Journal of Clinical Cases

Arrythmogenic Right Ventricular Dysplasia: Case Report

Camila Araujo Nogueira[1*], Rodolfo Alves Antônio Silva do Nascimento[2], Michel Ulloffo do Nascimento[3] and Charlene Troiani do Nascimento[4]

[1]Medical Student at Faculdade de Medicina de Presidente Prudente
[2]Medical Student at Faculdade de Medicina de Presidente Prudente
[3]Co-advisor and Cardiologist at Hospital Regional de Presidente Prudente
[4]Advisor and Cardiologist at Hospital Regional de Presidente Prudente

[1*]Corresponding author:
Camila Araujo Nogueira,
Medical Student at Faculdade de Medicina de Presidente Prudente, Brazil,
Telephone: +55 67 99948-7452
E-mail: milanogueira@hotmail.com

Received Date: 28 March 2024
Accepted Date: 11 April 2024
Published Date: 17 April 2024

Citation:
Camila Araujo Nogueira. Arrythmogenic Right Ventricular Dysplasia: Case Report. Journal of Clinical Cases 2024.

1. Summary

Arrhythmogenic Right Ventricular Dysplasia (ARVD) is an inherited cardiomyopathy associated with the replacement of myocytes by fibrous and/or fibroadipose tissue, usually manifesting between the third and fifth decades of life. In the arrhythmic phase, when it becomes symptomatic, the patient may experience palpitations, syncope, and symptomatic ventricular arrhythmias originating in the right ventricle (RV). The absence of unique and specific diagnostic criteria is a factor that complicates and delays diagnosis. The main examinations performed are electrocardiogram (ECG), echocardiogram, and magnetic resonance imaging (MRI), often showing negative T waves, widening of the QRS complex with larger S waves, presence of late potentials, incomplete, complete, or atypical right bundle branch block, combined or isolated, in addition to the epsilon wave which is characteristic of ARVD. This article aimed to report the clinical case of a patient with ARVD, from the onset of signs and symptoms to the outcome of the case. The patient was admitted with a typical clinical picture of decompensated heart failure and during complementary exams, the possibility of ARVD was suggested, even with the nonspecific clinical presentation, later confirming the diagnosis with cardiac magnetic resonance imaging (MRI) and endomyocardial biopsy. ARVD is a disease with difficult early diagnosis, often confused with other pathologies due to presenting signs and symptoms characteristic of other heart diseases. Adherence to pharmacological treatment alleviates symptoms and improves quality of life, but in addition, lifestyle changes and regular follow-up are of paramount importance.

2. Keywords:
Arrhythmia; Arrhythmogenic dysplasia; Diagnosis; Treatment.

3. Introduction

Arrhythmogenic Right Ventricular Dysplasia (ARVD), also known as Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), is an inherited cardiomyopathy associated with the replacement of myocytes by fibrous and/or fibroadipose tissue [1,2,3]. The lesion may extend from the epicardium to the endocardium, usually located between the pulmonary infundibulum, apex, and inferior-posterior wall of the right ventricle (RV), an area known as the "triangle of dysplasia" [1]. The overall prevalence of ARVD is 1:2,000 to 1:5,000 individuals, with a predominance in the Caucasian population and athletes, usually manifesting between the third and fifth decades of life [4,5]. It is very rare in individuals under 12 years of age or over 60 years [4] of age and generally affects males, due to sex hormones and more intense exercise practice [6]. There are four classification phases described, depending on the progression of structural changes and clinical symptoms, namely: hidden phase, still asymptomatic, with discrete structural abnormalities; arrhythmic phase, with palpitations, syncope, and symptomatic ventricular arrhythmias originating in the RV; RV failure phase, compromising its functions and resulting in heart failure (HF); biventricular failure phase, the most advanced stage with involvement of the interventricular septum, resulting in congestive heart failure (CHF), and thrombus formation in aneurysms formed in the RV or due to atrial fibrillation (AF) [4]. This pathology usually manifests with RV dilation, extension to the left side, expression of late potentials on the electrocardiogram (ECG), and fibrofatty infiltration in ventricular biopsy samples, which may lead to HF and even sudden cardiac death (SCD) [1]. However, fatty infiltration is not considered a diagnostic criterion, with extensive loss of myocytes and a large amount of fibrous tissue being more indicative.

