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CASE REPORT

Arrhythmogenic right ventricular cardiomyopathy: A case report and review of literature

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Abstract

Arrhythmogenic right ventricular cardiomyopathy (also called arrhythmogenic RV dysplasia [ARVD]) is a heterogeneous inherited disease that results in fibrofatty infiltration of the right ventricle predominantly, although the disease can also affect the left ventricle (typically the posterior portion). It is a rare and life threatening cause of sudden cardiac death. ECG often carries the first clue to its diagnosis and a high degree of suspicion needs to be maintained to identify this condition in young patients presenting with syncope. We are presenting one such case of an young male who presented with syncope and one episode of documented VT who on evaluation turned out to be a case of ARVD.

Keywords: ARVD/ARVC; ventricular arrhythmias; sudden death; cardiac MRI; ICD

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Introduction

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/ARVD) is a rare familial cardiomyopathy characterized by progressive fibrofatty replacement of myocardium mainly involving right ventricle, rarely involving left ventricle. Clinically, it presents with life-threatening malignant ventricular arrhythmias arising from RV apex, which may lead to sudden death, most often in young people and athletes. ARVC/ARVD is difficult to diagnose. A previous Task Force criteria was highly specific but lacked sensitivity for early & familial disease. The present Task Force criteria 2010, incorporated imaging modalities like MRI, thus improving sensitivity & specificity for early diagnosis of ARVD. The therapeutic options at present are focused on the prevention of life-threatening cardiac arrhythmia, by using antiarrhythmic drugs, catheter ablation, and/or an implantable cardioverter defibrillator (ICD). A rare case of ARVD in young patient who presented with sudden onset of loss

of consciousness with documented RV apical VT on ECG is discussed here. The diagnosis was made on the basis of history, electrocardiography, 2D echocardiography [1, 2], and cardiac MRI [3, 4].

Case report

A 38-year-old male, farmer from Nalgonda district, Telangana, came to hospital with history of recurrent episodes of syncope preceded by palpitations and chest discomfort since one year. There was no family history of heart disease or sudden death. ECG revealed Broad QRS complex, tachycardia with superior axis (Figure 1) which was DC verted to sinus rhythm at a local hospital in Nalgonda. However, no specific etiology of this patient's arrhythmia was identified. At the time of admission at KIMS hospital, Secunderabad, patient had episodes of chest discomfort and light headedness. ECG showed an incomplete RBBB with T waves inverted in V1- V5 & II, III, aVF & epsilon waves in V1 & V2 (Figures 2,3,4). CK MB was normal & troponin-T was mildly elevated (? secondary to DC Shock). Chest X ray revealed mild cardiomegaly (Figure 5). 2D echocardiogram done at KIMS Hospital showed normally functioning left ventricle, dilated RVOT & RV cavity with good RV systolic function & mild tricuspid regurgitation (Figure 6). Patient was suspected to be a case of ARVD, based on abnormal ECG & 2D Echo (Dilated RV) & RV apical VT.

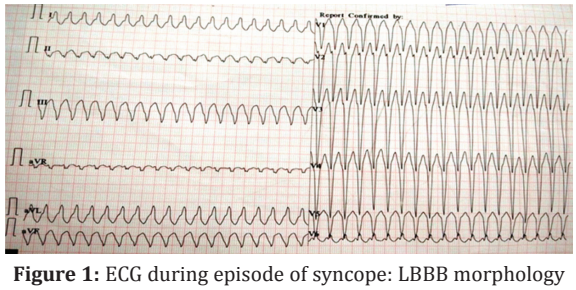

Figure 1: ECG during episode of syncope: LBBB morphology VT with superior axis.

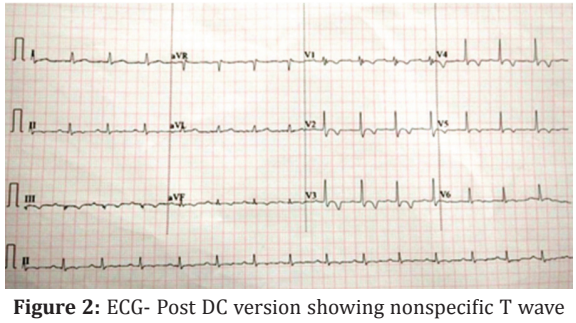

Figure 2: ECG- Post DC version showing nonspecific T wave changes.

