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OLGU YAZISI / CASE REPORT

APİKAL TROMBÜS İLE SEYREDEN ARİTMOJENİK SAĞ VENTRİKÜL DİSPLAZİSİ KARDİYOMİYOPATİLERİN ATİPİK BULGUSU

ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA WITH APICAL THROMBUS ATYPICAL PRESENTATION OF CARDIOMYOPATIES

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ÖZ

Aritmojenik sağ ventrikül displazisi (ARVD) nadir görülen bir kardiyomiyopatidir. ARVD çoğunlukla genç yaşlarda tanı alır ve kendisini ventriküler aritmiler, çarpıntı, baş dönmesi, kalp yetmezliği ve hatta ani kardiyak ölüm ile gösterebilir. Görüntüleme yöntemleri ile sağ ventrikül (SV) dilatasyonu ve apikal anevrizma tipik bulgusudur. Fakat ARVD olgularında intraventriküler trombüs çok nadir görülmektedir. 19 yaşında erkek hasta, hastanemize çarpıntı ve bayılma şikâyetleri ile başvurdu. Elektrokardiyografisinde ön yüz derivasyonlarda T negatifliği bulunmakta idi. Ekokardiyografide sağ ventrikül dilate ve SV apeksinde anevrizmatik oluşum içinde trombüs görüldü (**Fig-1**) . Kardiyak manyetik rezonans incelemede sağ ventrikül genişlemesini, yağ infiltrasyonunu, fibrotik dokuları, SV duvar hareket bozukluğunu ve trombüslü apikal anevrizma doğrulandı. Antikoagulan tedaviyle üç ay sonra trombüsün rezole olduğu gözlendi ve ICD implante edildi. ARVD tanısında elektrokardiyografik, aritmik, histolojik ve ailesel özelliklerin yanında görüntüleme yöntemleri de büyük önem taşımaktadır. Sağ ventrikül dilatasyonu ve apikal anevrizması tanı sürecinde önemli kriterler olmakla birlikte bu gibi bulgular saptandığında trombüs varlığı da dikkatlice değerlendirilmelidir.

ANAHTAR KELİMELER: Aritmojenik Sağ Ventrikül Displazisi, Fibrofatty İnfiltrasyon, Trombüs

ABSTRACT

Arrhythmogenic right ventricular dysplasia (ARVD) is a rare form of cardiomyopathy. It commonly presents in young adults with ventricular tachycardia or sudden death. Right ventricular (RV) dilatation and apical aneurysm are the typical findings in imaging methods. However intraventricular thrombus is rarely seen in ARVD cases. A 19 year old male was admitted to hospital with palpitation and syncope. T wave inversion was detected on anterior surface electrocardiogram. Transthoracic echocardiography revealed dilated RV and apical aneurysm in which thrombus located (**Fig-1**). Cardiac magnetic rezonans imaging comfirmed RV enlargement, fatty infiltration, fibrosis, wall motion abnormalities and apical aneursym with thrombus. Anticoagulation theraphy commenced to the patient. After three months later trombus resoluted and ICD was implanted. Imaging methods have a great importance in the diagnosis of ARVD besides electrocardiographic, arrhythmic, histological and familial characteristics. While right ventricular dilatation and apical aneurysm are important criteria for the diagnosis process, the presence of thrombus should be evaluated carefully.

KEYWORDS: Arrhythmogenic Right Ventricular Dysplasia, Fibrofatty Infiltration,Thrombus

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INTRODUCTION

Arrhythmogenic right ventricular dysplasia(ARVD) is a rare form of cardiomyopathy in which the heart muscle of the right ventricle (RV) is replaced by fat and/or fibrous tissue. The right ventricle is dilated and contracts poorly. It commonly presents in young adults with ventricular tachycardia or sudden death (1). Researchers have found two patterns of inheritance for ARVD; autosomal dominant, the family members have a 50 percent chance of inheriting the condition, autosomal recessive, one form is called Naxos disease. ARVD is usually diagnosed at a young age and symptoms may include ventricular arrhythmias, palpitations, dizziness, heart failure and also sudden cardiac death. ARVD is diagnosed on medical history, physical exam, and tests (echocardiogram, Holter monitor, electrophysiologic testing, cardiac MRI, and/or cardiac CT scan). Cardiac MRI is an important test for the diagnosis as it visualizes fibrofatty infiltration of the right ventricular (RV) myocardium(2).