Lymphocytic inflammatory infiltrates, focal necrosis, and signs of apoptosis are commonly found in myocardial biopsies [1]. Diagnosing this cardiomyopathy remains a major challenge, given the absence of unique and specific diagnostic criteria, often confused with other arrhythmogenic diseases affecting the RV [1,3]. ARVD originates from the RV and was previously described as an isolated and predominant disease of the same, however, it is now known that in the initial phase, it is frequently biventricular, further widening the range of possibilities for other possible causes of signs and symptoms [1,7]. The ECG may show negative T waves, related to RV dilation. QRS complex widening may also occur, with larger S waves, presence of late potentials, incomplete, complete, or atypical right bundle branch block, combined or isolated. The epsilon wave is characteristic of ARVD and is present in the ECG

due to epicardial perivalvular activation, manifesting at the end of the QRS complex, in the ST segment, as a small-amplitude post-ventricular excitation electrical potential [1,8]. Transthoracic echocardiography (TTE) allows identification of some macroscopic alterations resulting from RV dilation and/or global systolic dysfunction. Regional akinesia, dyskinesia, or asynchrony, combined with RV dilation and/or dysfunction, can be observed [1]. Ejection fraction is usually reduced biventricularly [9]. Cardiac magnetic resonance imaging (MRI) allows morphological and kinetic analysis, with volume, mass, and thickness of cardiac chambers, being considered the gold standard [3]. It is frequently used in patients with ARVD, being the best way to identify regional fibrosis and diastolic dysfunction [10].

Treatment of patients with ARVD is important to reduce symptoms, improve quality of life, and aim to prevent complications resulting in HF or CHF, also reducing mortality due to these conditions and arrhythmic SCD [4]. Pharmacological treatment can be performed through chronic administration of beta-blockers or class 1 and 3 antiarrhythmic agents. Lifestyle changes are also necessary, as intense physical exercise is a factor in disease progression. Endocardial and/or epicardial catheter ablation and sympathetic denervation are also therapeutic options [7]. Radiofrequency catheter ablation is indicated for patients with sustained monomorphic ventricular tachycardia episodes (MVT) [6]. Finally, an implantable cardioverter-defibrillator (ICD) or heart transplant may also be indicated for these patients [4,6,11]. Screening of first-degree relatives should be done to identify possible cases of ARVD early, as it is an autosomal dominant inherited disease. Cardiac evaluation can preferably be initiated between 10 and 12 years of age, as manifestation of the disease before this age is rare. Exams may include electrocardiogram, echocardiogram, and if possible, MRI and 24-hour Holter monitoring, to be repeated every 2 years until 50 years of age [4].

4. Justification

The variable expression of ARVD complicates diagnosis, as it presents clinical symptoms and imaging findings that can easily be mistaken for various other pathologies. Therefore, it is necessary to establish more diagnostic criteria to facilitate recognition, contributing to early identification. Providing scientific basis to assist in disease management, from initial clinical assessment, symptom monitoring, formulation of possible diagnosis, observation of findings in tests, therapeutic possibilities, to case outcome, is of utmost importance for better elucidation of this arrhythmogenic cardiomyopathy and the patient's prognosis.

5. Goal

To report the clinical case of a patient with ARVD, from the onset of signs and symptoms until the case outcome. In addition to understanding the disease beyond its theoretical aspect and addressing the characteristic and differential findings of ARVD.

6. Methodology

The data were collected through the review of both printed and electronic medical records, obtained at the Regional Hospital of Presidente Prudente, following the participant's informed consent and authorization from local committees. Medical, familial, and psychosocial history were observed. Findings from physical examinations were reported and elucidated, as well as the results of diagnostic methods, while considering differential diagnoses and challenges encountered in diagnostic elucidation, therapeutic possibilities, and prognosis. Similarly, therapeutic interventions performed were described, including dosage and posology, as well as preventive measures for disease complications. Finally, the outcome was described by associating data obtained from the patient's medical records regarding the case's progression and the literature studied.

