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Case Report

Ventricular Tachycardia in Arrhythmogenic Right Ventricular Cardiomyopathy: How to Manage?

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ABSTRACT

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a condition characterized by fibrofatty replacement of the RV myocardium due to genetic abnormality. Structural changes may be absent or minor in the early stages of the disease and be localized in a specific region of the RV. Clinically it appears as RV electrical instability. To reduce the risk of arrhythmic events or sudden cardiac death, device therapy and pharmacotherapy may be recommended. In this paper, we describe a case of a female with ARVC and a brief discussion based on a literature review. The patient presented with chest discomfort accompanied by palpitation. An electrocardiogram (ECG) showed ventricular tachycardia of RV apex origin, and convert to symmetric inverted T-waves and probable epsilon waves in the right precordial leads, mimicking a pseudo-right bundle branch block (RBBB) pattern following electrical cardioversion. The parasternal short-axis view of echocardiography shows severe right ventricular dilatation. Subsequent workup using CMR was planned but the patient refused. We diagnosed this patient with ventricular tachycardia on a background of suspicious arrhythmogenic right ventricular cardiomyopathy. We were able to provide accurate diagnosis and treatment, avoiding potentially fatal consequences. As a result, it is critical to recognize potential ARVC ECG findings and to know when to pursue further research and implement therapies.

Keywords: T wave inversion; epsilon waves; monomorphic ventricular tachycardia; arrhythmogenic right ventricular cardiomyopathy; implantable cardioverter-defibrillator

INTRODUCTION

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a genetical condition characterized by fibrofatty replacement of the right ventricle (RV) myocardium.(1) In the early stages of the disease, structural changes may be absent or minor, and they may be localized to a specific region of the RV, such as the inflow tract, outflow tract, or apex, known as the "triangle of dysplasia".(2) The posterior lateral wall of the left ventricle (LV) is commonly affected and the development of more extensive RV disease is common. Predominant LV disease has also been reported previously.(4) Extensive sampling and transillumination may be required for postmortem diagnosis.(5) Sickness manifests itself in a variety of ways. People in the early

phases of the "hidden phase" are frequently asymptomatic but are at danger of sudden cardiac death, especially if they exert themselves.[6] Individuals with symptomatic arrhythmias and RV structural anomalies appear on conventional imaging immediately during the overt "electrical phase." Widespread illness may result in biventricular heart failure and ventricular arrhythmia. The final phenotype could resemble dilated cardiomyopathy (DCM). The clinical signs differ depending on the age of patient and the stage of the disease.[7]

With more information about arrhythmic outcomes, risk factors, and life-saving therapeutic approaches becoming available, it is more important than ever to critically address and place issues related to the clinical management of ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy ARVC patients. Some consensus statements give a complete summary of the current risk assessment algorithms and treatment options, both pharmacological and non-pharmacological, which can be challenging for cardiovascular experts and other practitioners to understand.

CASE ILLUSTRATION

A 65-years-old woman suffered from chest discomfort 1 day before admission, which occurs while eating, and lasting more than 30 minutes. It was accompanied by nausea vomiting and palpitation. It was getting worsen in the last 2 hours before admission. Her family said that she was no cough, fever, diarrhea, or urinary tract disturbances. It was not getting improve by resting position. The family history of syncope, palpitations or sudden cardiac death were denied. Due to her worsening condition, her family brought her to hospital. At hospital, she suffered from cardiogenic shock and got inotropic agent. An electrocardiogram (ECG) showed ventricular tachycardia RV apex origin (Fig. 1). The patient was kept under observation while blood samples for cardiac enzymes were sent because the chest pain was unusual for coronary artery disease. The result of laboratory examination showed increase of cardiac enzyme. The first ECG (Fig. 1) shows ventricular tachycardia RV apex origin with heart rate 180 bpm. Because of VT with unstable hemodynamics, an electrical cardioversion performed and the ventricular tachycardia was terminated. The second ECG (Fig. 2), showed symmetric inverted T-waves and probable epsilon waves in the right precordial leads, mimicking a pseudo-right bundle branch block (RBBB) pattern.

