CASE REPORT

A CASE REPORT OF ARRYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA PRESENTING WITH STABLE VENTRICULAR TACHYCARDIA AND LEFT VENTRICULAR DYSFUNCTION

Ali Nawaz Khan[1], Erum Shahzadi Malik[1], Zeeshan Shaikh[1], Safina Shabbir[1], Jawad Abbas[1], Mahesh Kumar Harwani[1]

[1]PNS Shifa Hospital, Pakistan

Abstract: Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVD) is regarded to be one of the highest common cause of death especially in athletes due to sudden cardiac arrest. Epidemiologically, 1 among 5000 populations has estimated prevalence of ARVD. ARVD clinical indications or symptoms before the age of 12 are difficult to diagnose and it is also rare to acquire ARVD symptoms after the age of 60. 34-year-old male patient with no-known co-morbid received at Emergency Department of PNS Shifa Hospital Karachi. This case report is a typical case of ARVD in stage 4 with bi ventricular involvement.

Keywords: Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVD), Left bundle branch block (LBBB), right ventricular outflow tract (RVOT)

Citation: Khan AN, Malik ES, Shaikh Z, Shabbir S, Abbas J, Harwani MK. A Case Report of Arrythmogenic Right Ventricular Dysplasia Presenting with Stable Ventricular Tachycardia and Left Ventricular Dysfunction. Pak Heart J. 2022;55(04):417-420. DOI: https://doi.org/10.47144/phj.v55i4.2332

INTRODUCTION

Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVD) is regarded to be one of the commonest cause of death among young adults, children, and especially in athletes due to sudden cardiac arrest. It came fore to medicine world in 1977 by Guy Fontaine as a hereditary cardiomyopathy. It is caused by mutation in non-desmosomal and desmosomal genes. A fibro-fatty replacememt of the right ventricular myocardium and life threatening arrthymias are characteristic features of ARVD.[1] Various names for this disease have been used, including arrhythmogenic cardiomyopathy, arrhythmogenic RV dysplasia, and arrhythmogenic ventricular tachycardia. Epidemiologically, 1 among 5000 populations has estimated prevalence of ARVD. Patients frequently appear with syncope, palpitations, light-headedness, or even abrupt death. ARVD clinical indications or symptoms before the age of 12 are difficult to diagnose and it is also rare to acquire ARVD symptoms after the age of 60.[2]

CASE REPORT

A 34 year old male patient with no-known co-morbid received at Emergency Department of PNS Shifa Hospital Karachi with the complaint of atypical chest pain and palpitations for the last 2 hours. He was hemodynamically stable. His systemic examination revealed bilateral crepitation in the chest, while rest of the examination was unremarkable. ECG depicted run of sustained monomorphic ventricular tachycardia of Left bundle branch block (LBBB) involving right axis which reverted to sinus rhythm spontaneously (Figure 1).

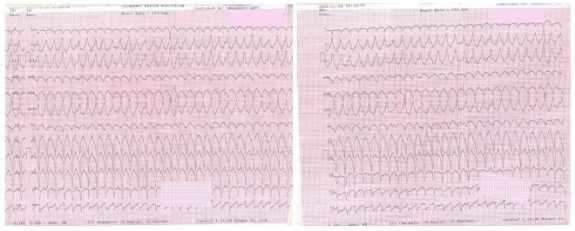

Figure 1: 12 lead ECG indicative of Monomorphic Ventricular Tachycardia. The VT morphology is LBBB involving inferior axis

Repeat ECG revealed epsilon wave with sinus rhythm (Figure 2). His baseline bio chemical profile revealed Hb of 14.6 g/dl, TLC of 7.9, Platelets 158, Trop I 0.100, Pro BNP 3484 pg/ml, S. Bilirubin 29 µ mol, ALT 24 U/L, Alk Phosp. 233 IU/L, S. Ca+2 2.31 mmol/L, S. Mg 0.80 mmol/L, S. Albumin 37 g/L. Thyroid Profile TSH 2.830 mIu/m, Free T3 7.240 pmol/L and Free T4 16.13 pmol/L.