7. Case Description

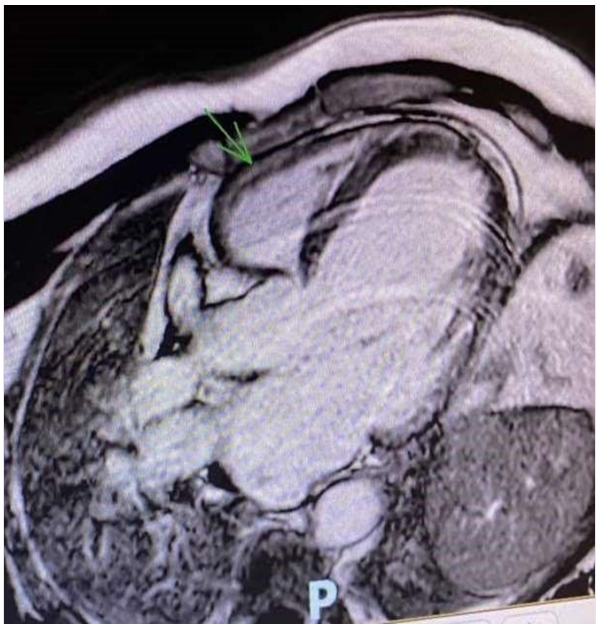
A 49-year-old male patient presented to the Regional Hospital of Presidente Prudente complaining of progressive dyspnea, with significant worsening over the past day. He reported experiencing cold sweats with minimal exertion and lightheadedness three days ago, followed by marked dyspnea with minimal exertion one day prior to seeking medical attention. The patient reported a history of progressively worsening dyspnea over the past 7 years, initially occurring during strenuous activities. He sought specialized care where he was diagnosed with heart failure with reduced ejection fraction (HFrEF) of 29% (Simpson's method), concentric left ventricular hypertrophy, and grade II diastolic dysfunction. Since then, he had been undergoing pharmacological treatment with dose adjustments and changes in medication classes, with irregular follow-up and persistent hypertension control issues and HF decompensations, necessitating medical attention. Additionally, he experienced weight gain during this period, with a decrease in ejection fraction to 20.9% over time and outpatient cardiac catheterization (resulting in markedly dilated left ventricle and diffuse hypokinesis ++++/4), indicating a non-ischemic etiology of HF. His medical history included systemic arterial hypertension (SAH) for the past 8 years, obesity, sedentary lifestyle, alcoholism, and anxiety. Regarding family medical history, he mentioned that his father died suddenly at 27 years old, without further details. Upon admission, physical examination revealed a fair general condition, blood pressure of 160/100 mmHg, heart rate of 78 bpm, respiratory rate of 25 breaths per minute, peripheral oxygen saturation of 92% on room air, and mild dyspnea at rest worsening with minimal exertion. Bilateral basal crackles were heard on pulmonary auscultation. The patient was admitted to the hospital for clinical and hemodynamic stabilization and further diagnostic tests. Intensive care with vasoactive drugs was initiated, starting with dobutamine followed by nitroglycerin, considering the functional class and profile C of HF presented, along with respiratory physiotherapy with non-invasive ventilation and oxygen supplementation, as well as symptomatic treatment.

Initial diagnostic tests included an electrocardiogram (sinus rhythm with supraventricular extrasystole, left chamber overload, and secondary

