ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC)

Zahid Aslam Awan, Farhat Abbas, Kamran Bangash

Department of Cardiology,
Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar

ABSTRACT

Objective: *To see the presentations of patients with arrhythmogenic right ventricle cardiomyopathy (ARVC).*

Material and Methods: *The study was conducted in the Department of Cardiology Postgraduate Medical Institute, Hayatabad Medical Complex from Jan 2003 to Dec 2004. Patients who fulfilled the diagnostic criteria of ARVC were included. Twelve channels ECG, 24 hours ECG monitoring, transthoracic echo and signal average ECG (SAECG) were done for all patients.*

Results: *Sixty-two patients presenting with LBBB type of broad complex tachycardia were studied. Only twelve patients could fulfill the diagnostic criteria of ARVC. Mean age at presentation was 34± 8 years. Monomorphic ventricular tachycardia (VT) of LBBB type with inferior axis was the commonest presentation. T-wave inversion in surface ECG was seen in right precordial leads in all the patients. SAECG was abnormal in only one patient. Epsilon waves in right precordial leads were seen in one patient. Transthoracic echo revealed RV dilatation in 11 of the 12 cases. VT was responsive to amiodarone in all the cases.*

Conclusion: *ARVC commonly presents with ventricular arrhythmia of LBBB type and 12 leads resting ECG is abnormal in almost all cases. RV is mostly dilated and response to amiodarone is good.*

Keywords: *Arrhythmogenic Right Ventricle Cardiomyopathy (ARVC), Ventricular Tachycardia, Resting ECG., Sudden Death.*

INTRODUCTION

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a heart muscle disease of unknown etiology characterized by peculiar right ventricular (RV) involvement[1]. Distinctive pathologic features are myocardial atrophy and fibro-fatty replacement of the RV free wall. Clinical presentation is usually related to ventricular tachycardias with a left bundle branch block pattern or ventricular fibrillation leading to cardiac arrest, mostly in young people and athletes[2]. Later in the disease evolution, progression and extension of RV muscle disease and left ventricular involvement may result in right or biventricular heart failure[3,4]. The diagnosis of ARVC may be difficult because of several problems with specificity of ECG abnormalities, different potential etiologies of ventricular arrhythmias with left bundle branch morphology, assessment of RV structure and function and interpretation of endomyocardial biopsy findings. A definite diagnosis relies on histopathologic demonstration of fibrofatty infiltration of the RV free wall reaching the endocardium. This possibility is limited to postmortem analysis because enodomyocardial biopsy rarely reflects transmural changes[5]. Genetic chromosomal analysis is possible but is not yet practical for routine use[6]. A standardized diagnostic criterion have been proposed by the Study Group on ARVC of the European Society of Cardiology[7,8]. According to these guidelines, the diagnosis of ARVC is based on the presence of major and minor criteria encompassing electro-cardiographic, arrhythmic, morphological, histopathologic and genetic factors. Since the assessment of sudden death risk in patients with ARVC is still not well established, there are no precise guidelines to determine which patients need to be treated and what is the best management approach. The therapeutic options include beta-blockers, antiarrhythmic drugs, catheter ablation, and implantable cardioverter defibrillator (ICD). The ICD is the most effective safeguard against arrhythmic sudden death.

However, its precise role in changing the natural history of ARVC by preventing sudden and non-sudden death needs to be evaluated by a prospective study of a large series of patients[9].

In patients in whom ARVC has progressed to severe RV or biventricular systolic dysfunction with risk of thromboembolic complication, treatment consists of current therapy for heart failure including anticoagulant therapy. In case of refractory congestive heart failure, patients may become candidates for heart transplantation.

The purpose of this study is to highlight different presentations of ARVC so that although uncommon but not rare this fatal disorder should be identified in time and those at high risk for sudden cardiac death (SCD) may be benefited by ICD.

MATERIAL AND METHODS

This prospective study was conducted in cardiology department of Hayatabad Medical Complex Peshawar over a period of two years from January 2003 to December 2004. The patients were admitted through outdoor patient department, emergency room and private clinics.

The diagnostic criterion proposed by the study group on ARVC of the European Society of Cardiology[7,8] was utilized for diagnosis. On the basis of this classification, diagnosis of ARVD/C is fulfilled in the presence of 2 major criteria, or 1 major plus 2 minor criteria, or 4 minor criteria from different groups (Table 1).

