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Case report

VENTRICULAR ARRHYTHMIAS IN PATIENT WITH ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

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ABSTRACT

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a rare genetic disorder characterized by the replacement of the right ventricular myocardium with fibrous and fatty tissue, increasing the risk of ventricular arrhythmias and sudden cardiac death (SCD), particularly in young people and athletes. We would like to present a case report of a 23-year-old female who presented with out-of-hospital cardiac arrest due to ventricular fibrillation. Initial resuscitative approaches included cardiopulmonary resuscitation, defibrillation shock and administration of amiodarone, followed by intensive care management. The patient was diagnosed with ARVC and underwent implantable cardioverter-defibrillator (ICD) placement for secondary prevention of SCD. With a review of medical literature, we would like to discuss our approach, diagnosis, and treatment for ARVC.

Key words: *Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), sudden cardiac death (SCD), ventricular arrhythmias, implantable cardioverter-defibrillator (ICD).*

I. INTRODUCTION

Arrhythmogenic right ventricular dysplasia/ cardiomyopathy (ARVD/C) is the most studied and best-characterized disease within the phenotypic spectrum of arrhythmogenic cardiomyopathy (ACM), is an inherited heart muscle disease characterized by ventricular arrhythmias, an increased risk of sudden cardiac death (SCD), and predominant right ventricular dysfunction. ARVD/C is a rare condition and has an estimated prevalence of 1:2000 to 1:5000, depending on geographic location [1]. ARVD/C typically present in the 2nd to 4th decade of life. Approximately 20% of the patients present after age of 50 years. Men are more commonly affected with earlier onset than women and have worse outcomes once diagnosed, that may be explained by sex-related difference in hormone profiles and exercise participation. The presentation of ARVD/C varies considerably: palpitations (30 - 60%), lightheadedness (20%), and syncope (10 - 30%). Up to 19% of ARVD/C patients present as cardiac arrest [2, 3]. Thus far, there have not been many reports on the manifestation of arrhythmogenic right ventricular cardiomyopathy, particularly in Vietnam. Therefore, we would like to share a case of ARVD/C at the Emergency - Interventional Cardiology Department, Hue Central Hospital.

II. CASE REPORT

A 23-year-old female patient had neither a medical history nor a family history of cardiovascular disease, and was hospitalized because of out-of-hospital cardiac arrest (OHCA). The patient at the Emergency Department was unconsciousness, no carotid pulse, with wide, unresponsive pupils, no spontaneous respirations. Cardiopulmonary resuscitation (CPR) with advanced life support was applied. Following the patient's placement of electrocardiography (ECG) electrodes, the ECG monitor showed ventricular fibrillation (VF), and immediately delivered defibrillation shock 270J, and continued with CPR and ventilation, along with epinephrine 1mg/3 min and loading dose of

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amiodarone 300mg IV as well as the maintenance dose of amiodarone 1mg/min. After about 30 minutes, the pulse was checked, also the rhythm was showed on the monitor with fast sinus rhythm 150 bpm, the patient was still unconscious, the blood pressure was 100/70 mmHg, the pupils reacted to light, and the pulse was checked clearly. The monitor displayed a fast sinus rhythm of 150 bpm. On a 12-lead ECG fast sinus rhythm with 150 bpm, with some R-on-T premature ventricular contractions (PVCs) (Figure 1). The patient was transferred to the intensive care unit (ICU).

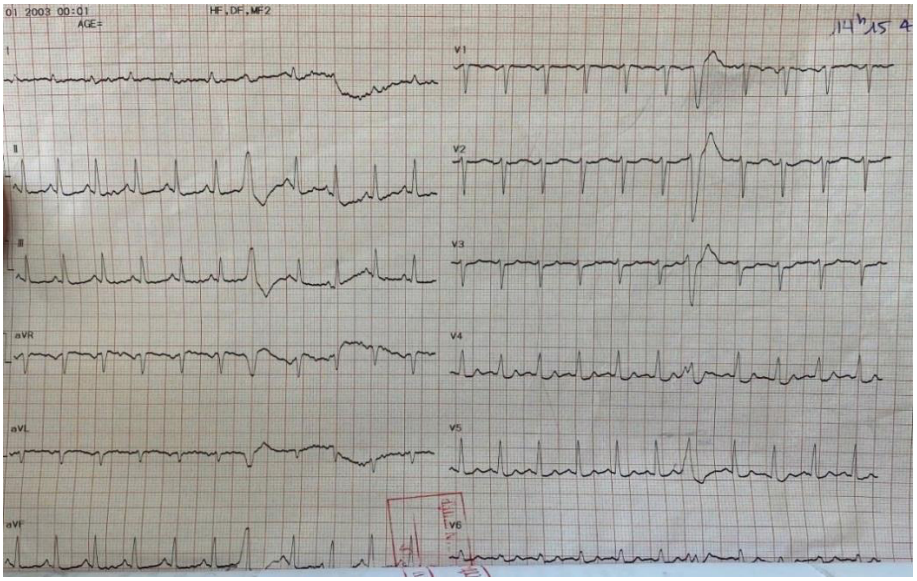

Figure 1: Post-defibrillation 12-lead ECG: R-on-T PVCs and T-wave inversion in V1 - V3

