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CASO CLÍNICO

Arrhythmogenic Left Ventricular Cardiomyopathy: A Successful Case of Extracorporeal Cardiopulmonary Resuscitation

Miocardiopatia Arritmogénica do Ventrículo Esquerdo: Um Caso de Sucesso de Ressuscitação Cardiopulmonar Extracorporal

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ABSTRACT

A 24-year-old man suffered a witnessed cardiac arrest after a padel game. Basic life support was immediately provided. The pre-hospital emergency services team continued the resuscitation efforts, and the patient was accepted for extracorporeal cardiopulmonary resuscitation. The return of spontaneous circulation was achieved in 45 minutes. The initial assessment revealed a ST-segment elevation in leads V_4-V_6 and a dilated left ventricle with severe systolic dysfunction. Coronary angiography was normal. An improvement in left ventricular systolic function was observed and extracorporeal cardiac support was discontinued after 48 hours. Cardiovascular magnetic resonance imaging demonstrated hypokinesia and subepicardial fatty infiltration of the left ventricle lateral wall. Genetic testing detected a variant of uncertain significance in the *ANK2* gene. The diagnosis of arrhythmogenic left ventricular myocardiopathy did not fulfill all the current diagnostic criteria, but it is a very likely diagnosis. An implantable cardioverter-defibrillator was placed. The patient was discharged without physical or cognitive impairment.
Keywords: Arrhythmogenic Left Ventricular Cardiomyopathy; Cardiopulmonary Resuscitation; Extracorporeal Membrane Oxygenation; Heart Arrest/therapy

RESUMO

Homem de 24 anos sofreu uma paragem cardiorrespiratória presenciada após um jogo de padel. O suporte básico de vida foi imediatamente iniciado. A equipa de emergência pré-hospitalar manteve os esforços de ressuscitação e o doente foi aceite para ressuscitação cardiopulmonar extracorporal. O retorno da circulação espontânea foi atingido de imediato após 45 minutos. A avaliação inicial evidenciou elevação do segmento ST nas derivações V_4-V_6 e dilatação do ventrículo esquerdo com disfunção sistólica grave. Angiografia coronária sem alterações. Foi observada uma melhoria da função sistólica do ventrículo esquerdo e a oxigenação por membrana extracorporal veno-arterial foi suspensa após 48 horas. A ressonância magnética cardiovascular demonstrou hipocinésia da parede lateral e infiltração gordurosa subepicárdica na parede lateral do ventrículo esquerdo. O teste genético revelou uma variante de significado incerto no gene *ANK2*. Apesar do diagnóstico de miocardiopatia arritmogénica do ventrículo esquerdo não preencher todos os critérios diagnósticos atuais, é, no entanto, um diagnóstico muito provável. Foi colocado um cardioversor desfibrilador implantável. O doente teve alta sem compromisso físico ou cognitivo.
Palavras-chave: Miocardiopatia Arritmogénica do Ventrículo Esquerdo; Oxigenação por Membrana Extracorporal; Paragem Cardíaca/tratamento Ressuscitação Cardiopulmonar

INTRODUCTION

Sudden cardiac death is a devastating event that occurs unexpectedly. A significant number of cases are attributed to non-coronary causes with a genetic basis, such as cardiomyopathies, channelopathies and malignant arrhythmias.

The arrhythmogenic cardiomyopathy (ACM) is a heart muscle disease that affects the right ventricle (RV), the left ventricle (LV) or both, according to the 2020 International criteria for ACM. It is characterized structurally by a myocardial scar (fibro or fibrofatty myocardial replacement) and functionally by ventricular dysfunction. This myocardial scar is a predisposing factor for ventricular arrhythmias, which could present as sudden cardiac arrest, regardless of the severity of pump failure.[1,2]

The diagnosis of ACM is made by meeting the Padua criteria. A definitive diagnosis of arrhythmogenic left ventricle cardiomyopathy (ALVC) must meet one major structural LV criterion along with the presence of a gene mutation for ACM.[1,3]

A complete understanding of the genetic basis of certain cardiac conditions is an area of medical knowledge that has significant potential for development. Advances in genomic technology and research have allowed for the identification of specific genes and mutations that play a role in the development of these conditions.