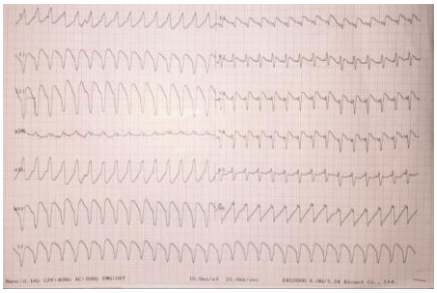

Figure 1. Patient's ECG showed ventricular tachycardia RV apex origin

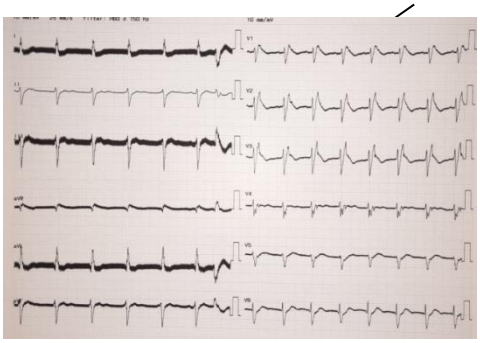

Figure 2. Patient's second ECG showed symmetrically inverted T-waves and probable epsilon waves in the right precordial leads, mimicking a pseudo-right bundle branch block (RBBB) pattern

CXR showed cardiomegaly. From parasternal short-axis view of echocardiography showing severe right ventricular dilatation.

From 4-chamber view showed RA and RV dilatation (Fig. 3). Patient also had right ventricular systolic dysfunction and akinetic wall motion at right ventricular outflow tract wall. The coronary angiogram revealed thrombus and stenosis 50% in distal right coronary artery (Fig. 4). We diagnosed this patient as ventricular tachycardia on a background of suspicious arrhythmogenic right ventricular cardiomyopathy.

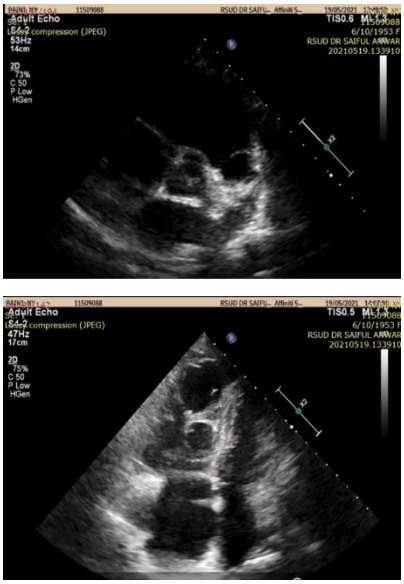

Figure 3. Parasternal short-axis view of echocardiography showing severe right ventricular dilatation. From 4-chamber view showed RA and RV dilatation

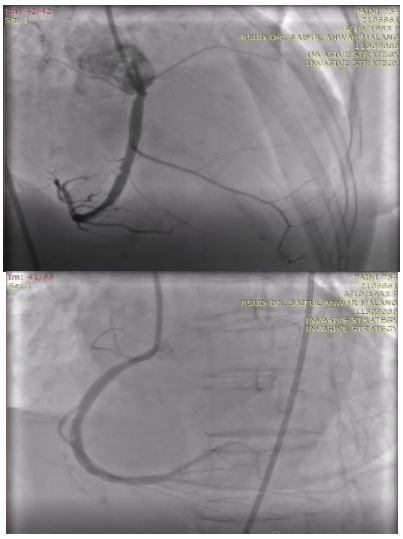

Figure 4. Coronary angiogram showed thrombus and stenosis 50% in the distal right coronary artery

The patient is planned for implantable cardioverter-defibrillator (ICD) implantation after establishing the diagnosis using CMR. The patient was supposed to get a cardiac magnetic resonance imaging (CMRI) at an outpatient clinic, but she rejected. She was discharged in hemodynamically stable condition and ECG on discharge revealed heart rate 83 bpm and symmetrically inverted T-waves in the right precordial leads with epsilon wave and PVC occasional. At the time of discharge, she was given bisoprolol 2,5 mg a day. It's always exciting to come across rare pathological entities with classic clinical findings, especially when they pose a diagnostic challenge. We were able to provide accurate diagnosis and treatment, avoiding potentially fatal consequences. As a result, it is critical to recognize potential ARVC EKG findings and to know when to pursue further research and implement therapies.

