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Case Report

Late presentation of arrhythmogenic right ventricular cardiomyopathy : role of non invasive modalities for the diagnosis

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Abstract

Background : Arrhythmogenic right ventricular cardiomyopathy(ARVC) is an inherited myocardial disease affecting predominantly young people and manifests as sustained ventricular tachycardia, sudden cardiac death (SCD) or heart failure. However, its first manifestation in older patients is infrequent. Diagnosis of ARVC remains a clinical challenge and need further investigation. Our case report investigated role of non invasive modalities for diagnosis of ARVC patient.
Case presentation : A 65 year old man was admitted to the hospital with symptoms of palpitationand near syncope. An Electrocardiogram (ECG) showed a sustained VT with LBBB morphology and inferior axis. The patient was cardioverted to sinus rhytm with a single 100J shock. Postcardioversion ECG showed an epsilon wave in right precordial leads. Echocardiography revealed extensive RV enlargement and reduce function. Our patient had three major (RV aneurysm, epsilon wave and T wave inversion) and one minor criteria (sustained LBBB type–VT with inferior axis)making the diagnosis of ARVC definite according to the revised Task Forced Criteria.
Conclusion : ARVC mayhave a very late presentation and this diagnosis should be considered as a potential cause of sustained VT of RV origin among the elderly. ECG and echocardiography as non invasive modalities have an important role for the diagnosis of patients with suspected ARVC.

Keywords : Arrhythmogenic right ventricular cardiomyopathy,ventricular tachycardia, sudden cardiac death, diagnosis.

INTRODUCTION

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited myocardial disease affecting predominantly young people. It characterized by fibrofatty replacement of the right ventricular (RV) myocardium that predisposes patients to life threatening ventricular arrhythmias and slowly progressive ventricular dysfunction. Biventricular and left-dominant forms of the disease are increasingly recognized.[1] Clinical manifestations develop most often between the second and third decade of life and are related to ventricular tachycardia (VT) or ventricular fibrillation (VF) which may lead to sudden death, mostly in young people while heart failure symptoms and signs typically appear later in life. Its first presentation as sustained VT in older patients without preceding symptoms of heart failure is infrequent. Clinical diagnosis of ARVC is often difficult due to the nonspecific nature of disease features and the broad spectrum of phenotypic manifestation, ranging from severe to concealed forms. Early detection and preventive therapy especially for highest risk patients of experiencing sudden cardiac death may modify the natural history of the disease.[2,3]

Epidemiology

The prevalence of the disease in the general population is estimated at 0.02% to 0.1% (average 1:5.000) but is dependent on geographic circumstances. In certain regions of Italy (Padua, Venice) and Greece (Island of

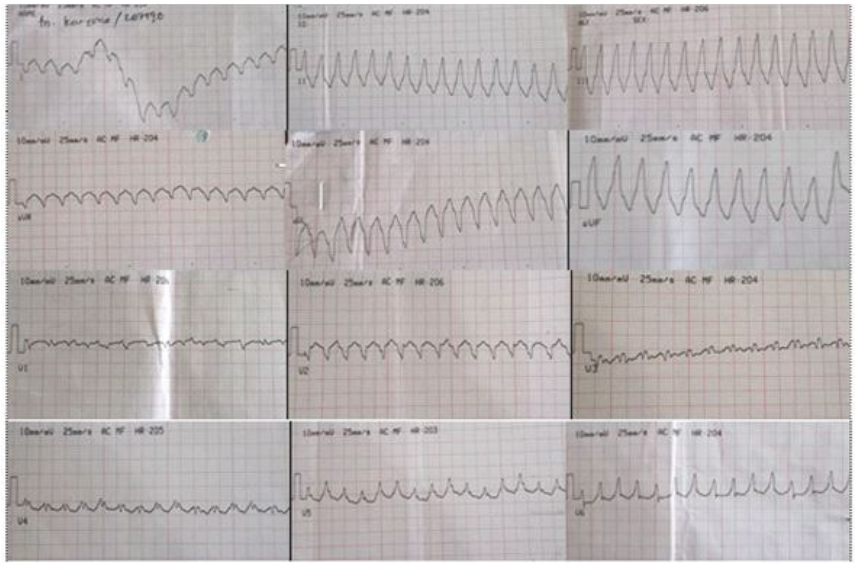

Figure 1. 12 leads ECG of our patient showing VT morphology with LBBB pattern and inferior axis