The authors consider that this case report serves as an important warning about the association between mutations in the *ANK2* gene with structural changes in the myocardium, which can increase the likelihood of malignant arrhythmias and sudden death.

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CASE REPORT

We describe a case of a 24-year-old man, without relevant personal or family history. The individual suffered a witnessed cardiac arrest after a padel game. Basic life support (BLS) was immediately provided by laypeople. Eight minutes later the pre-hospital emergency services team arrived and continued the resuscitation efforts in accordance with Advanced Life Support (ALS) best practice. The initial arrest rhythm was ventricular fibrillation (VF). The field team established early liaison with the Intensive Care Unit (ICU), and the patient was accepted for extracorporeal cardiopulmonary resuscitation (eCPR). During transport, quality mechanical chest compressions were assured. The patient arrived at the ICU 40 minutes after the onset of cardiac arrest in refractory VF. The right common femoral artery and vein were cannulated percutaneously with ultrasound guidance, and veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was started within five minutes. The return of spontaneous circulation was achieved 45 minutes after the onset of cardiac arrest in sinus rhythm (with eight minutes of BLS, 32 minutes of ALS, and five minutes for canulation to establish VA-ECMO). For distal limb perfusion, the ipsilateral superficial femoral artery was cannulated.

The initial 12-lead electrocardiogram presented with a ST-segment elevation in leads V_4-V_6 (Fig. 1). Transthoracic echocardiography (TTE) revealed a dilated LV with severe systolic dysfunction due to global diffuse hypokinesia. The cardiac output was severely depressed [left ventricular outflow tract velocity time integral (LVOT VTI) of 4.8 cm], a non-dilated RV with a mild systolic dysfunction on visual assessment. Coronary angiography revealed normal coronary vessels.

For neuroprotection, the patient underwent deep sedation monitored by continuous electroencephalogram and therapeutic temperature management (33ºC) with an external cooling device in the first 24 hours.

Initially, the patient was kept on VA-ECMO support (blood flow of 2.5 – 3.0 L/minute and sweep gas flow of 1 L/minute). Limb perfusion was monitored with bilateral near-infrared spectroscopy.

After 24 hours of neuroprotection bundle, the patient was slowly reheated to normothermia. With sedative reduction, the patient had spontaneous eye opening and was able to follow the observer and obey commands.

As cardiac function improved, VA-ECMO support was slowly reduced with no cardiovascular dysfunction or perfusion imbalance. TTE revealed an improvement of LVOT VTI to 17.6 cm and RV function (tricuspid annular plane systolic excursion of 18 mm and S´ RV of 11 mm). A mild acute renal injury was observed in the acute phase and was rapidly resolved.

After 48 hours of VA-ECMO, the patient was successfully weaned and decannulated. Respiratory function was normal, and he was successfully extubated. No other organ support was required. Repeated clinical neurological examination revealed a progressive improvement in brain function to a cerebral performance category (CPC) score of 1 (CPC 1 – good cerebral performance).

Four days after the cardiac arrest, the patient was transferred to the Cardiology ward for further studies to clarify the cause of cardiac arrest.

Cardiovascular magnetic resonance imaging (CMR) demonstrated non-dilated moderately impaired LV [LV ejection fraction (EF) of 48%], hypokinesia of the lateral wall and subepicardial fatty infiltration of the LV lateral wall. T2 mapping was increased in the lateral walls suggesting myocardial oedema. Extensive subepicardial late gadolinium enhancement (LGE) was noted in the anterior, lateral and inferior walls. Preserved systolic function of RV (RV EF 51%) with no regional wall motion abnormalities and no LGE in the RV wall was also noted (Fig. 2).

Based on the clinical history and the imaging findings, ALVC was the most likely diagnosis. Genetic tests were performed. An implantable cardioverter-defibrillator (ICD) was placed for secondary prevention of sudden cardiac death.

The patient was discharged from the hospital on the 18th day after cardiac arrest. The patient demonstrated no physical or cognitive impairment and was found to be completely independent (with Medical Research Council sum-score of 60 – normal strength) and CPC 1.[4] The 12-lead electrocardiogram at the time of discharge showed no abnormalities (Fig. 3). The patient received follow-up in the cardiomyopathy clinic and in the following seven months there were no arrhythmic events.