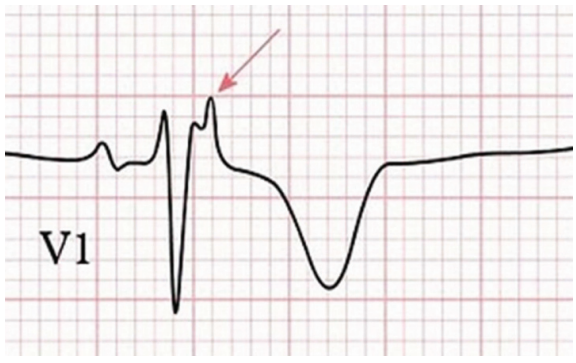

Figure 3: Line diagram showing epsilon wave in anterior, inferior precordial leads and epsilon wave, lead V1.

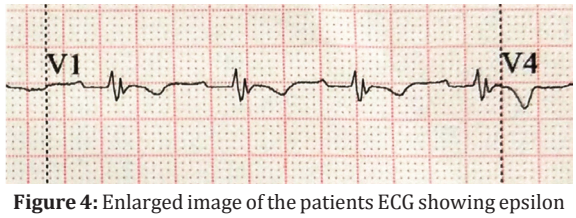

Figure 4: Enlarged image of the patients ECG showing epsilon wave in lead V1.

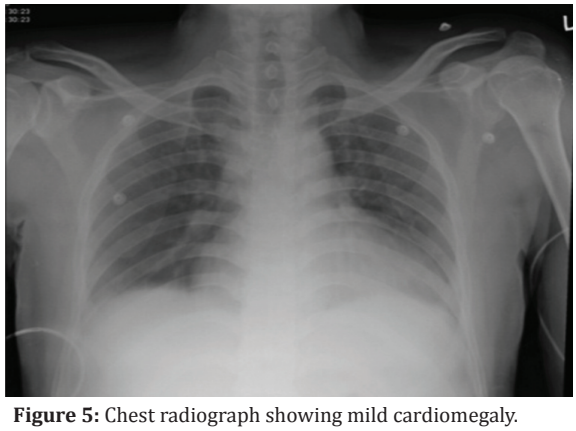

Figure 5: Chest radiograph showing mild cardiomegaly.

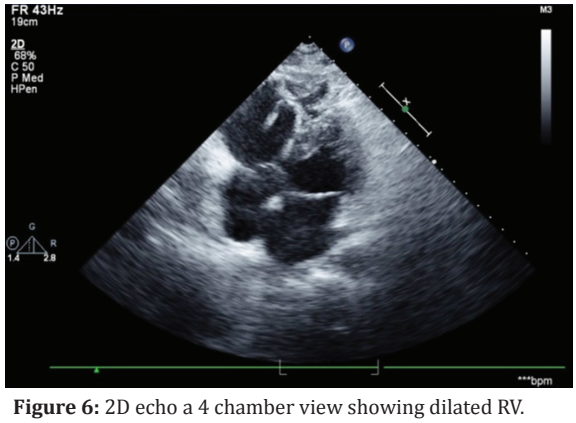

Figure 6: 2D echo a 4 chamber view showing dilated RV.

With the above history & investigations, cardiac MRI was done which showed Dilated, akinetic right ventricle with thinning of right ventricular wall &

fatty infiltration of right ventricular free wall (Figures 7, 8, 9, 10). Provisional diagnosis of arrhythmogenic RV dysplasia was made and was discharged on oral drug therapy (Beta blockers/Cardarone). He was advised to have ICD implantation for secondary prevention of ventricular dysrhythmia.

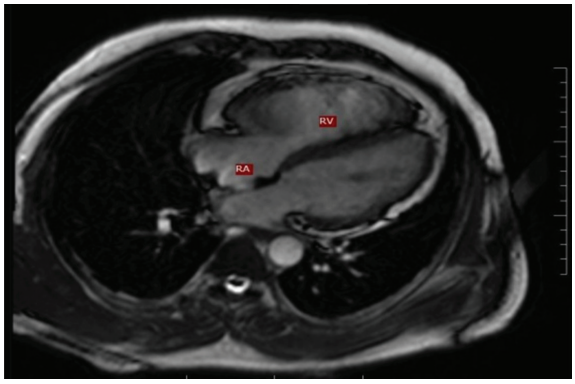

Figure 7: MRI 4 chamber showing dilated RV.