A fixed protocol was followed for all patients with LBBB type broad complex tachycardia. Those who fulfilled the diagnostic criteria of ARVC were included (12 pts). Others with evidence of pre-excitation on resting ECG (6 pts), Coronary artery disease (36 pts) and RVOT-VT (8 pts) were excluded. 12 lead ECG during sinus rhythm, an ECG during ventricular tachycardia, transthoracic echocardiography and signal average ECG (SAECG) was performed for

CRITERIA FOR DIAGNOSIS OF ARVD/C

I.	Family history **Major** Familial disease confirmed at necropsy or surgery **Minor** Family history of premature sudden death (<35 years) due to suspected ARVD/C (clinical diagnosis based on present criteria)
II.	ECG depolarization/conduction abnormalities **Major** Epsilon waves or localized prolongation (=110msec) of the QRS complex in the right precordial leads (V_1-V_3) **Minor;** Late potentials seen on signal-average ECG
III.	ECG repolarization abnormalities **Minor;** Inverted T waves in right precordial leads (V_2 and V_3) in patients > 12 years and in the absence of right bundle branch block.
IV.	Arrhythmias **Minor** Sustained or non-sustained left bundle branch block-type ventricular tachycardia documented on ECG, Holter monitoring, or during exercise testing Frequent ventricular extrasystoles (>1,000/24 Hours on Holter monitoring)
V.	Global and/or regional dysfunction and structural alteration **Major** Severe dilation and reduction of right ventricular ejection fraction with no (or only mild) left ventricular involvement. Localized right ventricular aneurysms (akinetic or dyskinetic area with diastolic bulging) Severe segmental dilatation of the right ventricle. **Minor** Mild global right ventricle dilation and/or ejection fraction reduction with normal left ventricle Mild segmental dilatation of the right ventricle. Regional right ventricular hypokinesia
VI.	Tissue characteristics of walls **Major** Fibrofatty replacement of myocardium on biopsy.

Table 1

all patients with ARVC.

SAECG was done by using PPG Hellige EK56 system. The following indexes were derived from this waveform of the filtered QRS: total filtered QRS duration (fQRS), the root-mean-square voltage of the terminal 40ms (RMS), and the duration of the low-amplitude signal (LAS) < 40 micro V in the terminal portion of the filtered QRS. Two hundred fifty to 400 beats were averaged to obtain a noise level <0.7 micro V. For 40Hz high-pass filter, the normal values were: fQRS<122 ms for men; fQRS<115 ms for women; LAS<41 ms and RMS > 20 micro V for both genders. Late potentials were considered positive if at least 2 of the above-mentioned variables were abnormal[10].

Transthoracic echocardiography was performed using a Core Vision system (Toshiba). All patients with ventricular arrhythmia were screened for electrolyte imbalance and drugs effect. Coronary artery disease was excluded on the basis of history of chest pain or ECG evidence of ischemia.

RESULTS

Only 12 patients of those who presented with ventricular arrhythmia and having no evidence of coronary artery disease could fulfill the diagnostic criteria of ARVC. All patients were male with mean age of 34 years. Six presented with palpitation, four with exertional dyspnea and two with dyspnea at rest. Frequent sustained VT with spontaneous remission was commonly seen in 24hrs ECG monitoring in CCU. The VT was of LBBB type with inferior axis in all these cases (Fig 1). One patient with VT was unstable hemodynamically and was soon electrically cardioverted with 200j DC shock. Rest of the patients responded to amiodarone 150mg bolus in 10 mins and 800mg in 18 hrs infusion.