After 7-day duration of ICU treatment with targeted temperature management and medications (antibiotics, enoxaparin, amiodarone maintenance dose at 0.5 mg/min), this patient was transferred to the Emergency - Interventional Cardiology Department. The patient had a normal pulse of 74 bpm, normal blood pressure, warm upper and lower limbs without weakness. The 12-lead ECG showed profound negative T waves in leads V1-V3, T-wave inversion in numerous leads, and particularly epsilon waves in leads V1-V3 (Figure 2).

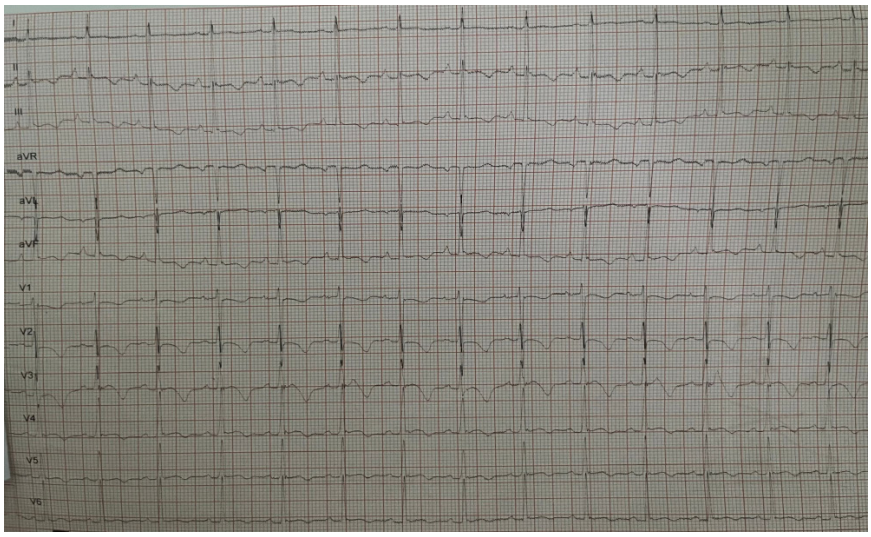

Figure 2: 12-lead ECG in our department: T wave inversion in many leads, deep negative T waves and Epsilon waves in lead V1 - V3

The laboratory results showed that normal complete blood count, normal potassium, magnesium and thyroid hormones. The echocardiography shows that no dilated ventricles and FE = 61%. Cardiovascular Magnetic Resonance (CMR) was indicated to find the cause of her arrhythmias. Her CMR result showed abnormal signals and morphologies of the right ventricle: diffuse thinning of the myocardium and fibro-fatty infiltration (Figure 3).

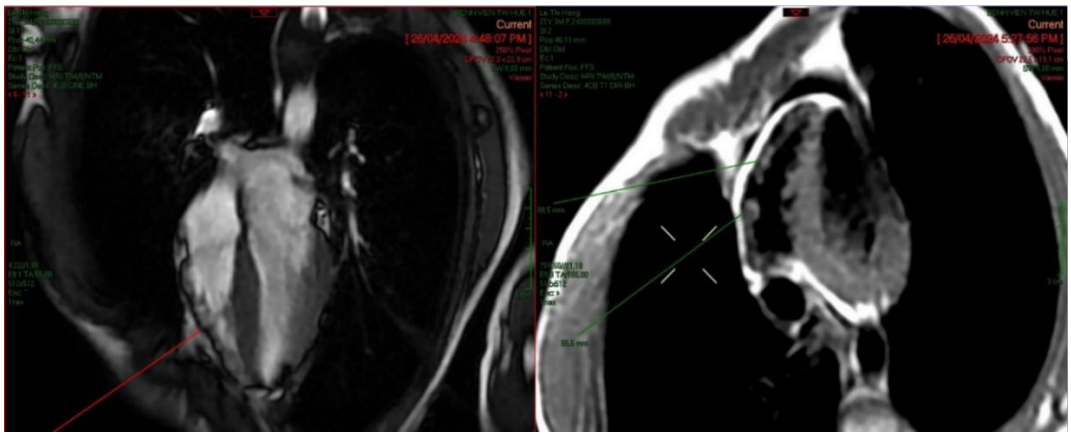

Figure 3: CMR result of the patient with diffuse thinning of RV myocardium and fibro-fatty infiltration

