Case Report

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Arrhythmogenic Right Ventricular Dysplasia: Case Report and Literature Review

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Introduction

Arrhythmogenic right ventricular dysplasia (ARVD) is an inherited cardiomyopathy anatomically and pathologically characterized by fibrofatty replacement of the right ventricular (RV) myocardium, causing RV electrical instability and structural abnormalities, resulting in ventricular arrhythmias.[1] The RV is usually more affected, however, the left ventricle (LV) may also be involved.[2]

Patients present different symptoms, especially after puberty and before the age of 50.[3] In addition, family history is present in 30% to 70% of cases due to autosomal dominant inheritance.[4]

Natural history is characterized by electrical ventricular instability, mainly by ventricular tachycardia (VT), which can evolve in 5 to 20% of cases for sudden death (SD), more prevalent in young patients and athletes.[1,3]

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A 42-year-old female patient reported chest discomfort, dyspnea and syncope. On physical examination, she had tachycardia (HR = 200 bpm); electrocardiogram (ECG) showed VT with left bundle branch block pattern (Figure 1A). Electrical cardioversion (ECV) was performed and, after stabilization, a new ECG was performed (Figure 1B). On physical examination, after ECV, the patient had regular heart rhythms, normal-sounding sounds and no murmurs; vesicular murmur present in both hemithorax, without adventitious noises and laboratory tests (cardiac enzymes; electrolytes; renal function; negative Chagas' disease serology; thyroid function) were normal.

Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) revealed increased RA (indexed volume = 73.5 ml/m^2 — reference value: 25 ± 7ml/m^2); increased RV (baseline diastolic diameter = 50.8 mm -

reference value: up to 40 mm; right ventricular proximal outflow tract in longitudinal parasternal axis view = 51.3 mm — reference value: 21-35 mm; outflow tract diameter in transverse parasternal axis view = 37.1 mm — reference value: up to 27mm); diffuse hypokinesia and RV dysfunction (TAPSE = 13.5 mm — reference value: greater than 17 mm; S' on TDI = 7.46 cm/s — reference value: greater than 9.5 cm/s and FAC = 31% — reference value: greater than 35%); preserved LV systolic function (Figures 2 and 3). Atrial septum was intact and the pulmonary and tricuspid valves did not present morphological changes.

HOLTER evidenced left branch conduction disorder; 337 supraventricular extrasystoles; 8747 ventricular extrasystoles; 7 nonsustained VT episodes.

Modified ECG was performed with Fontaine leads (Figure 4), revealing the epsilon wave.

Based on the Task Force criteria (2010), ARVD was diagnosed and the drug therapy was started, recommending implantable cardioverter defibrillator (ICD).

Discussion

In 1994, the World Health Organization classified ARVD as part of nonischemic cardiomyopathies.[5,6]

It is more common in males (3: 1), young people, and is an important cause of SD in young athletes, accounting for less than 10% of SD in people younger than 65.[6]

The clinical condition usually appears between the second and fourth decades of life. Patients may report palpitations consequent to ventricular extrasystoles, VT, signs of heart failure, syncope and even SD. ARVD is often underdiagnosed.[7]

ARVD is associated with two syndromes: Naxos and Carvajal. Naxos syndrome is an autosomal recessive disorder related to the mutation of the placogobine gene (17q21), characterized by cardiocutaneous impairment: right ventricular arrhythmogenic dysplasia, sheep wool hair and palmoplantar hyperkeratosis. Carvajal syndrome is related to the mutation of the desmoplaquine gene (6p24) and is characterized by curly hair, palmoplantar hyperkeratosis and dilated cardiomyopathy.[7]

Diagnosis is based on ECG findings (Table 1), HOLTER, endomyocardial biopsy, family history and imaging tests (Task Force: 2 major or 1 major and 2 minor or 4 minor of different categories)[6,7] revised in 2010 that raised sensitivity and maintained specificity.