Genetic testing detected a variant c.11081A>G, p.(Lys3694Arg), in the *ANK2* gene which is classified as a variant of uncertain significance. The diagnosis of ALVC does not fulfill all the current diagnostic criteria.

DISCUSSION

This case represents a successful case of eCPR in refractory cardiac arrest. The following factors predicted a high probability of survival with favorable neurological outcome: younger age, no comorbidities, witnessed arrest, no-flow interval of less than five minutes, initial cardiac rhythm of VF, transportation with high quality chest compressions, refractory VF and low-flow interval of less than 60 minutes. For the same reason, those are typically considered the inclusion criteria for admission to eCPR.[5]

This case is compatible with the diagnosis of ALVC due to the clinical picture of recovered cardiac arrest after a refractory VF, imaging findings with mild LV systolic dysfunction and myocardial scar on CMR, and exclusion of ischemic, valvular, or infectious disease. Genetic testing did not fully confirm the hypothesis since it is a poorly described mutation without definitive clinical relevance.

The *ANK2* gene mutation was initially identified as a causative mutation for long QT syndrome and later for Brugada syndrome.[6,7] Interestingly, the *ANK2* gene mutations have also been found in individuals with structural myocardial changes, even without a prolonged QT interval, which increases their susceptibility to malignant arrhythmias and sudden death.[8,9] Therefore, additional genotyping and phenotyping studies are necessary and encouraged.

According to the International criteria for ACM, it is mandatory to have ACM-related genetic mutations associated with LV structural abnormalities to confirm the diagnosis.[1] In fact, morpho-functional and structural LV abnormalities of ACM do not provide sufficient disease specificity because of the overlap with the phenotypic features of other heart muscle diseases, and hence the stricter criteria.[3]

This patient fulfilled one major criteria (LV LGE) and two minor criteria (global LV systolic dysfunction and regional LV hypokinesia of LV free wall). Therefore, the diagnosis of ALVC was not confirmed, although it is very likely.[2]

As the diagnostic criteria for arrhythmogenic cardiomyopathies have changed with the development of knowledge about the diseases, the diagnostic criteria that define ALVC may change, or other genetic mutations related to ACM may be found in the future.

These types of conditions do not have a specific treatment and ICD implantation is the only strategy that may prevent sudden cardiac death.

The authors consider this case report helpful to other clinicians or researchers in various aspects. First, we demonstrated a successful case of an eCPR in the presence of adequate patient selection, teamwork and appropriate interventions in the different stages of patient care. Second, it adds to the literature by highlighting a possible additional genetic pathway to be explored and researched in future cases of cardiac arrest, arrythmia, heart muscle diseases and ALVC.

AUTHOR CONTRIBUTIONS

MG: Conceptualization, writing, review and editing of the final version of the manuscript.

IC, MPA, SAR, PGC, PF: Writing, review and editing of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

PF has received support for attending meetings and/or travel from Hamilton Medical and Getinge.

All other authors have declared that no competing interests exist.