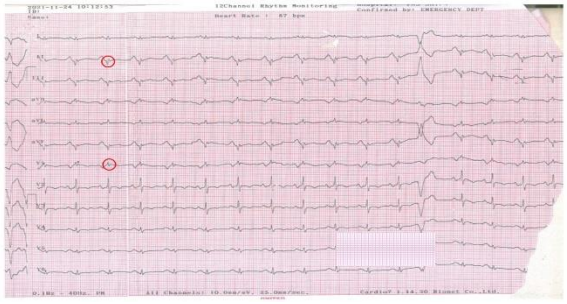

Figure 2: 12 Lead ECG indicating Epsilon Wave in V1 with Sinus Rhythm and premature ventricular contractions (PVCs)

2D Echocardiography revealed severe LV dysfunction and global hypokinesia with an EF of 10% along with grossly dilated RA and RV with severe RV systolic dysfunction. Spontaneous Echo contrast was seen in RA and RV and marked trabeculations of RV were observed (Figure 3). RVOT proximal Plax was recorded as 47 mm, RVOT proximal Psax recorded as 45 mm. Fractional area change was measured as 10%. Chest X Ray revealed marked cardiomegaly (Figure 4). On the basis of Echo and ECG findings a presumptive diagnosis of ARVD was made as per Revised Task Force Criteria 2010. On anamnesis one of his family members had similar complaint of palpitations and had ICD implanted.

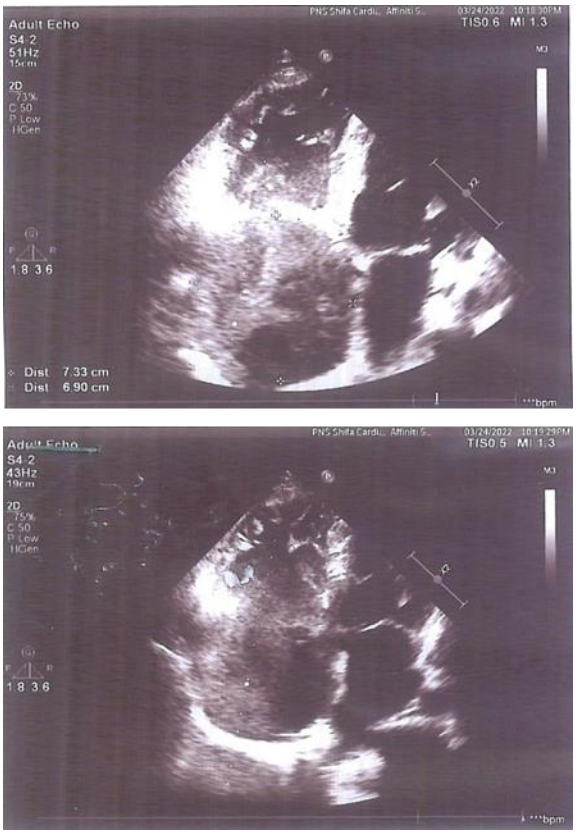

Figure 3: Echo Cardiograph Report indicating grossly dilated RA and RV, Right Atrium 69x73 mm, severe RV Systolic Dysfunction, Spontaneous Echo Contrast in RA & RV with Marked Trabeculations of RV

Cardiac MRI was done which was suggestive of ARVD involving both RV and LV (Report at Table I). The presumptive diagnosis was hence confirmed as the patient met all the major criteria as spelled in Revised Task Force Criteria 2010.

The patient was managed in hospital and kept on Tab loprin, Tab Rivaroxaban 15 mg, Tab Lasix 20 mg, Tab metoprolol 50 mg, Tab pantoperazole 40mg and Tab Amiodarone 200 mg. Later he was referred to a specialist centre for an electrophysiologist opinion and placement of ICD. ICD was subsequently placed in the patient who is currently asymptomatic and recovering well.