CASE REPORT

A 19 year old male was admitted to hospital with palpitation. There was no family history of heart disease or sudden death. On admission he was haemodynamically stable and was not in heart failure. T wave inversion was detected on surface ECG and had no other abnormalities. Laboratory tests contain complete blood count, liver-thyroid-renal parameters, serum electrolytes and cardiac markers and all of them were normal. Echo showed: dilated right ventricle with outpouching in the right ventricular cavity and apex aneurysm with thrombus in it (**Fig-1**). Due to his palpitation history Holter ECG was performed but no arrhythmogenicrythm was detected. Cardiac MRI revealed right ventricular enlargement, fatty infiltration, fibrosis, wall motion abnormalities and apical aneurysm with thrombus. Anticoagulation started with ACE (angiotensin converting enzyme) inhibitor,and beta blocker, after three months thrombus resolute and ICD was implanted.

DISCUSSION

ARVD is a leading cause of sudden death among young athletes. But it can affect people of all ages and all activity levels. The major condition which needs to be differentiated from ARVD/C is idiopathic ventricular tachycardia arising from the outflow tract (3). The electrocardiogram (ECG) provides important diagnostic information in patients suspected of having right ventricular cardiomyopathy/dysplasia. Normally, the free wall of the right ventricle is the last part of the heart to undergo depolarization. If there is selective damage to the right ventricular free wall musculature, there may be fragmentation and selective slowing and prolongation of the end of the QRS complex and this can be seen in the anterior precordial leads. The delay in depolarization may be extremely prolonged and may be visible as reproducible low frequency waves that extend beyond the QRS complex and before the T wave. These are known as postexcitation or epsilon waves (4,5). They are of low amplitude and are usually visible only on the ECG leads overlying the right ventricle.

Fig-1 Echocardiography of RV

International Task Force proposed criteria for the clinical diagnosis of ARVD/C, based on structural, electrocardiographic, arrhythmic, histological and familial characteristics of ARVD/C. On the role of emerging diagnostic modalities and advances in the genetics of ARVC/D, and although 1994 criteria were highly specific, but they lacked sensitivity for early and familial disease, Marcus et al revised the task force (6). Comparison between the Original and Revised Task Force Criteria is shown in the (**Table-1)**.

Table-1 Comparison of Original and Revised Task Force Criteria

Original task force criteria	*Revised task force criteria*
*I. Global or regional dysfunction and structural alterations**	
Major	
	By 2D echo:
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	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	
	By 2D echo:
Mild global RV dilatation and/or ejection fraction reduction with normal LV Mild segmental dilatation of the RV	Regional RV akinesia or dyskinesia and 1 of the following (end diastole):
Regional RV hypokinesia	✓ PLAX RVOT 29 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%
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
	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 wave (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 (SAECG)	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 (fQRS) 114 ms
	Duration of terminal QRS ,40 mV (low-amplitude signal duration) 38 ms Root-mean-square voltage of terminal 40 ms 20 mV Terminal activation duration of QRS 55 ms measured from the nadir of the S wave to the end of the QRS, including R0 , 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)
Minor	
Left bundle-branch block-type ventricular tachycardia (sustained and nonsustained) (ECG, Holter, exercise)	Nonsustained 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
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/D confirmed in a first-degree relative who meets 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	
Family history of premature sudden death (,35 years of age) due to suspected ARVC/D	History of ARVC/D in a first-degree relative in whom it is not possible or practical to determine whether the family member meets current Task Force criteria
Familial history (clinical diagnosis based on present criteria)	Premature sudden death (,35 years of age) due to suspected ARVC/D in a first-degree relative ARVC/D confirmed pathologically or by current Task Force Criteria in second-degree relative