The patient was diagnosed with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C). The patient and her family were explained about placing an implantable cardioverter-defibrillator (ICD) to prevent arrhythmias in the future and they agreed. After that, she was discharged from hospital with an ICD. We prescribed metoprolol 25mg/day for the patient. After a three-month follow-up, the patient had improved her condition and had experienced no arrhythmia events.

III. DISCUSSION

Arrhythmogenic right ventricular dysplasia/ cardiomyopathy (ARVD/C) is a genetic disorder that primarily impacts the heart muscle of the right ventricle (RV). It is marked by the gradual loss of RV myocardial tissue, which is then replaced by fibrous and fatty tissue [1, 2]. First recognized in 1977 during a surgery to map and treat ventricular tachycardia at the Hospital de La Salpêtrière (France) and first described by Fontaine and Marcus in 1982, ARVD/C is a significant cause of sudden cardiac death (SCD) or sudden arrhythmic death (SAD) in young individuals and athletes [4]. Recent medical advances have greatly enhanced our understanding of the disease's pathogenesis, clinical symptoms, and long-term progression. Initially termed dysplasia due to the belief it was a congenital defect in RV myocardial development, it was later reclassified as a cardiomyopathy after discovering that a genetic defect in cardiac desmosomes is responsible, leading to its inclusion in the American Heart Association's (AHA) cardiomyopathy classification [5, 6].

Based on the development of structural modification and clinical symptoms, the natural progression of ARVD/C, in its classic form where RV is primarily affected, can be split into 4 distinct phases: Occult phase: This is the subclinical phase, where the patient shows no symptoms and may have only subtle or no structural abnormalities in the right ventricle. Sudden cardiac death (SCD) might be the first indication of the disease. Arrhythmic phase: The patient experiences palpitations, syncope, and typically symptomatic ventricular arrhythmias originating from the right ventricle, often triggered by physical exertion. These arrhythmias can vary from isolated ventricular ectopies (non-sustained ventricular tachycardia) with a left bundle-branch block (LBBB) pattern to episodes of SCD caused by ventricular fibrillation (VF). Right ventricular failure: At this stage, the ongoing replacement of myocardial tissue with fibrous and fatty tissue gradually impairs right ventricular function, potentially resulting in heart failure. Biventricular failure: In the advanced stage of the disease, the

interventricular septum becomes affected, leading to congestive heart failure. During this phase, mural thrombosis can develop, particularly in aneurysms that form in the right ventricle or in the presence of atrial fibrillation (AF). The disease's presentation may resemble advanced dilated cardiomyopathy, making it difficult to distinguish between the two conditions in the later stages [7].

To standardize the clinical diagnosis of ARVD/C, an international task force criteria (TFC 2010) proposed guidelines, introducing a qualitative scoring system with major and minor criteria, including six categories namely global or regional dysfunction and structural alterations, tissue characterization, repolarization abnormalities, depolarization abnormalities, arrhythmias, family history [5]. CMR is recommended in patients with suspected ARVC (IB) [8]. For this reason, we recommended CMR for the patient and discovered some important signs of ARVC in the patient: diffuse thinning of RV myocardium and fibro-fatty infiltration.

Despite being the current gold standard, TFC 2010 does not address the predominant forms of left chamber involvement, therefore, it was introduced Padua Criteria 2020 (or International Criteria 2020) [9]. The Padua criteria are divided into two separate sets to identify clinical signs of RV and LV involvement based on six categories: Morpho-functional ventricular abnormalities, Structural myocardial abnormalities, ECG repolarization abnormalities, ECG depolarization abnormalities, Ventricular arrhythmias, Family history/genetics [9]. The Padua criteria are classified as "major" and "minor", with the diagnosis being categorized as possible, borderline, or definite based on the number of criteria met. However, to diagnose ACM, at least one morpho-functional or structural criterion, whether major or minor, must be satisfied (Figure 4).