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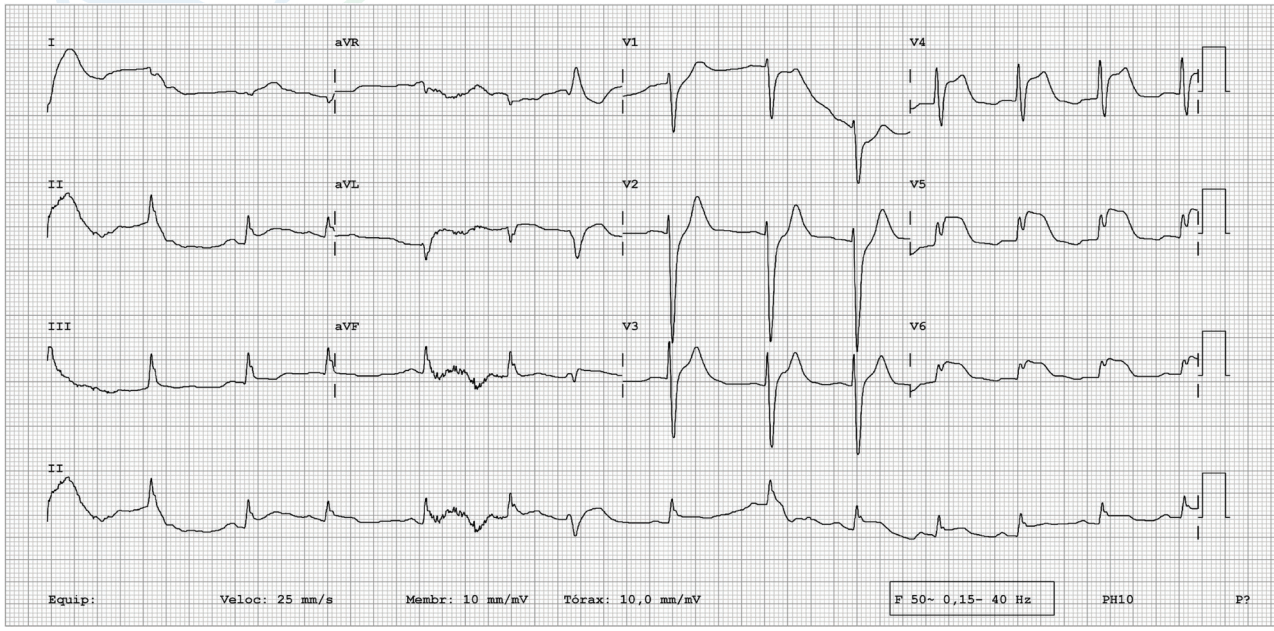

Figure 1 – Initial 12-lead electrocardiogram presented with a ST-segment elevation from V_4 to V_6