DISCUSSION

In 1982, Marcus first identified ARVC as hereditary cardiomyopathy that progresses with

an elevated risk of arrhythmias at cardiac ventricle and sudden death. On histological analysis, the RV myocardium is replaced with fibrofatty tissue, causing in RV dilatation and systolic failure.[1] ARVC can affect the left ventricle, resulting in left-sided heart failure, despite its nomenclature. It was estimated that the prevalence would be between 1:2000 and 1:5000. The underlying pathophysiology is thought to involve mutations in multiple genes encoding desmosomes, which are necessary for cell-to-cell adhesion. Desmosome dysfunction causes myocyte separation and cell death, as well as constant mechanical stress and cardiac contraction. In the early phase, inflammation occurs in the affected myocardium, followed by apoptosis and fibrofatty replacement of the myocardium. In ARVC, ventricular fibrillation (VF) is linked to fibrofatty scarring, while reentrant ventricular tachycardia (VT) is linked to cell death. In autosomal dominant ARVC, nondesmosomal gene mutations have also been documented.[2,3]

Some persons may have palpitations, dizziness, cardiogenic syncope, heart failure, ventricular arrhythmias, or cardiac arrest, even if they are asymptomatic. ECG abnormalities such as inverted T waves and epsilon waves in the right precordial leads have been seen in roughly 30% of patients (V1, V2 and V3). Epsilon waves occurs as a result from low-amplitude positive signals at the end of QRS complexes which caused by the delayed depolarization of the RV myocardium. Monomorphic VT with an LBBB pattern is the most prevalent of the related ventricular arrhythmias.[4,5] Supraventricular arrhythmias have been reported in the past. In individuals with ARVC, the major causes of cardiovascular mortality are progressive heart failure and SCD, in that order. Those who had previously had ventricular fibrillation were more likely to develop SCD.[6] The amount of exercise has a substantial correlation with phenotypic penetrance. Endurance activity levels influence disease phenotypic penetrance and the onset of VT and SCD in athletes, according to James, et al.[7] This was also discovered during an animal investigation.[8] On echocardiography, regional RV wall motion abnormalities, increased RV dimensions (particularly at the RV outflow tract), and diminished RV EF can all be seen. Despite the fact that CMRI has played a critical role in detecting ARVC with great sensitivity and specificity due to advances in technology, interobserver variability has been discovered.[9] To detect inducible VTs, EPS can be used as a diagnostic tool. Electroanatomic mapping also can be done to determine the extend of disease.[10] Endomyocardial biopsy can also be guided with EPS, but it still controversial in a patchy myocardial involvement and low sensitivity due to sample mistakes.[11]

When the diagnosis of ARVC still can't be established and a concentrated genetic screening of first-degree relatives is expected, genetic testing may be informative. The use of EMB or genetic testing as the first step in determining the diagnosis is not advised. According to the research, around 50% of people with ARVC are related to one another, which could lead to an underestimate. The disease can be autosomal dominant or autosomal recessive, with autosomal dominant being the most frequent. Autosomal dominant illness has been linked to a number of genes. The plakophilin-2 gene (PKP-2) encodes the desmosomal protein plakophilin-2 and is the most prevalent mutation in North America. Patients with PKP-2 mutations experience symptoms and arrhythmias

at a younger age, with an average start age of 28. (11 years).[2,12]

It is critical to make the accurate diagnosis; yet, this might be difficult. The 2010 Task Force Criteria were provided by Marcus et al.15, and they included the following six categories.