Journal of Clinical Cases

ventricular repolarization changes), chest X-ray (cardiomegaly and signs of pulmonary congestion), and laboratory tests. A transthoracic echocardiogram (TTE) was scheduled to be performed after clinical improvement. To further evaluate the differential diagnosis of dyspnea, a chest computed tomography (CT) scan was requested after clinical stabilization, including ruling out lung involvement due to SARS-CoV-2 infection, considering the peak of the COVID-19 pandemic. Until then, the complementary exams were suggestive of HF decompensation. After clinical improvement, a TTE revealed a significant worsening of HFrEF (15% - Simpson's method) and diastolic dysfunction (grade III with restrictive pattern). At this point, cardiac magnetic resonance imaging (MRI) (Figure 1) was requested for further diagnostic elucidation, which showed significant biventricular systolic dysfunction [Left ventricular ejection fraction (LVEF) = 7% and right ventricular ejection fraction (RVEF) = 12%], late gadolinium enhancement, and mild enhancement of the right ventricle, possibly corresponding to ARVD. It was decided to perform endomyocardial biopsy, which was carried out without complications, and await the anatomopathological report.

Figure 1: Cardiac Magnetic Resonance Imaging (MRI) elucidating, indicated by the arrowhead, the late gadolinium enhancement and mild enhancement of the right ventricle.



During the 24-hour Holter monitor, isolated supraventricular ectopic activity was recorded, with 29 isolated supraventricular extrasystoles observed during the examination and only 1 episode of paired supraventricular extrasystoles. Regarding isolated polymorphic ventricular ectopic activity, 2,913 isolated polymorphic ventricular extrasystoles were observed, along with 823 episodes of paired supraventricular extrasystoles and 71 episodes of non-sustained ventricular tachycardia (NSVT), consisting of 3 consecutive complexes. The longest NSVT episode occurred at 06:16:36 hours, with a frequency of 146 bpm. The patient clinically remained stable, without new complaints, and free from cardiovascular symptoms. Hospital discharge was decided for continuation of care in an outpatient setting, with instructions to await the anatomopathological report and emphasizing the importance of follow-up, correct medication use, life style changes, as well as the risks of poor therapeutic adherence and alarm signs, with instructions to seek medical attention if necessary. The diagnosis at discharge was HFrEF of etiological investigation, restrictive cardiomyopathy, systemic arterial hypertension (SAH), obesity, social alcoholism, in addition to a family history of paternal sudden death at 27 years old. ARVD remained as a suspected diagnosis, pending the definitive biopsy report. The discharge prescription included losartan 50 mg every 12 hours, carvedilol 6.25 mg every 12 hours, spironolactone 25 mg/day, dapagliflozin 10 mg/day, allopurinol 300 mg after lunch, and furosemide 40 mg in the morning. After approval by the high-cost pharmacy, losartan would be replaced by sacubitril/valsartan 24/26 mg/day. During the outpatient follow-up visit after discharge, the biopsy result revealed hypertrophy of muscle fibers and areas of hyalinization (Figure 2), corresponding to the histopathological pattern of ARVD. Therapeutic management included increasing the carvedilol dose to 25 mg every 12 hours, adjusting the sacubitril/valsartan dose to 12/12 hours, and initiating amiodarone 200 mg/day. A new Holter monitor was requested after these medication adjustments, along with laboratory tests, and a follow-up appointment in 3 months. In the diagnostic conclusion, the patient has biventricular HFrEF due to ARVD, systemic arterial hypertension (SAH), non-sustained ventricular tachycardia (NSVT), and hyperuricemia, under regular outpatient follow-up.