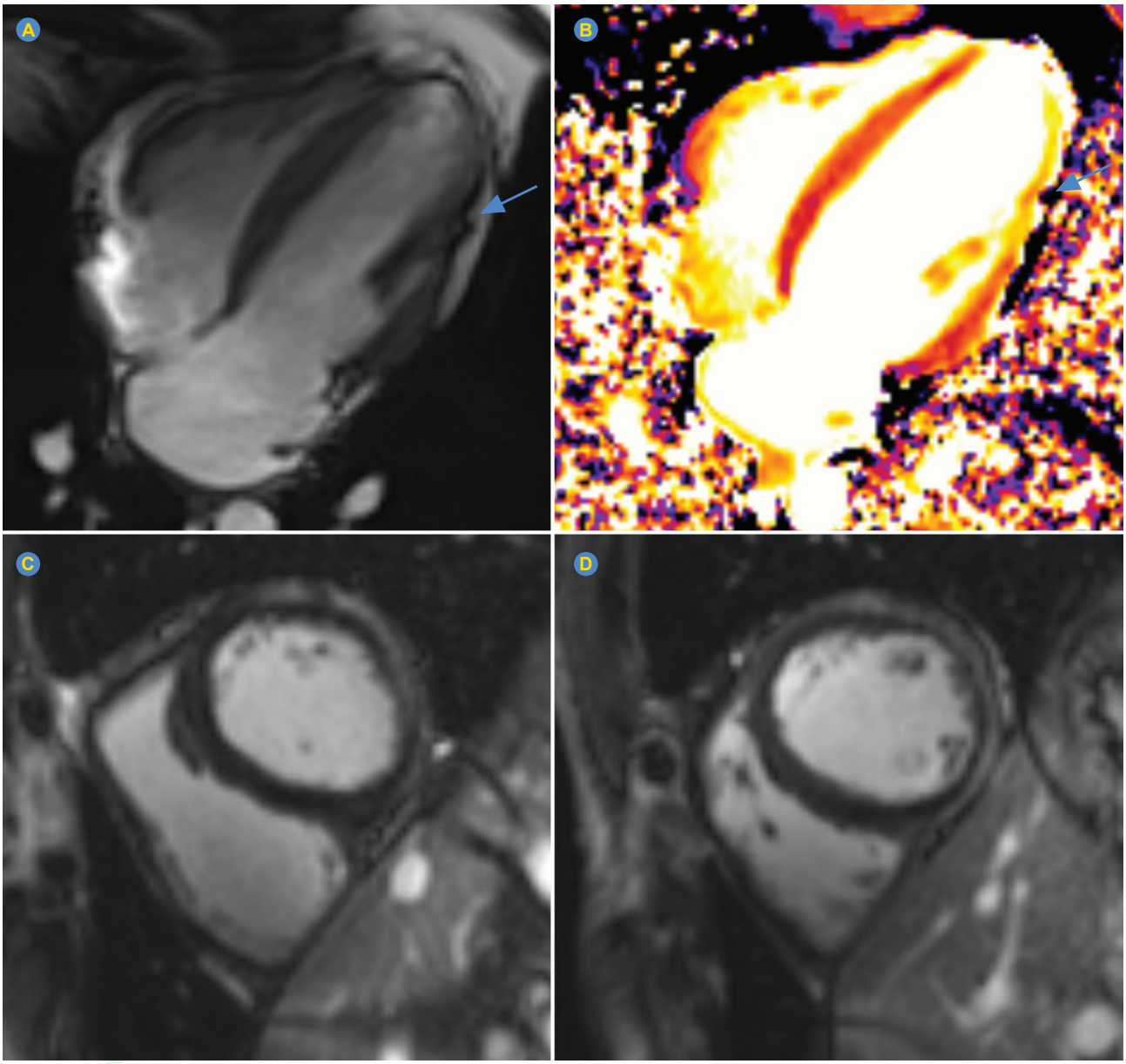

Figure 2 – Cardiovascular magnetic resonance imaging showing subepicardial fatty infiltration of the left ventricular lateral wall (arrows) in cine images (A) and native T1 mapping (B); extensive subepicardial late gadolinium enhancement in the anterior, lateral and inferior walls (C and D)

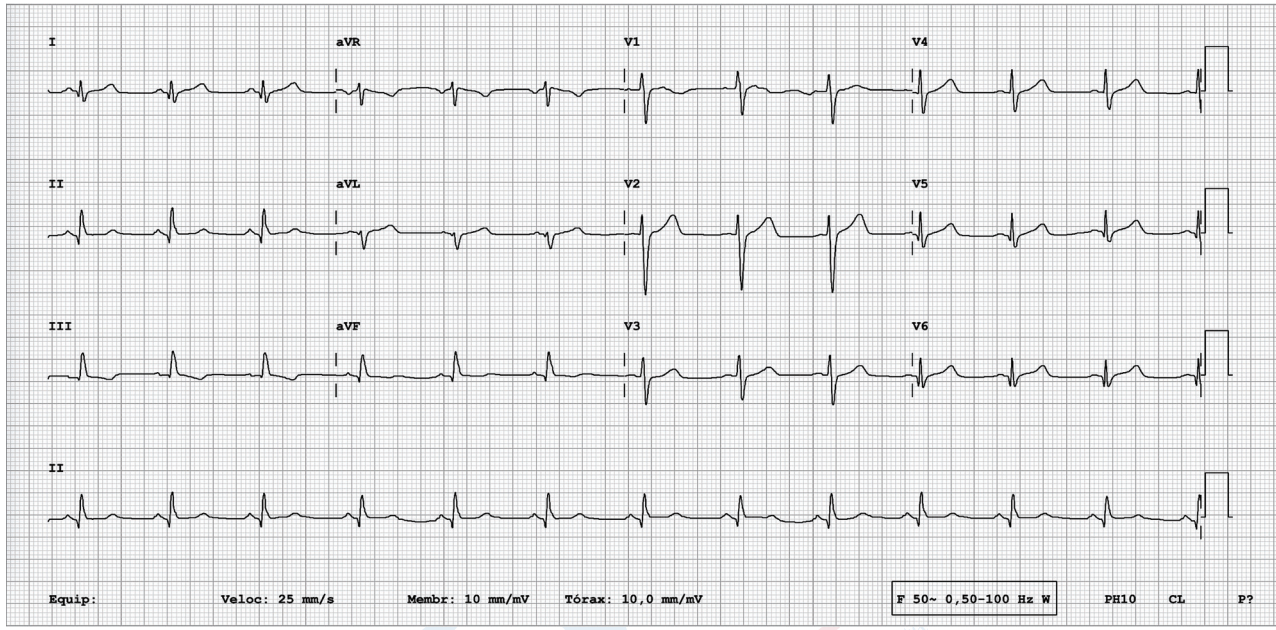

Figure 3 – The 12-lead electrocardiogram at discharge without alterations