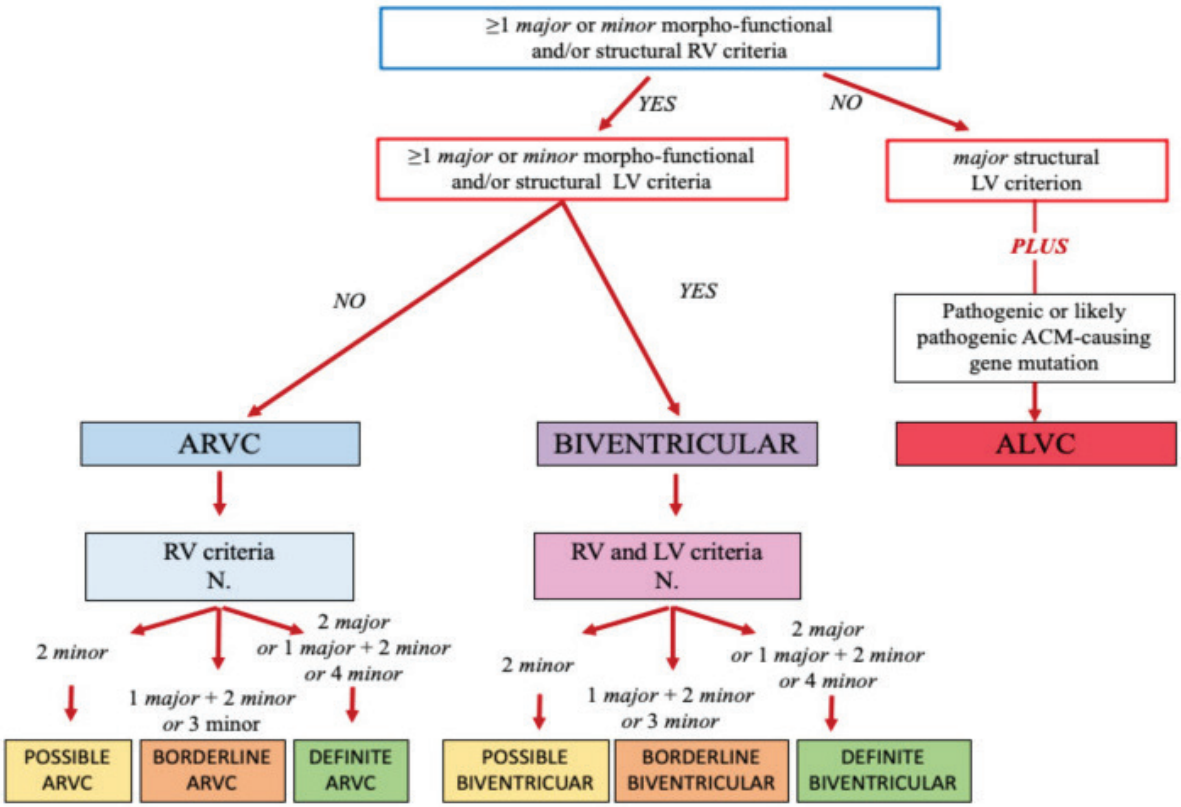

Figure 4: Identifying the phenotype of arrhythmogenic cardiomyopathy [9]

Return to this patient, she had abnormal signals and morphologies of the right ventricle, including diffuse thinning of the myocardium and fibro-fatty infiltration, as well as inverted T waves and epsilon waves in V1-V3. According to the criteria, the patient was diagnosed with "definite" ARVD/C.

Arrhythmogenic right ventricular dysplasia/ cardiomyopathy is predominantly inherited in an autosomal-dominant manner, characterized by incomplete penetrance and variable expressivity. Recently. many gene mutations have been identified to cause ARVD/C, with three common ones being PKP2 (plakophilin-2), DSP (Desmoplakin), and DSG2 (Desmoglein-2). Among the probands diagnosed with the disease, a screening of first-degree relatives allows the identification of the presence of genetic mutations in approximately 50% of cases, regardless of gender. According to a recent study, one third of first-degree relatives develop ARVD/C with siblings having the highest risk of disease [10]. Although we suggested the patient undergo the gene mutation test, the patient's family declined our advice.

Based on the identified risk factors and the estimated probability of life-threatening arrhythmic events, the International Task Force Consensus Statement on ARVD/C treatment categorizes patients into high (>10% per year), intermediate (1–10% per year), or low-risk groups (<1% per year) [11]. This classification is helpful when discussing the risk-benefit balance with patients and their families regarding the appropriateness of recommending an ICD. Another important consideration is the patient's individual preferences and values [11]. Return to our patient, she had a prior cardiac arrest due to VF, the strongest predictor of life-threatening arrhythmia. Therefore, this patient was classified as high-risk, and ICD placement was class I indication for the secondary prevention of SCD and treatments of ventricular arrhythmias according to ESC 2022 [8]. There are also different recommendations for ICD placement in ARVD/C patients (Figure 5) [12].