Abnormalities on electrocardiography are found in more than 90% of patients with ARVD.[8] About 40% of patients may present normal ECG, but all of them will present abnormalities

Keywords

Arrhythmogenic Right Ventricular Dysplasia/Genetic; Tachycardia, Ventricular; Electric Countershock; Electrocardiography; Echocardiography.
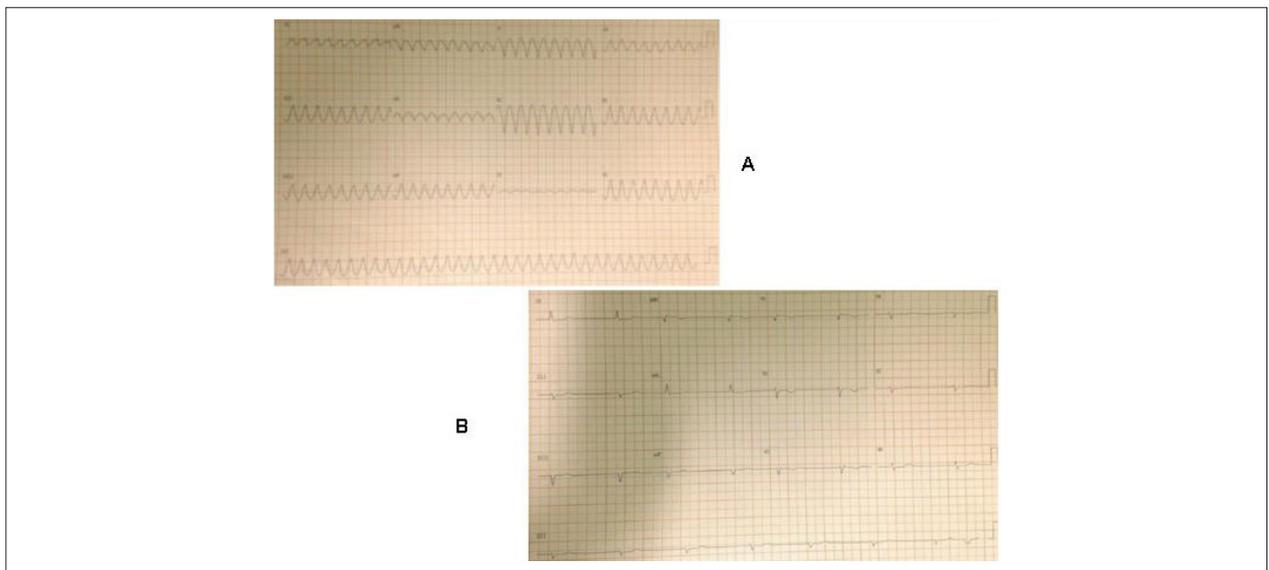
Figure 1 – *A: 12-lead ECG showing VT with left bundle branch block pattern. B: 12-lead ECG showing inverted T waves in V1, V2 and V3.*
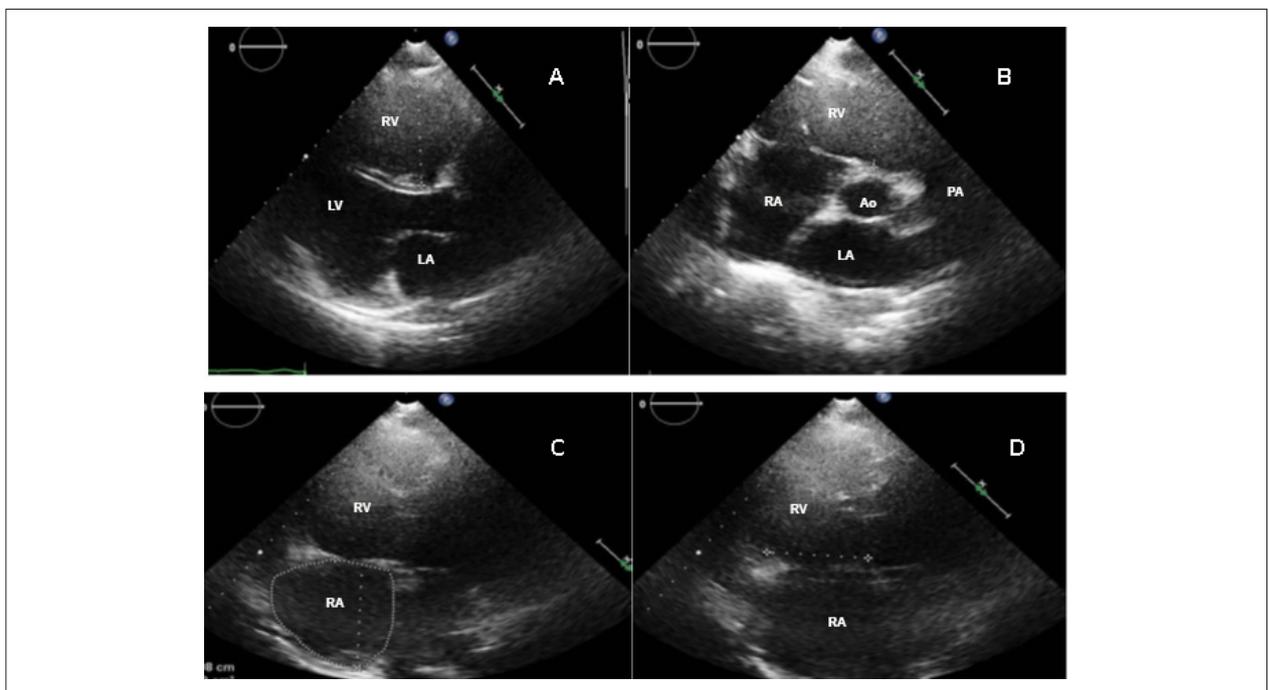