VENTRICULAR TACHYCARDIA IN ARVC

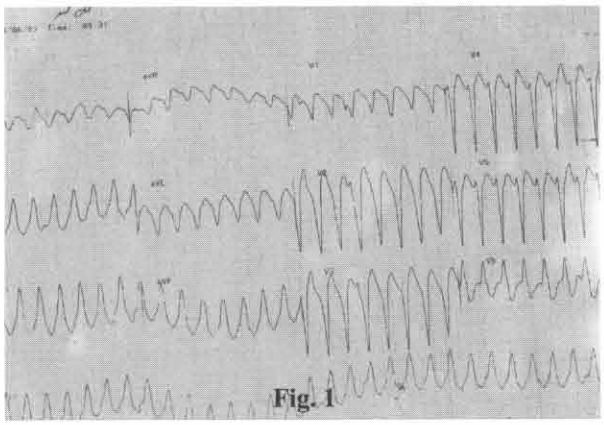

Fig. 1

In the 12 lead ECG of all the patients, T-wave inversion and QRS>110ms was seen in chest leads V_1-V_3. Epsilon wave in V_1, V_2 and V_3 was seen in only one patient (Fig 2). Late potentials were positive in one patient where fQRS>140 ms and RMS 15 micro V and LAS 60 ms was observed. Transthoracic echo revealed RV dilatation (mean RV 3.5cm) and poor contractility in eleven cases; one of these cases was also having LV enlargement (6.3cm). One patient had RV hypokinesia.

Of the fifty patients presenting with LBBB type of BCT which were excluded from study six were having evidence of pre-excitation on resting ECG, thirty six were having evidence of coronary artery disease and eight were labeled RVOT-VT on basis of Isoprel/exercise induced VT.

DISCUSSION

Documentation of 12 cases of ARVC in a tertiary care center in two years time indicates that ARVC is not uncommon in this part of the world. The actual magnitude of the problem is expected to be much more because in this study only those who were having refractory ventricular arrhythmia were referred to our unit. There are many who die suddenly and there are others who solely present with right heart failure or biventricular failure. ARVC prevalence in general population is 1 in 5000. In Veneto (Italy), it has been shown that 20% of all SCD are due to undiagnosed ARVC. In 50% of the cases it is inherited as autosomal dominant variant; however we have not been able

EPSILON WAVES

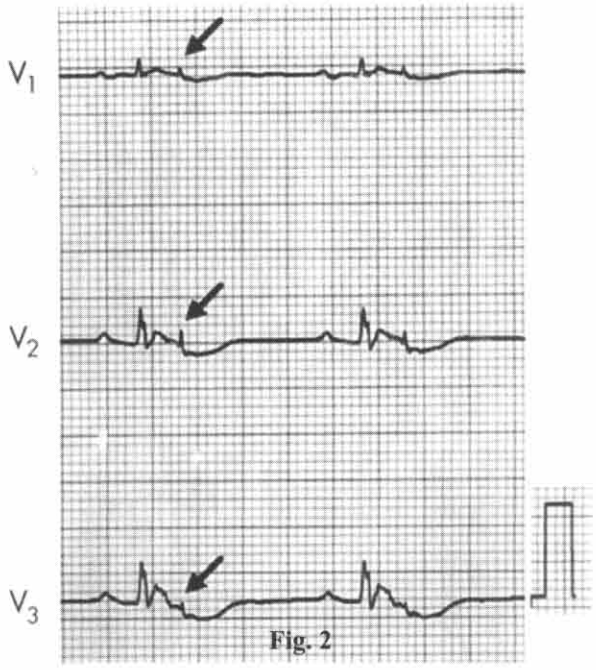

Fig. 2

DIFFERENTIATION OF ARVD/C FROM RVOT TACHYCARDIA ON SURFACE ECG, AND AS PROPOSED BY MARCUS

	ARVC	RVO-VT	Control
T-wave inversion > V2	54.3%	33.0%	1.4%
Max QRS duration (V1-3)	114±19ms	104±13ms	98±11ms
Max QRS >100ms (V1-3)	51.7%	21.0%	12.9%
QRS dispersion	40±13ms	34±10ms	33±9ms
QT dispersion	54±21ms	47±16ms	40±13ms
Epsilon potential	22.5%	2.8%	0
Late Potentials (25Hz)	41.4%	11.7%	3.0%
ARVD current opinion Cardiol 2001,16:8-16			

Table 2

to screen relatives in our cases because of multiple reasons. Right ventricular electrical instability in ARVC presentation ranges from isolated PVCs to sustained VT/VF. The LBBB morphology of VT indicates origin in RV however mean QRS axis if inferior suggests RV outflow and if superior suggests RV inferior wall or apical origin of VT. ECG depolarization and repolarization abnormalities especially T inversion in precordial leads V_1-V_3 are the most common finding. In our study 100% of the patients were having T changes in right precordial leads. Moreover due to delayed RV activation complete or incomplete RBBB or prolonged QRS in right precordial lead may be seen. All our patients were having QRS >110ms in V_1-V_3. Epsilon wave, which presents as small amplitude signal after QRS on surface ECG representing late potential is uncommon. In our study only 8.33% cases were having epsilon wave. Epsilon wave and late potentials reflect areas of slow coduction due to fibrofatty replacement.[10]