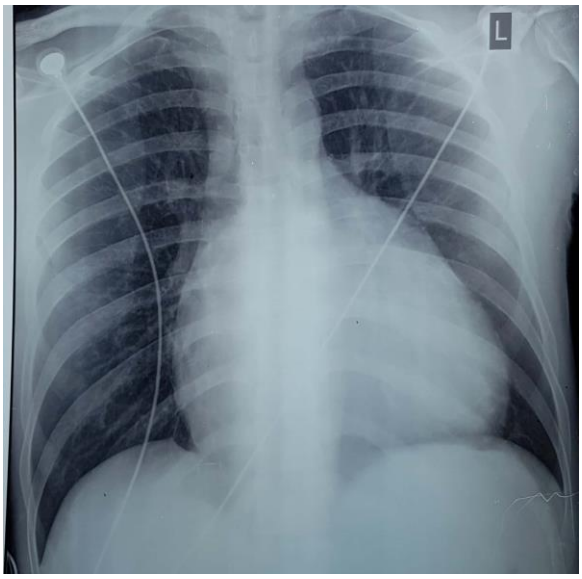

Figure 4: Chest X-Ray PA View showing Cardiomegaly

Table 1: MRI report findings suggestive of Arrhythmogenic Cardiomyopathy involving RV and LV

Functional Cine Images	Early Gadoline Images	Delayed Enhanced Images
Normal Sized LV with severe systolic dysfunction	No area of hypo enhancement in RV and LV cavities, suggestive of intra cavity thrombus	Diffused myocardial hyper enhancement of LV and RV
Dilated RV and RVOT		The volume of blood in RV at end load filling index for BSA was 152 ml/m^2
Dyskinetic segments in RVOT		
Normal valves		
Mild to moderate MR		

DISCUSSION

ARVD has an age-dependent penetrance, and the majority of individuals don't show symptoms until their 2nd to 4th decade of life. As a consequence of this, very little is known about the genotype, clinical features, or long-term prognosis of ARVC/D at an older age.[3] The *primary disease-causing gene* in ARVD/C was discovered by genetic foundation of Naxos. A desmosomal protein "Plakoglobin (JUP)", which is found on chromosome 17q21 is crucial in cell-to-cell adhesion. Following that, mutations in genes encoding various desmosomal proteins, such as

desmoglein-2 (DSG2), desmoplakin (DSP), desmocolin-2 (DSC2), and plakophilin-2 (PKP2) were discovered, all of which produce autosomal-dominant variants of ARVD/C.[4] PKP2 is the most often mutated gene (20–46%) among all index cases, followed by DSC2 (1–8%), DSP (3–15%), JUP (1%), and DSG2 (3–20%). Only around 10% of all pathogenic variations are caused by non-desmosomal genes. There have been attempts to link genetics to phenotypes. Patients with several mutations (4–16%) had a faster start of illness and poorer disease outcomes, such as arrhythmia, sudden cardiac death, and heart failure.[5] Desmosomes and gap junctions are involved in disease pathophysiology because they are important for signal transduction, cell adhesion, and electrical integrity. Desmosomal protein defects cause cardiac myocytes to lose adhesion, resulting in inflammation, fibrosis, mortality, and the development of fibrofatty tissue. Desmosomes are vital in intracellular and intercellular signal transmission in addition to enabling mechanical cell attachment.[6] Complete thickness of Free wall is observed at low magnification in RV histopathology in ARVD cases. This demonstrates a specific topographic pattern in which the epicardial layers have a lower quantity of myocardium, as well as fat and fibrosis. However, strands of cardiomyocytes may be seen within this fibro-fatty tissue, which are a pathognomonic histological hallmark of this illness. The RV, on the other hand, has two types of fibrosis i.e. interstitial fibrosis, and replacement fibrosis. This fibrosis is observed during Cardiac MRI and identified as a sign of superimposed myocarditis.[7]