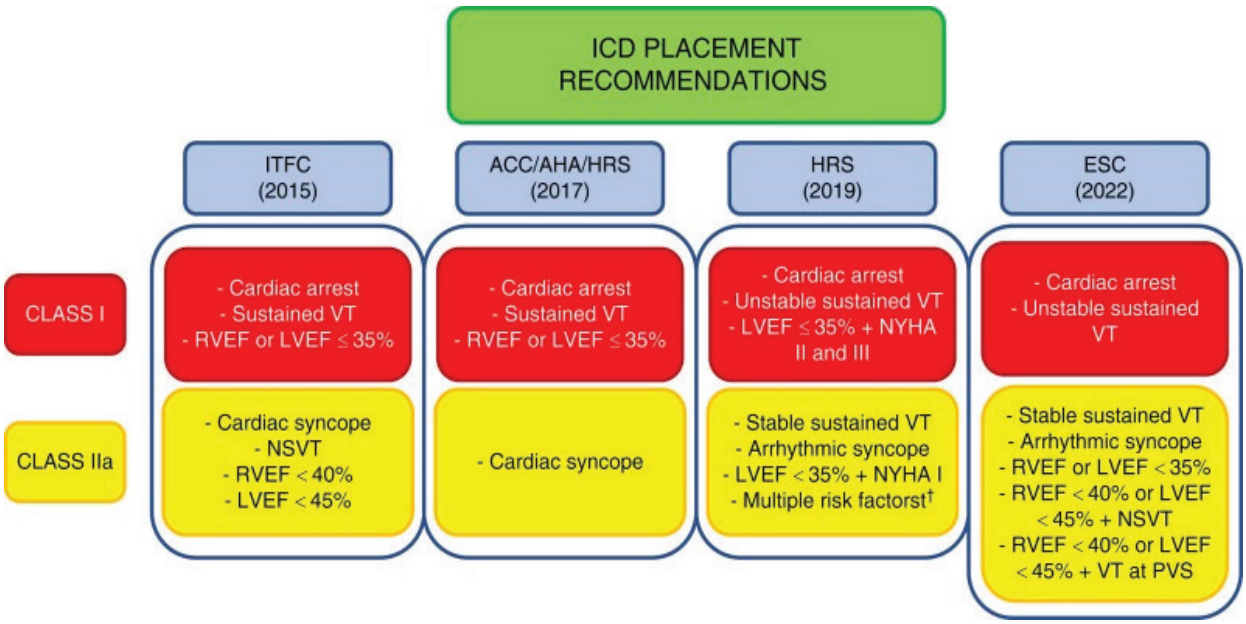

Figure 5: Summary of current guideline indications for ICD placement in patients with ARVD/C [12]

Single-chamber ICDs are recommended to reduce the risk of long-term lead-related complications, especially in younger patients. While a dual-chamber detection system can lower the number of inappropriate interventions, the additional lead increases the risk of both short-term and long-term complications and should only be used in cases of symptomatic bradycardia or AV block, which are extremely rare in ARVD/C patients [4]. The patient was indicated with single-chamber ICD.

Pharmacologic therapy is commonly utilized in the management of ARVD/C. Beta-blockers

are recommended as the first-line treatment for all confirmed ARVD/C patients, is based on the proven effectiveness of beta-blockers in preventing SCD in heart failure and on observations that ventricular arrhythmias in ARVD/C are often triggered by physical exertion and facilitated by catecholamines Anti-arrhythmic drugs are primarily used to reduce the frequency of arrhythmias and rarely eliminate the risk of sudden death [13, 14]. Additionally, ESC 2022 also recommended using beta-blocker therapy in patients with ARVC and non-sustained or sustained ventricular arrhythmias [8]. For the patient, we prescribed metoprolol 25mg/day. Following a three-month follow-up and ICD checkup, the patient had experienced no arrhythmia occurrences.

IV. CONCLUSION

Arrhythmogenic right ventricular cardiomyopathy (ARVC) can first manifest clinically as cardiac arrest. Early recognition in electrocardiography and cardiovascular magnetic resonance in order to prevent sudden cardiac death in affected individuals plays an important role of diagnosis and management of the ARVC patients. Implantable cardioverter-defibrillator is recommended to prevent secondary sudden cardiac death in ARVC patients with haemodynamically ventricular arrhythmias.

Disclosure

The authors report no other conflicts of interest in this work

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