content: Fernandes RM, Weber LC, Guedes MB, Azevedo DFC, Rabelo MMN.

References

1. Corrado D, Link MS, Calkins H. Arrhythmogenic Right Ventricular Cardiomyopathy. *N Engl J Med*. 2017;376(15):1489-90. doi: 10.1056/NEJMc1701400.
2. Corrado D, Basso C, Judge DP. Arrhythmogenic Cardiomyopathy. *Circ Res*. 2017;121(7):784-802. doi: 10.1161/CIRCRESAHA.117.309345.
3. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, et al. Diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia: Proposed Modification of the Task Force Criteria. *Eur Heart J*. 2010;31(7):806-14. doi: 10.1093/eurheartj/ehq025.
4. Elias J Neto, Tonet J, Frank R, Fontaine G. Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVC/D) - What We Have Learned after 40 Years of the Diagnosis of This Clinical Entity. *Arq Bras Cardiol*. 2019;112(1):91-103. doi: 10.5935/abc.20180266.
5. Calkins H, Corrado D, Marcus F. Risk Stratification in Arrhythmogenic Right Ventricular Cardiomyopathy. *Circulation*. 2017;136(21):2068-82. doi: 10.1161/CIRCULATIONAHA.117.030792.
6. Towbin JA, McKenna WJ, Abrams DJ, Ackerman MJ, Calkins H, Darrieux FCC, et al. 2019 HRS Expert Consensus Statement on

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

- Evaluation, Risk Stratification, and Management of Arrhythmogenic Cardiomyopathy. *Heart Rhythm*. 2019;16(11):e301-e372. doi: 10.1016/j.hrthm.2019.05.007.
7. Orgeron GM, James CA, Te Riele A, Tichnell C, Murray B, Bhonsale A, et al. Implantable Cardioverter-Defibrillator Therapy in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy: Predictors of Appropriate Therapy, Outcomes, and Complications. *J Am Heart Assoc*. 2017;6(6):e006242. doi: 10.1161/JAHA.117.006242.
 8. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. 2015 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J*. 2015;36(41):2793-867. doi: 10.1093/eurheartj/ehv316.



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