Although LBBB type VT in patients with RV pathology has been the commonest presentation of ARVC in our experience however differentiation from idiopathic right ventricular outflow tract tachycardia is important. The prognosis in later cases is good and definite treatment is available. Table 2 enlists differentiation between ARVC and RVOT-VT as proposed by Marcus.

Beside the LBBB type VT, the T-wave abnormality in right precordial leads and right bundle branch block pattern in V1 is common in ARVC and needs to be differentiated from Brugada syndrome which is also not uncommon in this part of world. The difference between Brugada syndrome and ARVC as proposed by Brugada are listed in Table 3.

DIFFERENTIAL DIAGNOSIS BETWEEN ARVD/C AND BRUGADA SYNDROME AS PROPOSED BY BRUGADA

	ARVD	Brugada
Age	Any	Any
Sex	M>F	M>F
Inheritance	Autosomal Dominant	Autosomal Dominant 50%
Dominant ECG	Inverted T, ST elev	Epsilon±RBB, V1-3
H-V Interval	Fixed abnormality	Dynamic changes
Echo/Angio	Normal	1/3 normal
MRI	RV dilation or aneurysms	Normal (almost)
Pathology	Fatty infiltration	Normal
VT type	Fibrosis, fatty infiltration	Normal
Exercise	Monomorphic	Polymorphic(VF)
Isoproterenol	No effect	Normal or worsening
Class I Drugs	No effect	Normalization
(Flecainide)	No effect (some)	? ST elevation
(Ajmaline)		
ARVD current opinion Cardiol 2001,16:8-16		

Table 3

Two dimensional echo has been the main tool of diagnosis in our cases. The most specific aspects for diagnosis are reduced global or regional ejection fraction and different degree of dilatation of RV and outflow tract. RV apex and inferior wall are mostly involved[11-13].

We have not used NMR (Nuclear Magnetic Resonance) because diagnostic criteria was already fulfilled in all patients. It has high sensitivity but low specificity and is of limited value in patients with normal RV function on echo. It is good for free wall thickness and contraction assessment[14].

Ventriculography has been gold standard for diagnosis of ARVC especially LAO 60 with Cran 25 and Caud 30 tilt and RAO 30 with Cran 15 and Caud 20 tilts to view apex and RV outflow tract[15]. We did not need it in our series because echo revealed RV abnormality in all cases.

Since ARVC is a common cause of SCD, we are following our patients for the last two years, one patient died in hospital due to refractory VF and one lost to follow up. The risk factors for SCD are[16-20]

1. History of CA or syncope.
2. Extension of ARVD/C as expressed by T-wave inversion in V3 or beyond.
3. Markedly abnormal late potentials
4. Marked RV dilatation or enlargement.
5. Motion abnormalities, assessed by echo or angiography.
6. Left ventricular involvement and dilatation.
7. ARVD/C, with a genetic locus on chromosome 1q42.43, associated with exercise-induced polymorphic VT and right ventricular apical aneurysms,.

The therapeutic options include beta-blockers, anti-arrhythmic drugs, catheter ablation, and implantable cardioverter defibrillator[21-23]. A variety of drugs have been tried, French have proposed amiodarone to be most effective antiarrhythmic while Italians prefer propaferone and Germans advise sotalol. In our experience amiodarone was found to be better than sotalol for control of VT. RFA has a limited role because of the patchy and progressive involvement of RV. ICD is recommended for aborted SCD.

CONCLUSION

ARVC is a heart muscle disease of genetic origin, which predominantly affects the right ventricle. Resting ECG and echocardiography is almost always abnormal in symptomatic cases. LBBB type VT with inferior axis is the commonest presentation. Late potentials in SAECG and Epsilon wave in resting ECG are not very common. Mostly the ventricular arrhythmias are responsive to amiodarone therapy.

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Address for Correspondence:

Dr. Zahid Aslam Awan
Cardiology Department
Hayatabad Medical Complex Peshawar.