

Arrhythmogenic right ventricular dysplasia: A case report

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ARTICLE INFORMATION

Received: September 18, 2014

Accepted: November 4, 2014

Competing interests

The authors declare no competing interests

Acronyms

ARVD: arrhythmogenic right ventricular dysplasia

ICD: implantable cardioverter defibrillator

LBBB: left bundle branch block

LV: left ventricle


MRI: magnetic resonance imaging

RV: right ventricle

VT: ventricular tachycardia

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ABSTRACT

Arrhythmogenic right ventricular dysplasia is a heart muscle disease that predominantly affects the right ventricle, bringing about the replacement of normal myocardium with fatty or fibrofatty tissue and causing sudden death in young individuals. Ventricular tachycardia is an important clinical manifestation, although there are reports of right or global heart failure. The diagnosis is confirmed by echocardiography and magnetic resonance imaging. The case of a 65-year-old former smoker, with hypertension and ischemic heart disease, a history of effort syncope symptoms and proven non-sustained ventricular tachycardia, with morphology of left bundle branch block, is reported. Relevant diagnostic studies were performed, and echocardiographic elements which were compatible with arrhythmogenic right ventricular dysplasia were found. Therefore, an implantable cardioverter defibrillator was implanted, after which the patient has had a favorable outcome.

Key words: Arrhythmogenic dysplasia, Right ventricle, Arrhythmia, Left bundle branch block

Displasia arritmogénica del ventrículo derecho. Presentación de un caso

RESUMEN

La displasia arritmogénica de ventrículo derecho es una enfermedad del músculo cardíaco que afecta predominantemente al mencionado ventrículo, provoca el reemplazo del miocardio normal por tejido adiposo o fibroadiposo y es causa de muerte súbita en individuos jóvenes. La manifestación clínica relevante es la taquicardia ventricular, aunque se han descrito casos de insuficiencia cardíaca derecha o global. El diagnóstico se confirma con ecocardiografía y resonancia magnética nuclear. En este artículo se presenta a un paciente exfumador, de 65 años de edad, con hipertensión arterial sistémica y cardiopatía isquémica, con antecedentes de cuadros sincopales al esfuerzo y presencia demostrada de taquicardias ventriculares no sostenidas, con morfología de bloqueo de rama izquierda. Se realizaron los estudios diagnósticos pertinentes y se constataron elementos ecocardiográficos compatibles con displasia arritmogénica de ventrículo derecho, por lo que se implantó un desfibrilador automático implantable, tras lo cual el paciente ha evolucionado favorablemente.

Palabras clave: Displasia arritmogénica, Ventrículo derecho, Arritmia, Bloqueo de rama izquierda

INTRODUCTION

Arrhythmogenic right ventricular dysplasia (ARVD) has been referred to be an arrhythmogenic cardiomyopathy characterized by a progressive loss of cardiomyocytes by replacement of fibrous and adipose tissue, associated with an increased risk of arrhythmias and sudden death¹. It is proposed that the genetic cause is linked to an autosomal dominant inheritance in a third of cases; the recessive trait has a high penetrance. The right ventricle (RV) is predominantly affected, involved in 60% of cases². However, in advanced stages of the disease, biventricular heart failure may develop.

The diagnosis and differentiation of ARVD is a real challenge. The clinical criteria for its identification have low sensitivity in early stages. Electrocardiographically is characterized by the presence of epsilon waves and right bundle branch block morphology. Contrast ventriculography or endomyocardial biopsy are used when non-lethal methods are not conclusive³.

Therapeutic variants include antiarrhythmic drug therapy, guided by programmed ventricular stimulation; as well as radiofrequency ablation and surgery. The implantable cardioverter defibrillator (ICD) alone or in combination with drug therapy, has a significant importance⁴.

To give a diagnosis of the case presented was challenging due to lack of genetic information and being performed by non-invasive diagnostic means. Subsequent evolution denoted favorable outcome.

CASE REPORT

The case of a 65-year-old former smoker with a history of hypertension, ischemic heart disease, and several hospital admissions due to effort syncope without a definitive diagnosis, is reported. In the last episode was observed a left bundle branch block (LBBB), which was interpreted as acute and probably having ischemic causes (**Figure 1**). So he was admitted to the Coronary Intensive Care Unit under strict monitoring, and consequential stud-

ies began.

In the first 24 hours after admission we were able to confirm non-sustained ventricular tachycardia (VT) with LBBB morphology during syncope (**Figure 2**).