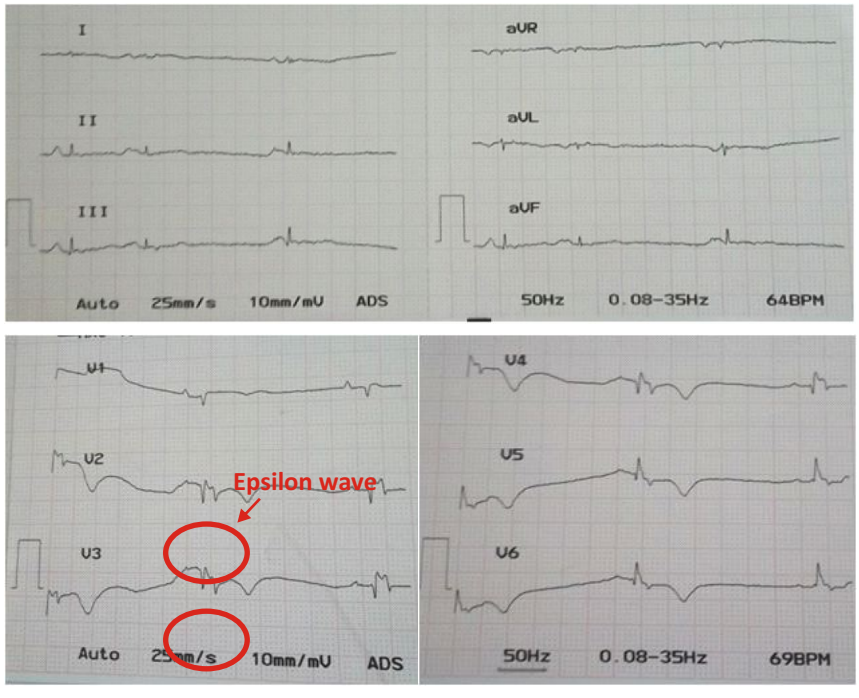

Figure 2. Patient's ECG after cardioversion. There is negative T waves at the anterior leads (V2–V5) and the presence of an epsilonwave in right precordial leads (red arrow).

Naxos), an increased prevalence of 0.4% to 0.8% for ARVC has been reported. 80% of the disease is diagnosed in patients younger than 40 years.[4] The real prevalence of AC, however, is unknown and is presumably higher due to many non diagnosed and misdiagnosed cases.[5]

CASE PRESENTATION

The unusual case of a 65 year old man, without prior history of heart disease was admitted to the hospital with symptoms of palpitation for several hours, chest discomfort and near syncope. Physical examination showed low blood pressure (90/60 mmHg) and a weak, regular and rapid pulse with peripheral oxygen saturation of 97% (in environmental air). Cardiac auscultation revealed an arrhythmic and very tachycardic heart, and it seemed like the presence of a third heart sound. Pulmonary and abdominal examination was normal.