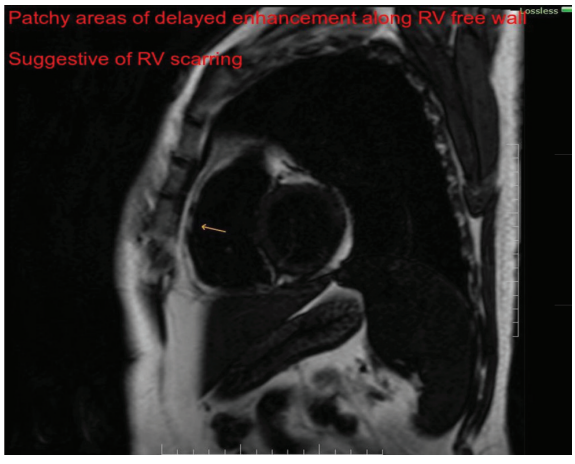

Figure 8: MRI suggestive of RV scarring.

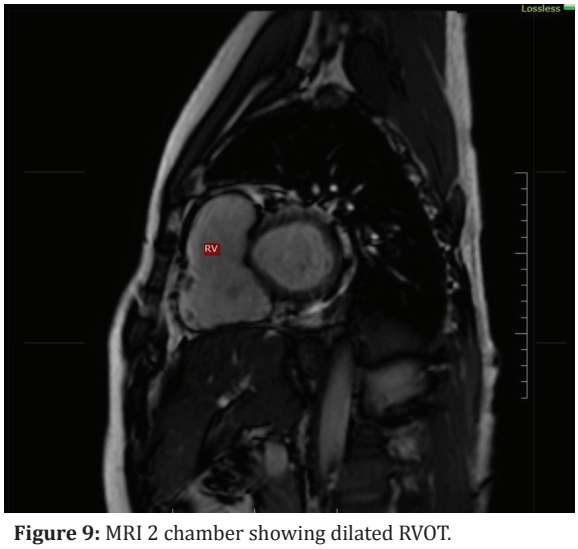

Figure 9: MRI 2 chamber showing dilated RVOT.

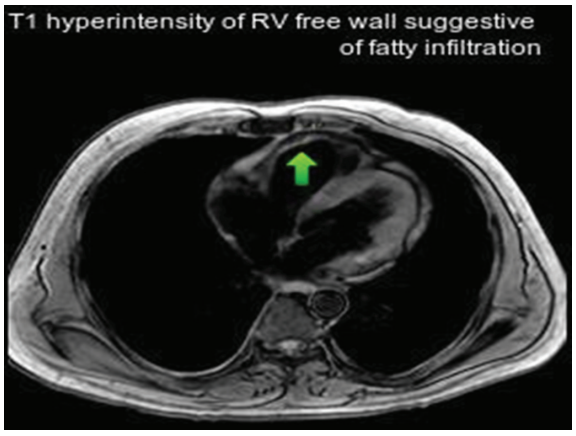

Figure 10: MRI showing T1 hyperintensity of RV free wall.

Discussion

Arrhythmogenic right ventricular cardiomyopathy (also called arrhythmogenic RV dysplasia [ARVD]) is a heterogeneous inherited disease that results in fibrofatty infiltration of the right ventricle predominantly, although the disease can also affect the left ventricle (typically the posterior portion) [5]. This fatty and fibrous tissue replacement of myocardium initially affects epicardium and then endocardium. This loss of muscle results in thinning and focal dilation of RV free wall and leads to systolic dysfunction. The IVS (Interventricular septum) is generally spared involving RV free wall. Endomyocardial biopsy generally obtained from IVS may be non-diagnostic. The predominant site of RV involvement is often the "triangle of dysplasia", an area involving the RV outflow tract, an area below the tricuspid valve, and the RV apex; this is the most common area of RV thinning, and aneurysm formation [6].

ARVD is a common cause of sudden death in young adult. It can affect any age group but the typical patient is a male patient in the third decade of life [7]. ARVD is characterized by progressive structural abnormalities of RV, associated with arrhythmia.