Figure 2 – *A: TTE — parasternal long axis window. Proximal diameter of RVOT = 37.1 mm. LA: left atrium; LV: left ventricle; RV: right ventricle; RVOT: right ventricular outflow tract; PA: pulmonary artery. B: TTE: parasternal short axis window. RVOT diameter = 51.3 mm. C: TTE — apical four-chamber window. RA indexed volume = 73.1 ml/m². D: TTE — apical four-chamber window. RV baseline diameter = 50.8 mm.*

over 6 years, with repolarization disorders being frequent. Delay in terminal activation and fragmented QRS are also prevalent. Low amplitude and fragmentation of QRS are independent risk factors for adverse events. The prevalence of epsilon waves is up to 30%, being one of the major criteria for the diagnosis of ARVD, but it has low specificity.[7,8]

Fontaine lead was developed to increase diagnostic sensitivity: the right arm electrode is placed in the sternal manubrium, the left arm electrode is placed in the xiphoid appendix and the left leg electrode is placed in the V4 position (Figure 4). Twice the speed (50 mm/s), double the voltage (20 mm/s) and 40 Hz filter are applied, increasing the sensitivity to detect the epsilon wave in 66% compared to the conventional ECG.[9]

HOLTER is also important because exercise-induced VT and ventricular ectopy are common manifestations. The high number of ventricular ectopies is associated with increased appropriate shock and recurrence of VT after ablation.[1]
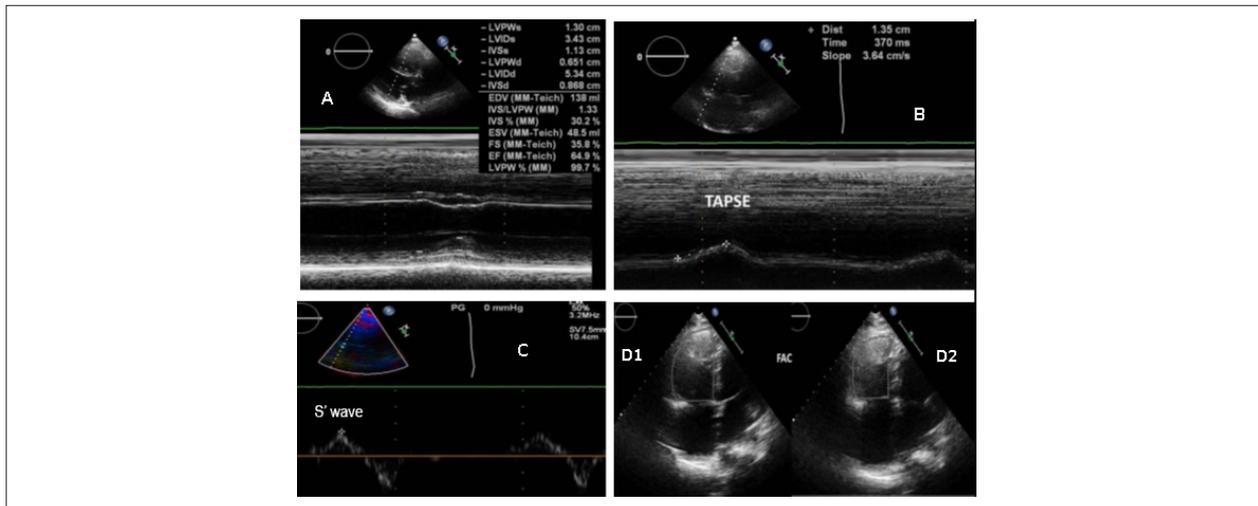
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Figure 3 – A: TTE. M-mode LV systolic function. B: TTE. M-mode RV systolic function. (TAPSE = 13.5 mm). TAPSE: tricuspid annular plane systolic excursion. C: TTE. RV systolic function on tissue Doppler (S' wave velocity = 7.46 cm/s). D: RV systolic dysfunction - FAC = 31% (D1: measured in diastole, D2: measured in systole). FAC: fractional area change.
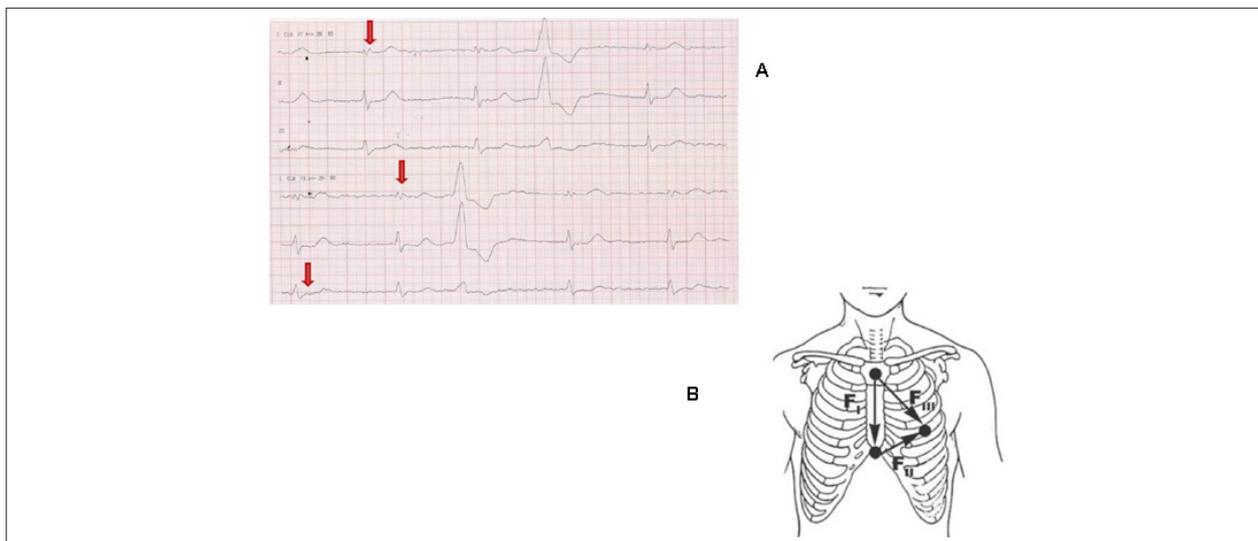

Figure 4 – A: 3-lead ECG - Fontaine leads showing the epsilon wave (red arrows). B: Positioning of the leads to record ECG with the Fontaine leads.