1) CMRI or echocardiography showed global or localized dysfunction and structural alterations.
2) Characterization of the wall tissue (fibrous replacement and %age of residual myocytes in the right ventricle)
3) EKG repolarization abnormalities (V1, V2, and V3 T-wave inversion) (epsilon waves in V1, V2, and V3)
4) Electrocardiographic depolarization/ conduction abnormalities (T-wave inversion in V1, V2, and V3) Arrhythmias
5) (VT with LBBB morphology and superior axis)
6) Family history (AVRC in a first-degree relative confirmed with task Force criteria or at autopsy)

Each category was further divided into major and minor. The diagnoses were as follows.

1) Definite ARVC was established with two major or one major and two minor criteria or four minor criteria from different categories
2) Borderline diagnosis of ARVC was made with one major and one minor or three minor criteria from different categories
3) Possible diagnosis is one major or two minor criteria from different categories.

Table 1. Diagnostic Criteria of ARVC[15]

	Original Task Force Criteria	Revised Task Force Criteria
I. Global or regional dysfunction and structural alterations		
Major	Severe dilatation and reduction of RV ejection fraction with no (or only mild) LV impairment Localized RV aneurysms (akinetic or dyskinetic areas with diastolic bulging) Severe segmental dilatation of the RV	By 2D echo: Regional RV akinesia, dyskinesia, or aneurysm And 1 of the following (end diastole): -PLAX RVOT > 32 mm (corrected for body size (PLAX/BSA) > 19 mm/m2) -PSAX RVOT > 36 mm (corrected for body size (PSAX/BSA) > 21 mm/m2) -or fractional area change < 33% By MRI: Regional RV akinesia or dyskinesia or dyssynchronous RV contraction And 1 of the following: -Ratio of RV end diastolic volume to BSA > 110 mL/m2 (male) or > 100 ml/m2 (female) -or RV ejection fraction < 40% By RV angiography: Regional RV akinesia, dyskinesia, or aneurysm
Minor	Mild global RV dilatation and/or ejection fraction reduction with normal LV Mild segmental dilatation of the RV Regional RV hypokinesia	By 2D echo: Regional RV akinesia or dyskinesia And 1 of the following (end diastole): -PLAX RVOT > 29 mm to < 32 mm (corrected for body size (PLAX/BSA) >16 to <19 mm/m2) -PSAX RVOT > 32 to <36 mm (corrected for body size (PSAX/BSA) > 18 to <21 mm/m2) -or fractional area change > 33% to < 40%

		By MRI: Regional RV akinesia or dyskinesia or dyssynchronous RV contraction And 1 of the following: -Ratio of RV end diastolic volume to BSA > 100 to <110 mL/m2 (male) or > 90 to <100 ml/m2 (female) -or RV ejection fraction >40% to < 45%
	Original Task Force Criteria	Revised Task Force Criteria
II Tissue Characterization of wall		
Major	Fibrofatty replacement of myocardium on endomyocardial biopsy	Residual myocytes <60% by morphometric analysis (or <50% if estimated), with fibrous replacement of the RV free wall myocardium in > 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy
Minor		Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated), with fibrous replacement of the RV free wall myocardium in > 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy
III Repolarization abnormalities		
Major		Inverted T waves in right precordial leads (V1, V2, and V3) or beyond in individuals >14 years of age (in the absence of complete right bundle branch block QRS > 120 ms)
Minor	Inverted T waves in right precordial leads (V2 and V3) (people age >12 years, in absence of right bundle branch block)	Inverted T waves in leads V1 and V2 in individuals >14 years of age (in the absence of complete right bundle branch block) or in V4, V5, or V6 Inverted T waves in leads V1, V2, V3 and V4 in individuals >14 years of age in the presence of complete right bundle branch block
IV Depolarization/ conduction abnormalities		
Major	Epsilon waves or localized prolongation (>110 ms) of the QRS complex in right precordial leads (V1 to V3)	Epsilon waves (reproducible low-amplitude signals between end of QRS complex to onset of the T wave) in the right precordial leads (V1 to V3)
Minor	Late potentials	Late potentials by SAECG in > 1 of 3 parameters in the absence of a QRS duration of > 110 ms on the standard ECG Filtered QRS duration > 114 ms Duration of terminal QRS <40 mcV (low amplitude signal duration) > 38 ms Root mean square voltage of terminal 40 ms < 20 mcV Terminal activation duration of QRS > 55 ms measured from the nadir of the S wave to the end of the QRS, including R', in V1, V2, or V3, in the absence of complete right bundle branch block
V Arrhythmias		
Major		Nonsustained or sustained ventricular tachycardia of left bundle branch morphology with superior axis (negative or indeterminate QRS in leads II, III, and avF and positive in lead avL) or of unknown axis
Minor	Left bundle branch block type ventricular tachycardia (sustained and nonsustained) (ECG, holter, exercise) Frequent ventricular extrasystoles (>1000 per 24 hours) (Holter)	>500 ventricular extrasystoles per 24 hours (Holter)
VI Family history		