It was decided to start treatment of oral impregnation with amiodarone 400 mg/day, linked to anti-ischemic treatment with oral antiplatelet therapy, intravenous nitroglycerin 0.5 mcg/kg/min and enalapril 20 mg/day.

As part of the study, a baseline echocardiogram was performed using imaging findings consistent with ARVD (**Figure 3**):

- Interventricular septum 13 mm, left ventricular (LV) posterior wall 5mm, LV diastolic diameter 66 mm, LV systolic diameter 56 mm, end diastolic volume 226 ml, end systolic volume 179 ml, LV ejection fraction 20.9% by the Teichholz method and 22.5% by Simpson.
- RV average diastolic diameter 46 mm, with dyskinesia at the level of apical and inferobasal segments. Increased thickness of the moderator band with trabecular aspect, irregular dilatation of the RV outflow tract 39mm, systolic excursion of the anterior leaflet of the tricuspid valve 9 mm, RV systolic function severely depressed.

The patient progressed without new syncopal episodes, with clinical and hemodynamic stability, and was referred to the territorial reference center (Cardiocentro Ernesto Che Guevara), in order to define the

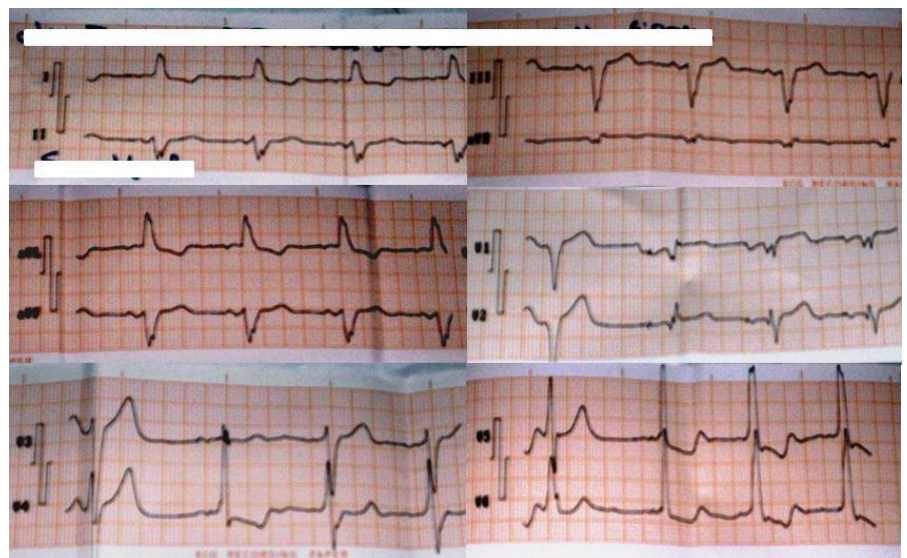


Figure 1. Electrocardiogram prior to syncope, performed in the Intensive Coronary Care Unit, showing a LBBB.

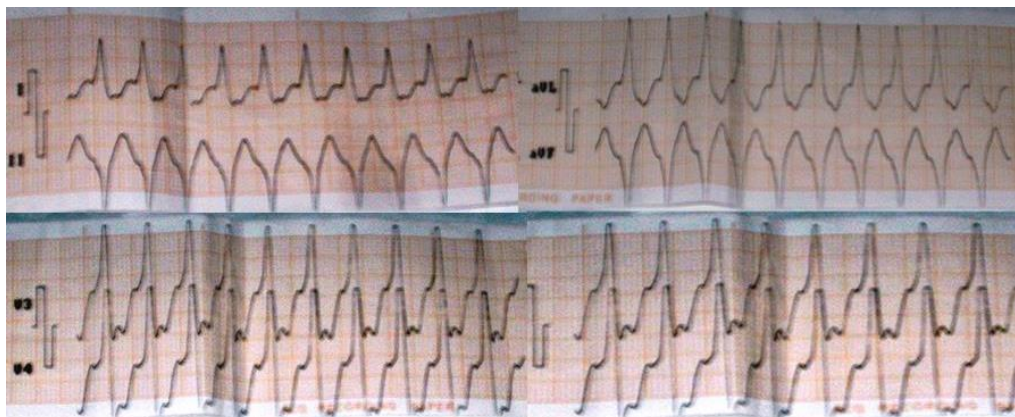


Figure 2. Electrocardiogram during syncope showing wide QRS tachycardia and atrioventricular dissociation compatible with non-sustained VT with LBBB morphology.

cause of the clinical picture. The coronariography showed a right coronary artery with chronic and diffuse calcifications in the middle and distal segments, with good distal beds, without percutaneous coronary intervention criteria due to the absence of significant lesions.