Table 1 – Electrocardiographic risk score for diagnosis of ARVD

Electrocardiographic risk score for ARVD	Score
Anterior T wave inversion in sinus rhythm	3
VT/VES:	
• QRS duration > 120 ms	2
• QRS deflection in (multiple leads)	2
• Transition in V5 or after	1
TOTAL SCORE	8

Score greater than or equal to 5 points differentiates ARVD from idiopathic VT in 93% of the times (sensitivity 84%, specificity 100%, positive predictive value of 100% and negative predictive value of 91%).

TTE is initially the first line test, as it is not invasive, but it is operator dependent and it is usually difficult to view the RV free wall. Structural and functional RV abnormalities are evaluated using this method. LV involvement may be present in some familial forms and has an impact on the prognosis of patients.[8] Furthermore, it is reported that LVEF and STRAIN of both ventricles are related to patient prognosis, having a decreased survival when LVEF < 50% and when they had altered strain, biventricular in relation to RV involvement only.[9] The RV longitudinal strain is superior to conventional echocardiographic parameters to identify cases of ARVD, and may be useful in diagnostic investigation in patients suspected of such pathology. However, its ability to differentiate ARVD from other RV changes is not yet known.[10]

Magnetic resonance imaging is an operator-independent test with better image definition. The criteria evaluated in the Task Force are: qualitative evaluation of regional kinetics (akinesia, dyskinesia, hypokinesia, micro or macroaneurysms; quantification of RV dimensions and functions (FE reduction and RV dilatation). Using gadolinium, myocardial fibrofatty replacement is observed and correlates with the endomyocardial biopsy and increased risk of VT induction, as it identifies areas of fibrosis, mapping the arrhythmogenic regions.[8] The most commonly observed locations are the "dysplasia triangle," which corresponds to the RV inflow tract, RV outflow tract and RV apex. However, it has been shown that the most affected regions are the epicardium of the subtricuspid region, the basal portion of the RV free wall and the LV lateral wall, with the RV apex and the endocardium generally spared.[11]

Finally, endomyocardial biopsy and immunohistochemical analysis establish the diagnosis, demonstrating myocardial fibrofatty replacement, but there is a possibility of a false negative.[1]

Treatment is based on the following three factors: risk stratification, minimization of arrhythmia and slowing of disease progression. Patients with a history of sustained VT or ventricular fibrillation are at high risk for arrhythmogenic events. Family history of SD is not a risk factor for adverse prognosis.[1]

The goals of antiarrhythmic drug treatment are to promote better quality of life and prevent VT. Amiodarone 400 to 600 mg per day can be used for 3 weeks; then 200 to 400 mg per day (maintenance), associated or not with beta-blockers. Beta-blockers are recommended in the treatment of patients with ARVD, who develop appropriate shock, recurrent VT, and in cases associated with supraventricular tachycardias.[3,12]

Patients with RV dilation have an annual incidence of 0.5% with complications due to thromboembolic phenomena. Therefore, in these patients, the use of anticoagulants is necessary.[3] In patients who develop right or left HF, treatment is based on the use of ACE inhibitors, beta-blockers and diuretics.[3]

Fatty replacement of the cardiac muscle results in the formation of arrhythmogenic substrate, favoring the recurrence of VT. In these cases, ablation of these areas can be performed, with success rates of 60% to 80%; however, the recurrence rate ranges from 50% to 70% in 3 to 5 years. Although there are no prospective randomized studies, a number of observational studies show that ICD increases the survival of patients with ARVD. In 10-15% of the cases, there are inappropriate shocks due to sinus tachycardia or AF. ICD is recommended in patients with sustained VT or aborted SD.[10,11] According to the 2006 AHA/ACC/ESC guideline, ICD implantation is recommended with class I for the prevention of sudden death in patients with right ventricular arrhythmogenic cardiomyopathy with documented VT and VF, under optimal clinical treatment, with life expectancy greater than one year. Class II indication includes patients with: Extensive ARVD; involvement of the left ventricle; family history of one or more members with aborted sudden death; syncope not diagnosed when TV or VF were not excluded as possible causes; optimized clinical treatment; life expectancy greater than one year.[11,12]

Conclusion

This report illustrates a case in which clinical criteria and complementary tests establish the diagnosis of ARVD.