Major	Familial disease confirmed at necropsy or surgery	ARVC confirmed in a first degree relative who meets current Task Force Criteria ARVC confirmed pathologically at autopsy or surgery in a first degree relative Identification of a pathogenic mutation categorized as associated or probably associated with ARVC in the patient under evaluation
Minor	Family history of premature sudden death (< 35 years of age) due to suspected ARVC Familial history (clinical diagnosis based on present criteria)	History of ARVC in a first degree relative in whom it is not possible or practical to determine whether the family member meets current Task Force criteria Premature sudden death (<35 years of age) due to suspected ARVC in a first degree relative ARVC confirmed pathologically or by current Task Force Criteria in second degree relative

The updated diagnostic criteria improved sensitivity while retaining specificity compared with the International Task Force Criteria at 1994. Our patient had an RV EF of 15%, T-wave inversions, epsilon waves in the right precordial leads, and VT of the LBBB pattern with an inferior axis were present in our patient.

In its natural history, ARVC can cause a wide range of ventricular arrhythmias, from premature ventricular complexes to persistent VT or ventricular fibrillation (VF). The morphology of ventricular arrhythmias with left bundle branch blockages usually points to a location of origin in the RV, such as the inferior axis from the RV outflow tract or the superior axis from the RV inferior wall or apex. The VT morphologies of the patients can vary. Overall, the incidence of cardiac arrest due to VF varies between studies, ranging from a low mortality rate in familial forms over an average follow-up of 8.5 years (0.08 % per year in the Nava et al. series) to a high mortality rate primarily due to congenital forms over an average follow-up of 8.5 years (0.08 % per year in the Nava et al. series) to a high mortality rate mostly due to SCD over an average follow-up of 4.6 years (3.6 % per year in the Lemola series).[19] VF is the mechanism underlying SCD In asymptomatic young people with ARVC, VF is the mechanism of SCD. VF is most likely associated with a clinical hot phase in this subset of patients, which is marked by acute myocyte death and reactive inflammation, as well as dynamic T-wave inversion, ST-segment elevation, and myocardial enzyme release. Scar-related hemodynamically stable VT is common in older adults with long-term illness. Conduction delay and ventricular arrhythmias have recently been proposed as potential substrates for conduction delay and ventricular arrhythmias in the prephenotypic phase of the disease, with experimental animal models supporting this hypothesis.[19]