The 12 lead electrocardiogram (ECG) showed a

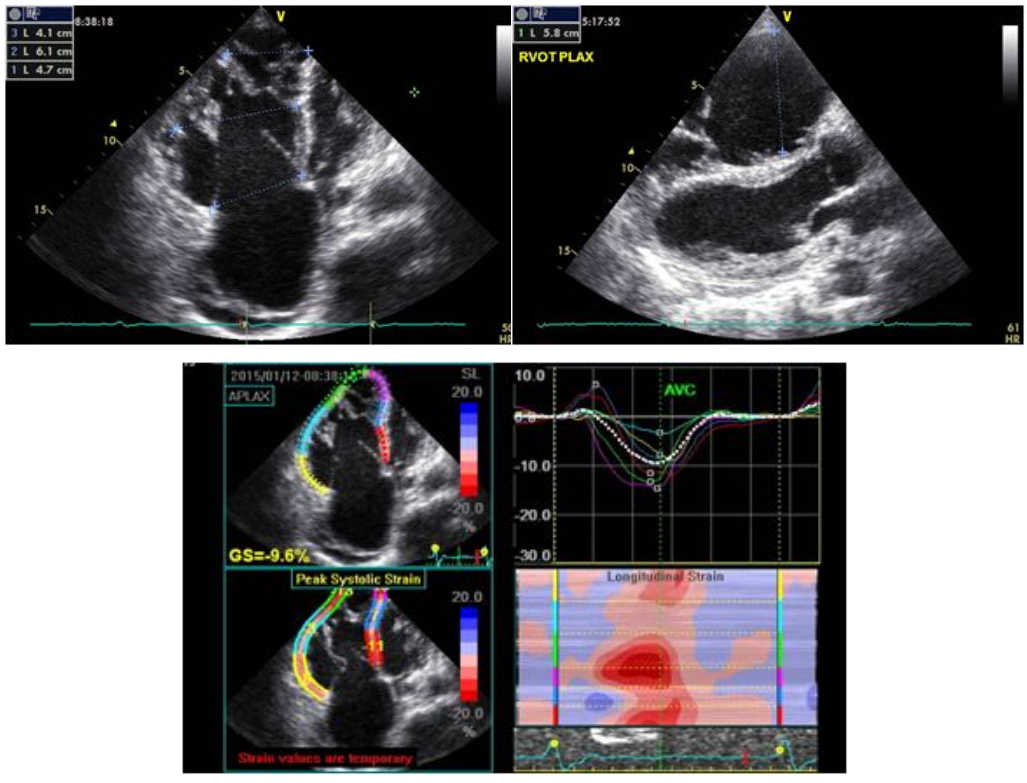

Figure 3. Echocardiographic measurement of the patient revealed extensive enlargement of RV and reduce ventricular function and strain pattern as well.

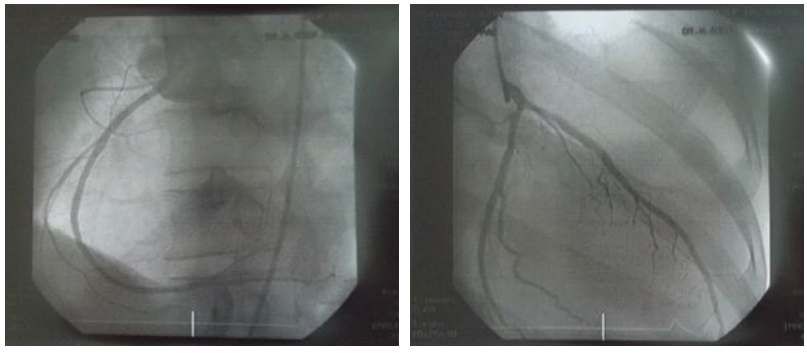

Figure 4. Coronary angiography showing no abnormalities (normal coronary artery)

wide QRS complex tachycardia with LBBB morphology and left axis deviation (Figure 1). Because of hemodynamic instability, the patient was cardioverted to sinus rhythm with a single 100 J biphasic shock. The ECG during the episode of the tachycardia wasconsistent with sustained VT of right ventricular origin. Post cardio version ECG showed sinus bradicardia with negative T waves at the anterior leads and the presence of an epsilon wave in right precordial leads. (Figure 2).

Laboratory examination showed normal limit with the exception of troponin which was positive. Transthoracic echocardiography revealed extensive RV enlargement with regional wall motion abnormalities, reduce RV function (FAC 24.9%, TAPSE 1.02cm, RV strain -9.6%) as well as LV function (LVEF 33%), dyskinetic areasand regional aneurysms in the RV was also present (Figure 3). Coronary angiography was also performed to our patient and showed no abnormalities (Figure 4).

Based on the clinicalpresentation and subsequent work–up, our patient fulfilled three major (RV aneurysm, epsilon wave and T wave inversion in right precordial leads) and one minor criteria (sustained LBBB type-VT with inferior axis) making the diagnosis of ARVC definite according to the revised Task Forced Criteria. The patient was treated with beta blocker and ACE inhibitor and further planned for ICD implantation.

DISCUSSION

ARVC is a cardiomyopathy whose fundamental structural anomaly is the right ventricular myocardial degeneration, which in advanced stages of the disease may spread to the left ventricle. The condition was initially believed to be adevelopmental defect of the RV myocardium, leading to the original designation of ''dysplasia''. This concept has evolved over the last 25 years intothe current perspective of a genetically determined''cardiomyopathy''. The estimated prevalence of ARVC in the general population ranges from 1 in 2000 to 1 in 5000. A familial background has been demonstrated in 30–50% of ARVC cases.[1,2]

The disease is characterized by progressive partial or massive replacement of the myocardium by adipose or fibrofatty tissue. This infiltration is a substrate for electrical instability and leads to variousarrhythmias, ranging from isolated premature ventricular contraction to sustain ventricular tachycardia (VT) or ventricular fibrillation (VF). ARVC is an inherited disorder. The disease shows a familial pattern in 40–70% of the cases and molecular geneticstudies demonstrated that ARVC is a desmosomal disease resulting from genetically defective cell adhesion proteins such as plakoglobin, desmoplakin, plaokophillin–2, desmoglein–2, and desmocollin.[1,3]