ARVD can exist in sporadic and familial forms (30-50% of cases). The inheritance of ARVD is primarily by autosomal dominant mode with variable expression and penetrance [8]. However, an autosomal recessive pattern has been reported in Naxos disease and in Carvajal syndrome [9, 10]. Mutations in genes that encode various proteins of the desmosome (plakoglobin, desmoplakin, plakophilin, desmoglein, and desmocollin) have been

found to cause the disease but are present in only approximately 50% of patients [11-13]. Ten genes for ARVD have been identified on chromosomes 1, 2, 3, 6, 10, 14 and 17. Major candidate genes identified are involved in encoding for desmoplakin (ARVD8) and plakoglobin (Naxos disease), a protein for cell to cell adhesion and ryanodine receptor, RYR2 (ARVD2), involved in ion channels [7, 10, 14, 15]. Desmosomal dysfunction should be considered as final pathway of ARVD pathogenesis [16].

Clinical presentation of ARVD varies from asymptomatic to Palpitations, syncope, arrhythmias, sudden cardiac death & heart failure. Typically the ventricular tachycardia in ARVD has LBBB morphology and superior QRS axis, indicating origin of arrhythmia from Right ventricle and Inflow tract. RVOT Ventricular tachycardia also presents with LBBB morphology but it is benign & has inferior axis or normal axis. ARVD forms about 3-4% of SCD in athletes. Heart failure is mainly right heart failure, although occasionally biventricular failure can occur due to concomitant left ventricular involvement.

ECG abnormalities in ARVD, usually show regular NSR with QRS duration >110msec in V1 and T inversion in right precordial leads beyond V1, (in absence of RBBB). RV late potentials, in the form of epsilon waves in V1–V3. 'T' wave inversion beyond V1, is normal in children up to 12 years and is present in 1-3% healthy population of age group 19–45 years and 87% patients with ARVD. Epsilon waves are seen only in 33% of patients [17].

Mechanism of VT in ARVD is twofold, with enhanced automaticity early in natural history of disease and scar mediated reentry in established disease, with recurrent sustained VT. The VT of enhanced automaticity is rapid, self-terminating, occurs at the beginning of exercise and beta blockade is highly effective. The VT that occurs due to reentry is often recurrent and sustained VT and needs more aggressive therapy like catheter ablation, in addition to antiarrhythmic drug therapy.

Provocative isoproterenol infusion – High dose of 45mcg/min x 3minutes – resulting in polymorphic PVC's/NSVT, is highly reliable for ARVD with sensitivity of 91.4% and specificity of 88.7%, early in the course of disease where it can be mistaken for RVOT tachycardia [18].

Diagnosis

Diagnosis of ARVD is based upon the presence of two or more abnormalities of RV structural, electrical abnormality (depolarisation and repolarization abnormality of RV, typical ventricular arrhythmias of RV inflow), tissue characteristics of RV free wall and family history.

A limitation of the previous Task Force criteria 1994, was the reliance on subjective criteria for assessing ventricular structure and function and for evaluation of myocardial histology which was highly specific but lacked sensitivity for early and familial disease [19]. Technical advances in MRI [3, 4] and 2-dimensional echocardiography [1, 2] have improved the capability to image the RV with reproducible measurements of volume and systolic function, which permits classification of severity and differentiation from normality & thus has improved the sensitivity & specificity in diagnosis of ARVD (Tables 1 and 2).

Table 1: Task Force criteria 2010 for diagnosis of ARVD [20, 21].

Definite diagnosis	2 major criteria or 1 major and 2 minor criteria or 4 minor criteria from different categories
Borderline	1 major and 1 minor criteria or 3 minor criteria from different categories
Possible	1 major or 2 minor criteria from different categories

Finally as per latest Task Force criteria, KIMS hospital patient fits into diagnosis of definite ARVD, where he satisfies 4 major criteria from 4 different categories: (i) 2D echocardiogram showing dilated RVOT, RV cavity; (ii) Repolarization abnormalities in ECG; (iii) Depolarization/ Conduction abnormalities in ECG; (iv) LBBB morphology with superior axis.

Emerging data suggest [22], increasing role for endocardial voltage mapping, in identifying scarring of RV, early diagnosis of disease, presence, location and extent of scar in RV by electro anatomic mapping and is useful in differential diagnosis of RVOT tachycardia. It also has prognostic implications, as scar related RVOT tachycardia has higher recurrence.

Table 2: Criteria.