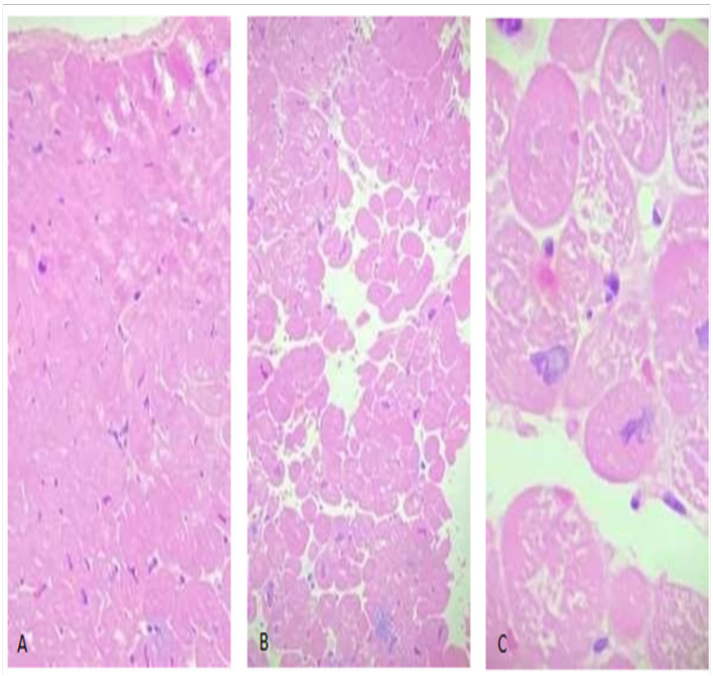


Figure 2: Electron microscopy slides obtained from endomyocardial biopsy. In A, an area of hyalinization can be observed. In B, hypertrophied cells with hyperchromatic nuclei and other cells without nuclei, along with areas of degeneration and increased spaces between cells. In C, severely hypertrophied cells.

Journal of Clinical Cases

8. Discussion

The patient experienced a late diagnosis, leading to complications of ARVD that could have been avoided and ultimately hindered the diagnosis, such as the patient's presentation with profile C HFrEF. Additionally, biventricular involvement was observed, which expands the diagnostic possibilities but is consistent with the pattern of involvement of the pathology in question [1,7]. Given that ARVD does not present with highly specific criteria, symptoms, and findings, the findings on cardiac MRI, the gold standard examination, were of paramount importance in diagnostic elucidation, indicating significant biventricular systolic dysfunction [3]. Furthermore, the identification of late gadolinium enhancement and mild enhancement of the right ventricle, which could correspond to ARVD, prompted endomyocardial and myocardial biopsy for further confirmation [1]. The anatomopathological report was crucial in concluding that the presentation was compatible with ARVD, showing hypertrophy of muscle fibers and areas of hyalinization, demonstrating that the disease does not always manifest with fatty infiltrations [1]. The transthoracic echocardiogram revealed an increase in the left ventricular diameter with significant contractile dysfunction, grade III diastolic dysfunction of the left ventricle, and a restrictive pattern. On the Holter monitor, several episodes of non-sustained ventricular tachycardia were observed, which is another common manifestation [1,9]. Regarding the clinical progression of the disease, symptoms such as palpitations, syncope, and symptomatic ventricular arrhythmias originating from the right ventricle belong to the arrhythmic phase [4]. The patient in this case did not present these symptoms; however, he experienced lightheadedness, a symptom that could potentially progress to syncope if left untreated.

Furthermore, there was a family history of sudden death in the father at the age of 27, raising the possibility that he also had ARVD, as the disease is hereditary and highly prevalent among first-degree relatives [1,2,3]. Pharmacological treatment alleviates symptoms and improves the patient's quality of life [4]. Chronic administration of amiodarone combined with beta- blockers is the most recommended therapy, given the synergistic effects of the antiarrhythmic properties of class III and beta-adrenergic blocking agentes [4]. Medications were prescribed for the patient during the consultation, and doses were optimized during outpatient visits. Additionally, it is important to raise awareness about the cessation of alcohol consumption and the need to properly adhere to medication regimens, along with regular outpatient follow-up, which the patient already receives. Lifestyle changes should be promoted, as intense exercise can exacerbate the progression of the disease [4]. Moreover, the patient is unable to adequately perform exercises due to the condition of heart failure, but cardiopulmonary rehabilitation assists in gradually increasing exercise intensity, leading to improved cardiovascular conditioning and quality of life.

9. Conclusion

ARVD is a disease that is difficult to diagnose early, often being mistaken for other pathologies due to presenting signs and symptoms characteristic of other heart diseases. MRI is crucial for indicating fibrosis, leading to confirmation of the definitive diagnosis through endomyocardial biopsy, supporting studies that dismiss the need for fatty infiltrations to confirm the diagnosis. Adherence to pharmacological treatment alleviates symptoms and improves quality of life, but it is also of paramount importance to make lifestyle changes and maintain regular follow-up.