ARVD is functionally divided into four stages, the first of which is the subclinical stage, which is characterised by structural abnormalities and covert functions. The second stage is the clinical stage, which is characterised by overt functions and structural abnormalities. There is overt electrocardiographic evidence of right ventricular (RV) arrhythmias found in second stage. In the third stage, there is substantial RVD with no involvement of the left ventricle (LV) in the process. During the fourth stage, there is bi-ventricular involvement, due to which severe right and left heart failure would occur.[8] It is important to high light that sudden cardiac death (SCD) can occur at any stage of ARVD/C. From diagnostic point of view, cardiac positron emission tomography (CPET) might be of critical importance. When there is substantial involvement on the left side, biventricular ARVD/C has the potential to resemble dilated cardiomyopathy. Congenital cardiac diseases such as abnormal venous return, Ebstein anomaly, pulmonary hypertension, Uhl's disease, or right ventricular infarction may also result in a dilated right ventricle.[9] To locate the areas of the heart that have the most delays i.e., the right ventricle, the right ventricular outflow tract (RVOT), and in the basal pre-tricuspid area, Invasive electro-anatomical mapping techniques can help in ARVD cases. Abnormal repolarization such as Twave inversion in leads V1–V2 occur in 3% of healthy adults, suggesting ARVD/C. The ST segment is usually normal in ARVD/C. However, LV participation has been linked to ST elevation. When the QRS axis is up with a positive aVL, ARVD/C is also suspectd.[10] P wave anomalies, including aberrant shape and extended P wave length (>_120ms), are common in ARVD/C but may not contribute to the diagnosis. Sino-atrial and atrioventricular blockages are rare early signs of ARVD/C. The SA-ECG characteristics suggest late potentials and are beneficial in ARVD/C including a fragmented QRS (>114ms). Ambulatory ECG Monitoring >500 PVCs in a 24-hour Holter is a minor updated Task Force Criteria. Additionally, exercise stress revealed hidden anomalies such e waves or TAD>_ 55ms.[11] Epsilon wave in long ECG is one of the key points of diagnosis recommendation of ARVD as per the 2010 Task Force, which was first identified in 1977 and to this date epsilon wave is considered as iceberg of ECG abnormalities in ARVD. Epsilon Wave was derived from ECG abnormalities occurring before QRS complex i.e., Presilon or at the top i.e., Topsilon or at the end i.e. Postsilon. Later on, in 2010 TFC constitutes independent wave on the ST Segment in V1 to V3 aside from QRS Complex is epsilon wave, However, this phenomenon would only be observed in advance cases of ARVD patients.

ARVC have been managed through five legs stool. The first step is to ensure that the accurate diagnosis has been made. ARVC is often misdiagnosed, owing to erroneous interpretation of MRI and maybe a lack of understanding of the 2010 Task Force Criteria for diagnosis. Secondly, the prediction of the probability of a prolonged ventricular arrythmia is performed in order to guide judgments regarding ICD placement. The third pillar is to keep ICD therapy to a bare minimum. Exercise restriction is used in conjunction with pharmaceutical treatment, including beta-blockers, antiarrhythmic medicines, and other drugs. The fourth is to prevent the illness from progressing. The fifth important leg is familial cascade screening. The increased use of genetic testing has aided this process. Moreover, an electrocardiogram or Holter monitor, echocardiogram or magnetic resonance imaging, and repeat cardiac examination should be done in every 2–3 years, targetly after puberty. If the proband has no harmful mutations, it has been proposed that all family members (first-degree) get cardiac testing every two to three years which depend

upon physical activity.[12] A recent consensus paper on the treatment of ARVC was published by an International Task Force comprising specialists from the United States and Europe. This publication from the International Task Force summarised information and recommendations for ICD implantation in ARVD patients. Cardiac arrest patients or persistent VT, as well as those who have significant LV or RV dysfunction, are classified as Class I patients. Patients who had just one major risk factor were classed as intermediate-risk, or Class IIa. Class III was assigned to one "minor" risk factor. Finally, there is a group with a minimal risk of SCD who does not need the implantation of an ICD. This also includes those patients who are gene carriers but do not follow ARVC diagnostic criteria as well as those who do have high risk of sudden cardiac death but meet the ARVD diagnostic criteria. Because a pathogenic mutation or family history of ARVC is an important diagnostic tool for ARVC, patients with no structural or arrhythmic symptoms may be identified with the illness.[13] Patients with ARVC who have had a prolonged ventricular arrythmia (VFL:a cycle duration of 240 milliseconds, sustained VT, or VF) are at an increased risk of recurrent persistent VF and VT. ARVD hemodynamically stable VT patients may not need the use of an ICD.[3] However, probands have a higher risk of arrhythmia than family members with ARVC. According to various studies, patients with more extensive RV or LV disease had a higher arrhythmic risk. Arrhythmias are more common in males with ARVC than in women. In a multivariable model research, several desmosomal gene mutations and male sex were shown to be independent predictors of lifespan.[14]

In conclusion, as explained ARVD/C is a herediatory cardiomyopathy with an inherent risk of arrhythmias leading to sudden cardiac death. This case report is a typical case of ARVD in stage 4 with bi ventricular involvement. It was picked during an ECG with positive epsilon wave after an episode of chest pain and palpitation. The patient has been implanted with an ICD device however due to limited resource country, the lack of genetic interpretation is considered a limitation of the study. The concluding note for health practioners in the case is to pick possible ECG findings of ARVD/C and the knowledge / understanding for further management.