The management of patients with ARVD has undergone important and crucial changes. Treatment is based on the prevention of SD and improvement of patients' quality of life, especially with implantation of ICD.

Authors' contributions

Research creation and design: Gouveia GNM; Data acquisition: Lima CJM; Data analysis and interpretation: Gonçalves BKB; Manuscript drafting: Alcantara ACB; Critical revision of the manuscript as for important intellectual content: Gomes CAM, Evangelista NL.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

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Academic Association

This study is not associated with any graduate program.

References

1. Philips B, Cheng A. 2015 update on the diagnosis and management of arrhythmogenic right ventricular cardiomyopathy. Curr Opin Cardiol. 2016;31(1):46-56. doi:10.1097/HCO.0000000000000240.

2. Watkins H, Ashrafian H, Redwood C. Inherited cardiomyopathies. N Engl J Med. 2011;364(17):1643-56. doi:10.1056/NEJMra0902923.

3. Prakasa KR, Calkins H. Arrhythmogenic right ventricular dysplasia/cardiomyopathy. Curr Treat Cardiovasc Med.2005;7(6):467-75. doi: PMID:16283974.

4. Naccarella F, Naccarelli G, Fattori R, Nava A, Martini B, Corrado D, et al. Arrhythmogenic right ventricular dysplasia: cardiomyopathy current opinions on diagnostic and therapeutic aspects. Curr Opin Cardiol. 2001;16(1):8-16. PMID:11247 13

5. Te Riele AS, Hauer RN. Arrhythmogenic right ventricular dysplasia/cardiomyopathy: clinical challenges in a changing disease spectrum. Trends Cardiovasc Med. 2015;25(3):191-8.

6. Asimaki A, Kleber AG, Saffitz JE. Pathogenesis of arrhythmogenic cardiomyopathy. Can J Cardiol. 2015;31(11):1313-24. doi:10.1016/j.cjca.2015.04.012

7. Corrado D, Wichter T, Link MS, Hauer RN, Marchlinski FE, Anastasakis A, et al. Treatment of Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia: An International Task Force Consensus Statement. Circulation. 2015;132(5):441-53. doi:10.1161/CIRCULATIONAHA.115.017944

8. Mast TP, Teske AJ, vd Heijden JF, Groeneweg JA, Te Riele AS, Velthuis BK, et al. Left Ventricular Involvement in Arrhythmogenic Right Ventricular

Dysplasia/Cardiomyopathy Assessed by Echocardiography Predicts Adverse Clinical Outcome. J Am Soc Echocardiogr. 2015;28(9):1103-13.e9. doi: 10.1016/j.echo.2015.04015

9. Gottschalk B, Gysel M, Barbosa-Barros R, De Sousa Rocha RP, Pérez-Riera AR, Zhang L, et al. The use of fontaine leads in the diagnosis of arrhythmogenic right ventricular dysplasia. Ann Noninvasive Electrocardiol. 2014;19(3):279-84. doi:10.1111/anec.12153.

10. Almeida ALC, Gjesdal O, Mewton N, Choi E-Y, Teixido-Tura G, Yoneyama K, et al. Speckle-Tracking pela ecocardiografia bidimensional – aplicações clínicas. Rev Bras Ecocardiogr Imagem Cardiovasc. 2013; 26(1):38-49.

11. Saguner AM, Brunckhorst C, Duru F. Arrhythmogenic ventricular cardiomyopathy: A paradigm shift from right to biventricular disease. World J Cardiol. 2014;6(4):154-74. doi:10.4330/wjc.v6.i4.154

12. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol. 2006;48(5):e247-346. doi:10.1016/j.jacc.2006.07.010.