The following are the most important clinical goals for patients with ARVC: (1) lower mortality, whether from sudden cardiac death or heart failure; (2) progression to RV, LV, or biventricular dysfunction and heart failure were prevented; (3) improving symptoms and quality of life by reducing/abolishing palpitations, VT recurrences, or ICD discharges (either appropriate or inappropriate); and (4) improving symptom of heart failure. Lifestyle adjustments, pharmaceutical medications, catheter ablation, ICD implantation, and heart transplantation are alternative treatment.[22] Given the substantial association between endurance activity and the incidence of ventricular arrhythmias, all patients with ARVC should change

their lifestyle. ARVC patients should avoid competitive sports as well as any physical exercise that causes palpitations or presyncope.[7,16] Exercise hastens disease progression, necessitating the use of -blockers to reduce sympathetic activity, which may improve clinical results. There is, however, limited evidence to support the usage of -blockers. Angiotensin-converting enzyme inhibitors may assist to prevent ventricular arrhythmias by reducing the structural progression of the disease.[1] Patients who develop heart failure as a result of ARVC should receive normal medical treatment.

Previous arrhythmic cardiac arrest and hemodynamically unstable VT have been demonstrated to be independent risk factors for life-saving ICD procedures in a large group of ARVC patients (i.e. shock on VF episodes).20 Patients who underwent implantation owing to VT but had minimal hemodynamic impairment had a better prognosis, with a reduced incidence of VF during follow-up. Resuscitated VF has a poor prognosis; in research by Canu et al., two out of three patients who died suddenly had a history of VF-related abortive SCD.[21]

Due to the finest algorithms for detecting supraventricular and ventricular arrhythmias, dual-chamber ICD implantation is the best strategy. According to specialists, ICD therapy is suggested for primary prevention in high-risk patients and secondary prevention in those who have a history of prolonged VT or aborted cardiac arrest.[17] However, there is no consensus on how to categorize high-risk patients, and the exact indications for ICD implantation in people with ARVC remain unknown. Randomized control trials, on the other hand, have shown that ICD therapy can prevent SCD in people who are at high risk. Prospective research found that anti-tachycardia pacing (ATP) successfully terminated ventricular tachyarrhythmias in patients with ARVC.[18] ICD therapy is related with pericardial effusion, perforation, device infection, and inappropriate shock, as it is in all settings with adequate implantation. Myocardial perforation and under-sensing of arrhythmias are particularly concerning in ARVC due to small parts of RV myocardium and growing fibro-fatty infiltration. Sotalol, an antiarrhythmic medication, may assist to lower the occurrence of ventricular arrhythmias. Antiarrhythmic medicines, on the other hand, are utilized as a supplement to ICD therapy in ARVC patients who already have one. Experts have also proposed that ARVC patients who are unable to tolerate ICD therapy be given sotalol or amiodarone.[17,19] Owing to the uneven involvement of the myocardium, radiofrequency ablation cannot be considered the final therapy. Surgery and heart transplantation are possible treatments for refractory ventricular arrhythmias and end-stage heart failure.

Given the clinical symptoms of palpitation, epsilon wave and T inversion in the right precordial ECG, dilatation and decreased systolic function in the RV in our patient, CMRI was advised as the next step in the diagnostic process. ICD was indicated as a main preventive therapy for patients with VT and unstable hemodynamics. This case started out as a diagnostic problem, but it also emphasizes the need of using medical tools properly, such as a cardiac MRI. Although many people with ARVC have a good quality of life, they are at a risk of ventricular tachyarrhythmias and heart failure. Due to age-related phenotypic penetrance, asymptomatic family members of affected patient may develop ARVC later in life. Patients with inducible sustained monomorphic VT are more likely to develop SCD; hence, EPS could

aid in risk assessment. According to the literature, ARVC has a better overall prognosis than other structural heart disorders that produce ventricular arrhythmias.[5,6,20]

CONCLUSION

ARVC is a type of inherited cardiomyopathy that increases the risk of ventricular arrhythmias and heart failure. The detection of an epsilon wave and T inversion in the right precordial ECG in our patient with VT and unstable hemodynamics led to the discovery of a potentially life-threatening illness. As a result, it's crucial to spot suspected ARVC EKG findings and to decide when to pursue additional investigations and therapy. ARVC has been extensively studied in terms of pathophysiology and management since its discovery in 1982. Nonetheless, key problems about risk categorization, effective medication, appropriate device approach, and illness prognosis remain unsolved.

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