ARVC is usually manifested in the form of VT episodes with left bundle of His branch block morphology and has its origin in the RV in apparently healthy adolescents or young adults. Ventricular arrhythmias may be asymptomatic and detected on routine ECG or can cause palpitations, syncope or sudden death. The age at which the first event occurs is between

	Major criteria	Minor criteria
RV systolic function and structure	By 2D echo: Regional RV akinesia, dyskinesia or aneurysm and one of the following (end diastole): PLAX RVOT ⩾ 32 mm, PSAX RVOT ⩾ 36 mm, Or fractional area change ⩽ 33% By MRI: Regional RV akinesia, dyskinesia or aneurysm or dyssynchronous RV contraction and 1 of following: Ratio of RV end-diastolic volume to BSA ⩾ 110 mL/m^2 or ⩾ 100 mL/m^2 (or RV EF ⩽ 40%) By RV angiography: Regional RV akinesia, dyskinesia or aneurysm	By 2D echo: Regional RV akinesia, dyskinesia or aneurysm and 1 of the following (end diastole): PLAX RVOT ⩾ 29 to < 32 mm, PSAX RVOT ⩾ 32 to < 36 mm, Or fractional area change > 33% to ⩽ 40% By MRI: Regional RV akinesia, dyskinesia or aneurysm 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/m^2 (female) or RV > 40% to ⩽ 45 % By RV angiography: Regional RV akinesia, dyskinesia or aneurysm
Tissue characterization	Residual myocytes < 60% by morphometric analysis with fibrous replacement of the RV free wall myocardium in ⩾ 1 sample, with or without fatty replacement of tissue on EMB	Residual myocytes 60% to 75% (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 EMB
Repolarization abnormality	Inverted T waves in right precordial leads (V1-3) or beyond in individuals > 14 yr of age (in the absence of complete right bundle - branch block QRS ⩾ 120 ms	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 V4-6 or inverted T waves in leads V1-V4 individuals > 14 yr of age in the presence of complete right bundle branch block
Depolarization abnormality	Epsilon waves in the right precordial leads (V1-3)	Late potential 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 mV or ⩾ 38 μs; Root-mean-square voltage of terminal 40 ms ⩽ 20 μV; Terminal activation duration of QRS ⩾ 55 ms measured from the nadir of the S wave to the end of QRS
Arrhythmias	Nonsustained or sustained ventricular tachycardia of left bundle branch morphology with superior axis Frequent ventricular extrasystoles (> 1000 per 24 h) (Holter)	Nonsustained or sustained ventricular tachycardia of RV outflow configuration, left bundle branch morphology with inferior axis or > 500 ventricular extrasystoles per 24 h (Holter)
Familial history	ARVC confirmed pathologically in the first degree or identification of a pathogenic mutation categorized as associated or probably associated with ARVC	History of ARVC in a first degree relative or premature sudden death (< 35 yr of age) due to suspected ARVC or ARVC confirmed pathologically or by current Task Force Criteria in second-degree relative

Table 1. Revised arrhythmogenic right ventricular cardiomyopathy diagnostic criteria (modified from Marcus *et al*.[8])

15 and 35 years. Clinical presentations include palpitations, fatigue, atypical chest pain, syncope and sudden cardiac death.The disorder affects men more often thanwomen, and it usually manifests in them with a broader expression of the disease. Symptomatic heart failure is a rare manifestation of ARVC and most often it occurs in advanced stages of the disease.[6]

The natural history of ARVC, in its classic "right dominant" form, has been classified into 4 distinct phases with progressive development of symptoms and structural abnormalities: (1) concealed phase: a subclinical asymptomatic phase with mild or absence of identifiable structural RV abnormalities. SCD may still occur in this stage of disease; (2) overt electrical disorder: with palpitations, syncope and typically withsymptomatic ventricular arrhythmias of RV origin usually triggered by effort. Arrhythmias may vary from premature ventricular beats, to non-sustained ventricular tachycardia with left bundle branch block (LBBB) morphology up to ventricular fibrillation leading to cardiac arrest; (3) RV failure: progressive loss of RV myocardium due to fibrofatty replacement impairs RV function and may result in pump failure; and (4) biventricular failure: an advanced stage with involvement of the interventricular septum and LV causing congestive heart failure (HF).[1,7]