Global & regional dysfunction & structural alterations		
	Major criteria	By 2-dimensional echocardiography: 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^2) PSAX RVOT ≥36 mm (corrected for body size—PSAX/BSA ≥21 mm^2) Fractional area change ≤33% By MRI: Regional RV akinesia or dyskinesia or dys synchronous RV contraction and 1 of the following: Ratio of RV end-diastolic volume to BSA ≥110 mL/m^2 (male) or ≥100 mL/m^2 (female) RV ejection fraction ≤40% By RV angiography: Regional RV akinesia, dyskinesia, or aneurysm
	Minor criteria	By 2-dimensional echocardiography: Regional RV akinesia or dyskinesia and 1 of the following (end diastole): PLAX RVOT ≥29 to <32 mm (corrected for body size—PLAX/BSA ≥16 to ≤19 mm/m^2) PSAX RVOT ≥32 to <36 mm (corrected for body size—PSAX/BSA ≥18 to <21 mm/m^2) 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/m^2 (male) or ≥90 to <100 mL/m2 (female) RV ejection fraction >40% to ≤45%
Tissue characterization of wall		
	Major criteria	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 criteria	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
Repolarization abnormalties		
	Major criteria	Inverted T waves in right precordial leads (V1, V2, and V3) or beyond in individuals >14 yr (in the absence of complete right bundle branch block QRS ≥120 msec)
	Minor criteria	Inverted T waves in leads V1 and V2 in individuals >14 yr (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 yr in the presence of complete right bundle branch block
Depolarization /conduction abnormalties		
	Major criteria	Epsilon wave (reproducible low-amplitude signals between the end of the QRS complex to the onset of the T wave) in the right precordial leads (V1 to V3)

	Minor criteria	Filtered QRS duration (fQRS) ≥114 msec Duration of terminal QRS ≤40 μV (low-amplitude signal duration) ≥38 msec Root-mean-square voltage of terminal 40msec ≤20 μV Terminal activation duration of QRS ≥55msec 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
Arrhythmias		
	Major criteria	Non-sustained or sustained VT of left bundle branch morphology with superior axis (negative or indeterminate QRS in leads II, III, and aVF and positive in lead aVL)
	Minor criteria	Non-sustained or sustained ventricular tachycardia of RV outflow configuration, left bundle branch block morphology with inferior axis (positive QRS in leads II, III, and aVF and negative in lead aVL) or of unknown axis >500 ventricular extrasystoles per 24hr (Holter)
Family history/ Genetics		
	Major criteria	ARVC/D confirmed in a first-degree relative who meets the current Task Force criteria ARVC/D confirmed pathologically at autopsy or surgery in a first-degree relative Identification of a pathogenic mutation† categorized as associated or probably associated with ARVC/D in the patient under evaluation
	Minor criteria	History of ARVC/D in a first-degree relative in whom it is not possible or practical to determine whether the family member meets the current Task Force criteria Premature sudden death (<35 yr) because of suspected ARVC/D in a first-degree relative ARVC/D confirmed pathologically or by current Task Force criteria in a second-degree relative

Treatment

1. *Drugs:* In asymptomatic patients or those with non-lethal arrhythmias, beta-blockers are agents of choice. Sotalol has been reported to be the most effective drug in suppressing ventricular arrhythmias in patients with ARVD. Amiodarone is also effective [23]. Drug therapy may be continued as an adjunct to an implantable cardioverter defibrillator (ICD) or as primary therapy for sustained arrhythmias.
2. *Radiofrequency ablation:* It has variable success rates and recurrence rates. It is used in patients not responding to drug therapy or those patients who received ICD but continues to have arrhythmias [24].
3. *ICD implantation:* Patients presenting with either hemodynamically unstable ventricular tachycardia or SCD should be considered for ICD implantation. ICD implantation is technically challenging in patients with ARVD due to thinning of RV wall with increased risk of RV perforation. Further as disease progresses, replacing more cardiac muscle with fibrous tissue, may lead to loss of sensing function in RV defibrillation lead, consequently lead revision may be necessary [25, 26].
4. *Surgery:* surgical resection of ventricular focus or cardiac transplantation in patients with refractory heart failure [27].

Conclusion

It is important to consider ARVD as one of the possible causes for RVOT VT in young patients who present with syncope or VT and high suspicion should be exercised by the clinician, so that the diagnosis can be clinched.

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Conflicts of interest

Authors declare no conflicts of interest.

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