AUTHORS' CONTRIBUTION: ANK and ESM: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. ZS, SS, JA, and MKH: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

REFERENCES

1. Li G, Fontaine G, Fan S, Yan Y, Bode P, Duru F et al. Right atrial pathology in arrhythmogenic right ventricular dysplasia. Cardiol J. 2020;26(6):736-43.
2. Gupta R, Tichnell C, Murray B, Rizzo S, te Riele A, Tandri H, et al. Comparison of Features of Fatal Versus Nonfatal Cardiac Arrest in Patients With Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy. Am J Cardiol. 2017;120:111-7.
3. Bhonsale A, Groeneweg JA, James CA, Dooijes D, Tichnell C, Jongbloed JD, et al. Impact of genotype on clinical course in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated mutation carriers. Eur Heart J. 2015;36:847-55.
4. Bhonsale A, Riele ASJM, Te Sawant AC, Groeneweg JA, James CA, Murray B, et al. Cardiac phenotype and long-term prognosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia patients with late presentation. Heart Rhythm. 2017;14:883-91.
5. Te Riele ASJM, Agullo-Pascual E, James CA, Leo-Macias A, Cerrone M, Zhang M, et al. Multilevel analyses of SCN5A mutations in arrhythmogenic right ventricular dysplasia/cardiomyopathy suggest non-canonical mechanisms for disease pathogenesis. Cardiovasc Res. 2017;113:102-11.
6. Mayosi BM, Fish M, Shaboodien G, Mastantuono E, Kraus S, Wieland T, et al. Identification of cadherin 2 (CDH2) mutations in arrhythmogenic right ventricular cardiomyopathy. Circ Cardiovasc Genet. 2017;10:e001605.
7. Saguner AM, Roland F, Li GL, Fontaine GH. 1933Superimposed myocarditis leading to heart transplantation in a young patient with arrhythmogenic right ventricular dysplasia. Eur Heart J. 2017;38(Suppl_1):ehx495.1933.
8. Mushtaque R, Mushtaque R, Baloch S, Idrees M, Bhatti H. Clinical Manifestations and Diagnostic Approach to Arrhythmogenic Right Ventricular Cardiomyopathy – A Case Report and Literature Review. Cureus. 2020;12(11):e11429.
9. Philips B, Madhavan S, James CA, Riele ASJM, Te Murray B, Tichnell C, et al. Arrhythmogenic right ventricular dysplasia/cardiomyopathy and cardiac sarcoidosis: distinguishing features when the diagnosis is unclear. Circ Arrhythm Electrophysiol. 2014;7:230-6.
10. 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;20(FI1):f3-f12.
11. Camm CF, James CA, Tichnell C, Murray B, Bhonsale A, Riele ASJMT, et al. Prevalence of atrial arrhythmias in arrhythmogenic right ventricular dysplasia/cardiomyopathy. Heart Rhythm. 2013;10:1661-8.
12. Bruna V, D_ıez-Villanueva P, Mart_ınez-Selle´s M, Datino T, Fern_andez-Avile´s F. Atrioventricular conduction disorder as a first manifestation of arrhythmogenic right ventricular dysplasia. Rev Esp Cardiol (Engl Ed). 2016;69(12):1222-4.
13. Li GL, Saguner AM, Fontaine GH, Frank R. Epsilon waves: Milestones in the discovery and progress. Ann Noninvasive Electrocardiol. 2018;23(6):e12571.
14. Orgeron GM, James CA, Te Riele A, Tichnell C, Murray B, Bhonsale A, et al. Implantable cardioverter-defibrillator therapy in arrhythmogenic right ventricular dysplasia/cardiomyopathy: predictors of appropriate therapy, outcomes, and complications. J Am Heart Assoc. 2017;6:e006242.

Address for Correspondence:

Dr. Erum Shahzadi Malik, Resident, Medicine-Cardiology Unit (CCU), PNS Shifa, Karachi, Pakistan.
Email: erummalik121@gmail.com