Diagnosis of arrhythmogenic cardiomyopathy (AC) is based on the presence of structural, histological, electrocardiographic, arrhythmic and genetic factors, and on family history. Accurate AC diagnosis is critical due to lifelong implications,not only for the index patient but also for family members.[5] According to the Task Force Report published by McKenna *et al*. in 1994, patients must meet two major criteria, or one major and two minor, orfour minor criteria for them to be considered affected by ARVC. A new modification of diagnostic criteria in order to increase the diagnostic sensitivity has recently been published.[8] There is no single gold-standard diagnostic test for ARVC, and the diagnosis relies on a scoring system with "major" and "minor" criteria based on the demonstration of a combination of defects in RV morphology and function, characteristic depolarization/ repolarization ECG abnormalities, characteristic tissue pathology, typical arrhythmias, family history, and the results of genetic testing.[8]

Electrocardiogram (ECG) and echocardiographic measurement plays important role as non invasive tools for screening and diagnosis of ARVC. The 12–lead ECG is one of themost important tools for the diagnosis, follow–up and SCD risk stratification of AC.[3] The ECG of patients with ARVCusually shows sinus rhythm, QRS duration >110 ms in lead V1. An invertedT waves in the right precordial leads beyond V1, without any right bundle of His branch block and right ventricular late potentials in the form of "epsilon waves" in leads V1–V3 as shown in our patient. T–wave inversion in these leads is awell-known feature of the ECG in ARVD and inabsence of right bundle of His branch block. Epsilon waves are "post–excitation" electrical potentials of small amplitude, occurring in the ST segment after the end of the QRS complex. These waves, which are observed in 33% of patients with ARVDare considered a major diagnostic criterion.[3,4,8] This Epsilon wave was also present to our patient.

The imaging techniques used to diagnose morphofunctional abnormalities consistent with ARVC include conventional angiography, echocardiography, computed tomography, radionuclide angiography and magnetic resonance imaging (MRI). Echocardiography is of paramount importance in the initial evaluation and follow up of AC patients because of its availability, ease of performance and interpretation, cost effectiveness and non invasive advantages.[3] As a non invasive technique, it is the first–line method for evaluating patients with suspected diagnosis of ARVC and for family screening. Echocardiography also allows serial examinations aimed to assess the diseaseonset and progression during the follow–up of affectedpatients and family members.[6]

The main objective of therapeutic strategy in ARVC is preventing sudden cardiac death.[4] The three main treatments are antiarrhythmic drugs, catheter ablation and use of implantable cardioverter defibrillator (ICD).[5] In patients with stable VT, antiarrhythmic drug treatment aims not only at the suppression of VT recurrences, but mainly at the prevention of sudden cardiac death.Various drugs have been investigated to suppress the sometimes life–threatening arrhythmias of ARVC including betablockers, sotalol, and amiodarone. The most efficacious drug seems to be sotalol with an overall efficiency rate of 68% and 83% to treatboth inducible and non inducible ventricular tachycardia in ARVC. Amiodarone, a class III drug, has shown efficacy in the treatment of malignant arrhythmias.[9,10] Current indications for catheter ablation in patients with ARVD are well tolerated monomorphic VT with localized forms of the disease and refractory to medication, or incessant VT or with frequent ICD discharges.[10]

ICD therapy improves long-term prognosis and survival when applied to a selected high–risk population and as secondary prevention. When the disease has progressed toright ventricular or biventricular failure, the currently prescribed treatment for heart failure should be applied, including diuretics, beta blockers, angiotensin converting enzyme inhibitors and anticoagulants.[2,4,5] Accepted indications for ICD therapy are prevention of sudden cardiac death in ARVC patients (1) with documented sustained VT or ventricular fibrillation (class I recommendation) and (2) with high–risk features such as extensive disease, positive family history, or undiagnosed syncope (class IIa recommendation).[10]

The patient described here was 65 yearsold when the diagnosis of ARVC was suspected, i.e., much older

than the age at which it is usually reported (between the second and fifth decades of life).[11] Afew cases of elderly people with this cardiomyopathy have been reported in the literature. The two oldest patients reported were both 82 years old: one was a manwith a previous history of syncope thatbegan 5 years earlier[12] and the second was a woman with sustained VT due to an initially diagnosed ARVC.[13]

CONCLUSION

Our case demonstrates that arrhythmogenic right ventricular cardiomyopathy may have a very late presentation and this diagnosis should be considered as a potential cause of sustained ventricular tachycardia of right ventricular origin among the elderly. ECG and echocardiography as non invasive modalities have an important role for the diagnosis of patients with suspected ARVC. Early diagnosis and appropriate treatment will improve outcomes and reduce morbidity and mortality.

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