Pertinent arrangements with the Department of Arrhythmia and Cardiac Electrophysiology from *Instituto de Cardiología y Cirugía Cardiovascular* from Havana (national reference center) were made, and the study was completed. The presumptive diagnosis was confirmed and an ICD was implanted as definitive treatment.

COMMENTS

The earliest references to ARVD were given by Dalla Volta in 1961, but only in 1977. After the death of a young Italian doctor while practicing tennis, a thorough investigation of this disease starts⁵. A year later, a definitive description was offered by Fontaine *et al.*⁶.

Its prevalence is estimated to be 1:5000 in the general population, indicating that sudden death may be the first symptom, generally in young people, mainly athletes. However, series of elderly patients have been published.

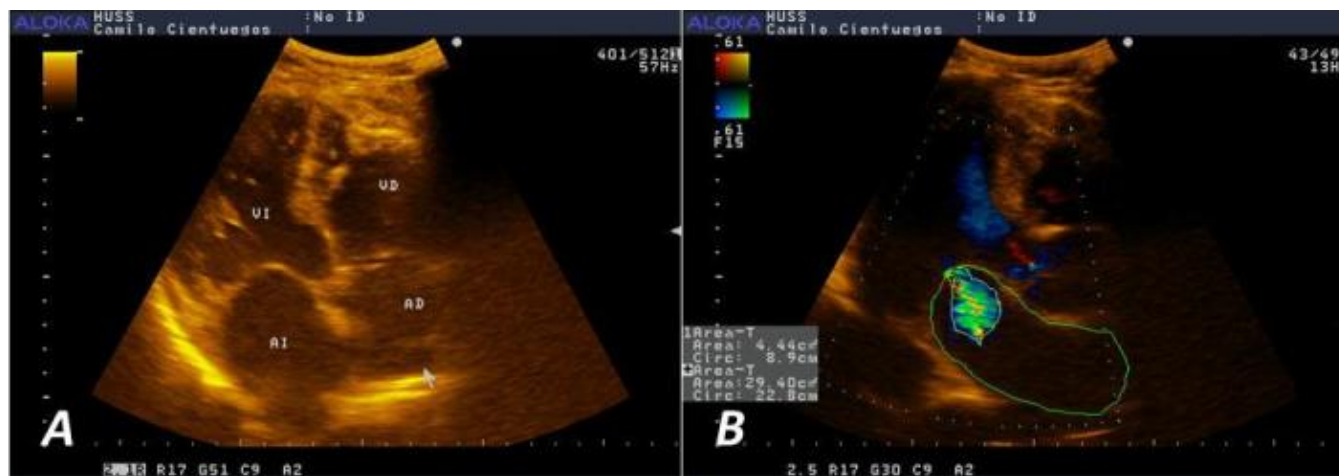


Figura 3. Echocardiography. **A.** Apical view showing dilatation of all cardiac cavities and anatomic changes of the RV. **B.** Mild mitral regurgitation.

This disease is associated with re-entrant ventricular arrhythmias originated in the right ventricle, so it shows a LBBB morphology. Palpitations may occur, induced by exercise, fatigue, dizziness, atypical chest pain and in some cases, syncope. A large number of patients are asymptomatic and the first manifestation is a sudden cardiac death which frequently occurs while physical activity is performed. Ventricular arrhythmias, –from isolated premature ventricular contractions to VT with an electrocardiographic pattern of LBBB– are the distinctive forms in which it appears⁷.

The pattern of inheritance is autosomal dominant in a third of cases and the recessive trait has a high penetrance, where the genetic abnormality is localized in chromosomes 1 and 14q23 also q24, and more recently chromosome 10 was identified with about 12 genes and *locus* linked to this disease.

These alterations determine encodings for desmosomal proteins, identified as Plakoglobin (JUP), Desmoplakin (DSP), plakophilin-2 (PKP2) Desmoglein-2 (DSG2) and Desmocollin-2(DSC2). Cell to cell adhesion strongly depends on the intracellular desmosomal interaction especially DSP and JUP. DSP deficiency causes increased expression of adipogenic and fibrogenic genes and abnormal deposition of fibro-fatty tissue, therefore, is also called as an intercellular bridge disease⁸.