PLAX indicates parasternal long-axis view; RVOT, RV outflow tract; BSA, body surface area; PSAX, parasternal short-axis view; aVF, augmented voltage unipolar left foot lead; and aVL, augmented voltage unipolar left arm lead.
Diagnostic terminology for original criteria: This diagnosis is fulfilled by the presence of 2 major, or 1 major plus 2 minor criteria or 4 minor criteria from different groups.
Diagnostic terminology for revised criteria: definite diagnosis: 2 major or 1 major and 2 minor criteria or 4 minor from different categories; borderline: 1 major and 1 minor or 3 minor criteria from different categories; possible: 1 major or 2 minor criteria from different categories.
* Hypokinesis is not included in this or subsequent definitions of RV regional wall motion abnormalities for the proposed modified criteria.
† A pathogenic mutation is a DNA alteration associated with ARVC/D that alters or is expected to alter the encoded protein, is unobserved or rare in a large non-ARVC/D control population, and either alters or is predicted to alter the structure or function of the protein or has demonstrated linkage to the disease phenotype in a conclusive pedigree

In the early stage of the disease, structural changes may be absent or subtle and confined to a localized region of the RV, typically the inflow tract, outflow tract, or apex of the RV, the "triangle of dysplasia (7)." Progression to more diffuse RV disease and left ventricular (LV) involvement, typically affecting the posterior lateral wall, is common (8). In the early "concealed phase," individuals are often asymptomatic but may nonetheless be at risk of sudden cardiac death, notably during exertion.Later, diffuse disease may result in biventricular heart failure, whereas ventricular arrhythmias may or may not be present. The ultimate phenotype may resemble dilated cardiomyopathy. Clinical manifestations vary with age and stage of disease (9).

Although being in autosomal dominant inheritance mostly, there are recessive forms (eg, Naxos disease, Carvajal syndrome) that are associated with cutaneous phenotype. Desmosomal variations lead to impairment of cell-to-cell binding. Seven genes have beenidentified that are associated with ARVC/D: plakoglobin (JUP), desmoplakin (DSP), plakop-hilin-2(PKP2), desmoglein-2 (DSG2), desmocol-lin-2 (DSC2), transforming growth factor beta-3 (TGF_3), and TMEM43.20 (10-12).

NIH registry showed that the mean age of di-agnosis of ARVC/D was 38±14 years with male predominance and T wave inversion beyond V? was present in 56% of newly diagnosed patients. In the first detailed clinical profile of this disease,6 T wave inversion in V1 to V4 was found in 86% (19/22 patients) in contrast to an incidence of 31%

of T wave inversion in V1 to V3 of newly diagnosed patients in the registry stated above(13). For this purpose Jain et al evaluate one hundred patients with ARVD and detected 17 patients with RBBB, 15 patients with IRBBB. T wave inversion through V3 demonstrated optimal sensitivity and specificity in both ARVD patients without a complete RBBB or incomplete RBBB.In this way, to identify patients with ARVD, they have made a chart summarizing an algorithm that can be used of an IRBBB or CRBBB (**Figure-2**) (13).

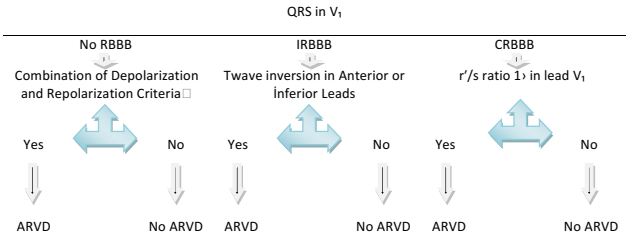

Figure-2; Electrocardiographic Evaluation for ARVD

Definite diagnosis is only possible after a comprehensive evaluation that includes evaluation of the family history, the structure and function of the RV, and screening for arrhythmias. There are two primary goals of treatment of ARVD/C; to reduce the frequency and severity of ventricular arrhythmias and to prevent or limit the worsening of ventricular function and heart failure. The proposed modifications of the original Task Force criteria represent a working framework to improve the diagnosis and management of ARVC/D. Awareness is growing that ARVC/D as such is the most well recognized form of a broad disease spectrum that includes left-dominant and biventricular subtypes. Lack of specific diagnostic guidelines contributes to under recognition of non-classic disease. Future revisions of the Task Force criteria may fill this gap.

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