References

1. Gandjbakhch E, Redheuil A, Pousset F, Charron P, Frank R. Clinical Diagnosis, Imaging, and Genetics of Arrhythmogenic Right Ventricular Cardiomyopathy / Dysplasia: JACC State-of-the-Art Review. J Am Coll Cardiol. 2018 Aug 14; 72 (7):784-804. doi: 10.1016/j. jacc.2018.05.065. PMID: 30092956.
2. Dolkar T, Nway N, Hamad AM, Jain H, Dufresne A. Arrhythmogenic Right Ventricular Cardiomyopathy. Cureus. 2022 Nov 13;14(11):e31446. doi: 10.7759 /cureus. 31446. PMID: 36523685; PMCID: PMC 9746880.
3. Manole S, Pintican R, Popa G, Rancea R, Dadarlat-Pop A, Vulturar R, Palade E. Diagnostic Challenges in Rare Causes of Arrhythmogenic Cardiomyopathy-The Role of Cardiac MRI. J Pers Med. 2022 Jan 31;12(2):187. doi: 10.3390/ jpm 12020187. PMID: 35207675; PMCID: PMC 8878419.
4. Elias Neto J, 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 Jan; 112(1): 91-103. doi: 10.5935/abc. 20180266. Erratum in: Arq Bras Cardiol. 2019 Feb; 112(2):214. PMID: 30673021; PMCID: PMC 6317628.
5. Valle NO do, Nobre M do N. Cardiomiopatia/ displasia arritmogênica do ventrículo direito: relato de caso. REAS. 2021 May; 13(5): e7881. DOI https://doi.org/10.25248/reas.e7881.2021
6. Cabalín CF, Staub KQ. Miocardiopatía arritmogénica del ventrículo derecho: particularidades del enfrentamiento diagnósticoen pediatría. Rev. Urug. Cardiol. 2018 Oct; 33 (3): 80-313. Disponible en: http://www.scielo.edu.uy/scielo.php? script=sci_arttext&pid = S 168804202018000 300280 & lng=es.
7. Elliott PM, Anastasakis A, Asimaki A, Basso C, Bauce B, Brooke MA, Calkins H, Corrado D, Duru F, Green KJ, Judge DP, Kelsell D, Lambiase PD, McKenna WJ, Pilichou K, Protonotarios A, Saffitz JE, Syrris P, Tandri H, Te Riele A, Thiene G, Tassopoulou A, van Tintelen JP. Definition and treatment of arrhythmogenic cardiomyopathy: an updated expert panel report. Eur J Heart Fail. 2019 Aug; 21(8): 955964. doi: 10.1002/ejhf. 1534. Epub 2019 Jun 18. PMID: 31210398; PMCID: PMC6685753.
9. Nunes de Alencar Neto J, Baranchuk A, Bayés-Genís A, Bayés de Luna A. Arrhythmogenic right ventricular dysplasia/ cardiomyopathy: an electrocardiogram based review. Europace. 2018 Jun 1;20(FI1):f3-f12. doi: 10.1093/europace/eux 202. PMID: 29272363.
9. Bosman LP, Te Riele ASJM. Arrhythmogenic right ventricular cardiomyopathy: a focused update on diagnosis and risk stratification.

Journal of Clinical Cases

Heart. 2022 Jan; 108(2):90-97. doi:. 1136/ heartjnl-2021 -319113. Epub 2021 May 14. PMID: 33990412.

10. Kubala M, Tschabrunn C, Marchlinski DF, Marchlinski FE. Overcoming challenges in the management of arrhythmogenic right ventricular cardiomyopathy. Kardiol Pol. 2020 May 25; 78(5): 386-395. doi: 10.33963/ KP.15374. Epub 2020 May 19. PMID: 32431133.

11. Wang W, James CA, Calkins H. Diagnostic and therapeutic strategies for arrhythmogenic right ventricular dysplasia/cardiomyopathy patient, EP Europace. 2019 Jan; 21(1):9-21. DOI https://doi.org/10.1093/europace/euy063