From the anatomopathological point of view is observed a thinning of the ventricular wall and fatty infiltration of the subepicardial regions; possibly showing a dilated RV with protrusions in infundibular, apical and subtricuspid regions, in the so-called triangle of dysplasia. Microscopy shows a replacement of the external and middle layers of the right ventricular myocardium and, to a lesser extent, of the left by adipose tissue and fibrosis limiting myocardial strips or groups of myocardial fibers. There are ordinary fibers or partially degenerated myofibrils which cause the slow driving and the reentrant phenomenon, being the cause of VT⁹.

The Working Group on Myocardial and Pericardial Diseases of the European Society of Cardiology and the Scientific Council on Cardiomyopathies have proposed some criteria to help diagnose the disease, with different case presentations, but have low sensitivity in early stages of the disease¹⁰.

The electrocardiographic finding established as major criterion is the presence of epsilon waves, ob-

served in 30% of cases, located at the beginning of the ST segment in right precordial leads due to the presence of late potentials or prolongation of QRS greater than 110 ms in V₁-V₃.

Minor criteria such as: inverted T waves in V₂-V₆ in patients over 12 years, without right bundle branch block; sustained or non-sustained VT with LBBB pattern, and frequent premature ventricular contractions (> 1.000 in 24 hours) are proposed.

Among the morphological and functional criteria that can be evaluated by echocardiography and magnetic resonance imaging (MRI) are found as major criteria: severe dilatation and reduction of RV ejection fraction, LV unaffected (or mildly affected), as well as aneurysms with severe segmental ventricular enlargement. As minor criteria: overall mild RV dilatation or reduction in its ejection fraction, or both, with normal LV; with discrete segmental dilatation and regional ventricular hypokinesia of the RV. Other important major criteria are added: histopathological finding of fibroadipose tissue replacing myocardial tissue that may be assessed by MRI or endomyocardial biopsy, and a diagnosed family history of ARVD. Family history of sudden death in people under 35 years, suspected of the disease, constitutes a minor criterion.

Thus the diagnosis is based on the existence of two major criteria or a major with two minor or, failing that, on the existence of four minor criteria.

In order to reach the diagnosis of the case presented, two major echocardiographic criteria were determined and one electrocardiographic defined as major, which was the timely discovery of non-sustained VT with LBBB morphology.

At present it is proposed the use of other combined techniques of signal-averaged electrocardiography with MRI, a great help in the differentiation of ARVD and idiopathic right VT¹¹. However, in the presence of typical echocardiographic findings, MRI and angiography can be avoided. Tomography shows the localized or diffuse involvement, RV dilation, thinning of its wall and hypokinesia. The distinctive feature is the noticeable increasing of subepicardial fat outlined by densitometric analysis of the tomographic image. Electrophysiology study and VD cineangiography are also included¹².

At present there is no set pattern for treatment; therefore, it is individualized and directed essentially to control malignant ventricular arrhythmias. Drug therapy is preferred in patients with arrhythmias that

do not involve life-threatening. If left ventricular function is normal, Class I antiarrhythmic drugs may be helpful. If ventricular function is depressed, some authors prefer amiodarone, which can be combined with beta blockers¹³.

Patients with sustained VT or ventricular fibrillation should receive a therapy guided by programmed ventricular stimulation. The ICD is the most effective way to prevent sudden death due to its capacity to provide anti-tachycardia therapy and electric shock. It represents the first choice in patients with syncope or cardiac arrest and non-inducible VT. Another interesting therapeutic measure is radiofrequency ablation, though recurrence of VT is seen in about half of cases and these recurrences can cause sudden death¹⁴.

The option to surgically isolate the right ventricular wall is used in selected cases, to prevent the transmission of abnormal rhythms to the LV, which is controversial because of the importance now granted to RV dysfunction in the different heart diseases. Heart transplantation is only indicated in cases of extreme right ventricular dilation or uncontrolled hemodynamic compromise, although in practice this is an uncommon form of therapy to control cardiac arrhythmias¹⁵.

The diagnosis of this disease becomes difficult when you do not have all the means, but the knowledge and constantly updating of its details is very important to define an adequate therapeutic conduct to save the patient's life.

The existence of subtle clinical and electrocardiographic data should lead to further investigations on the presence of ARVD. This way, it could probably acquire a greater prevalence than it has today.

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