Atrioventricular Conduction Disorder as a First Manifestation of Arrhythmogenic Right Ventricular Dysplasia

Trastorno de conducción auriculoventricular como primera manifestación de displasia arritmogénica del ventrículo derecho

To the Editor,

Arrhythmogenic right ventricular dysplasia (ARVD) has a prevalence in the general population of 1:2500 to 1:5000. Sudden death is the first manifestation of the disease in 11% to 22% of patients.[1] We present the case of a 58-year-old man, with no personal or family history of heart disease, who was admitted to our hospital with a 1-month history of dyspnea. The electrocardiogram showed sinus rhythm with second-degree atrioventricular block Mobitz I, narrow QRS with RR' pattern and epsilon wave in V1, inverted T waves from V1 to V4, and isolated ventricular ectopic beats with complete left bundle branch block (Figure 1A). Magnetic resonance imaging showed 31% ejection fraction of the right ventricle (RV), with ventricular volume in the upper limit of normal (end-diastolic volume indexed to body surface area, 92 mL/m^2), which was greater than the left ventricular volume (end-diastolic volume indexed to body surface area, 72 mL/m^2), with interventricular septum shift to the left due to volume overload in the right chambers (Figure 1B). We also observed dyskinesia, fibrosis and aneurysmal dilatation on the RV outflow tract and inferior wall. This combination of findings enabled us to confirm a diagnosis of ARVD.[1] In view of the patient's symptomatic atrioventricular block, a permanent pacemaker was indicated. We finally decided to insert an implantable cardioverter-defibrillator (ICD), due to intermediate risk of sudden death. During admission, telemetry showed no arrhythmia episodes. The patient was asymptomatic on discharge and genetic testing found no mutations associated with ARVD. One month later, the patient returned to our clinic to report an ICD discharge. The electrograms showed regular occurrence of atrial tachyarrhythmia, not previously observed, electrically-stimulated ventricular rhythm most of the time and several episodes of sustained ventricular tachycardia (SVT), all interrupted with antitachycardia pacing except 1, which received an ICD shock (Figure 2). Immediately before each SVT episode, we observed that the atrial arrhythmia did not reach the ventricle (appropriate mode switch), followed by detection of a ventricular beat, and then the SVT preceded by a paced ventricular beat. The patient was prescribed amiodarone, beta-blockers and anticoagulation therapy. Electroanatomic mapping in the electrophysiological study showed extensive areas of endocardial scarring on the RV inflow tract, basal portion of the inferior wall, and outflow tract. After receiving substrate ablation, the patient was discharged. He remains asymptomatic after 12 months of follow-up.

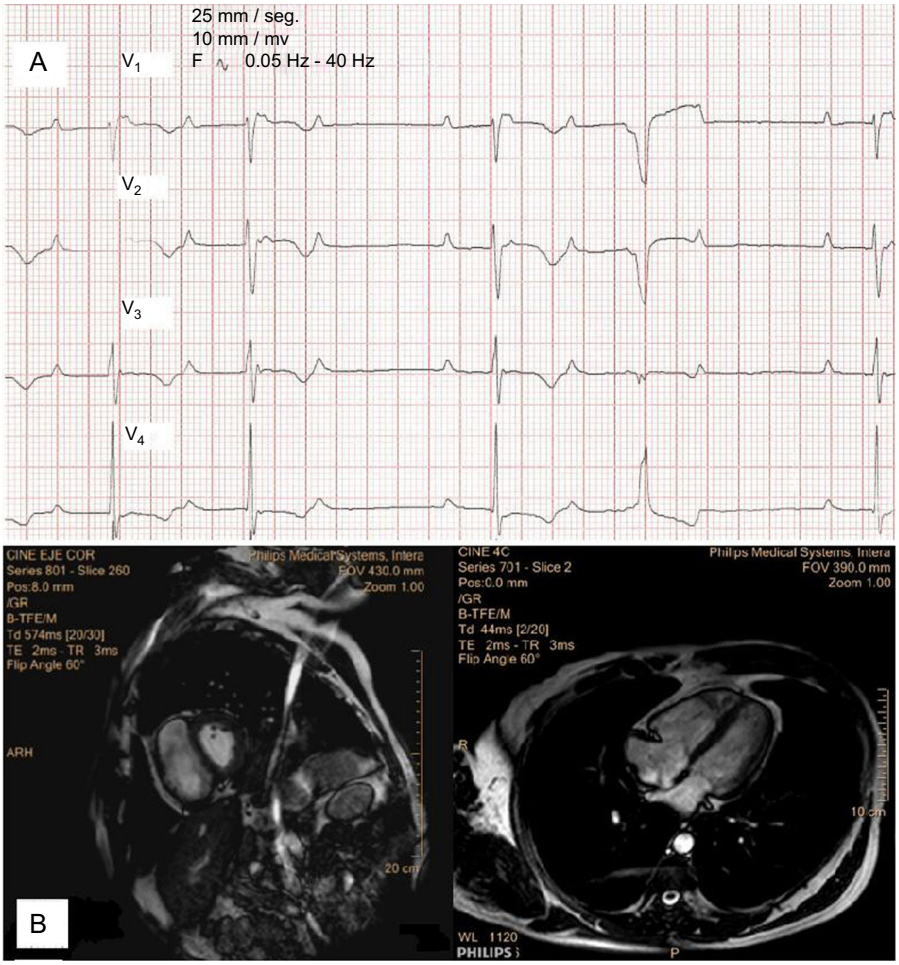

Figure 1. A: Electrocardiogram showing sinus rhythm with second-degree atrioventricular block Mobitz I, epsilon wave, inverted T waves from V1 to V4, and isolated ventricular ectopic beats with complete left bundle branch block. B: short axis and 4-chamber views of cardiac magnetic resonance imaging showing greater right ventricular volume than left ventricular volume and interventricular septum shift to the left.

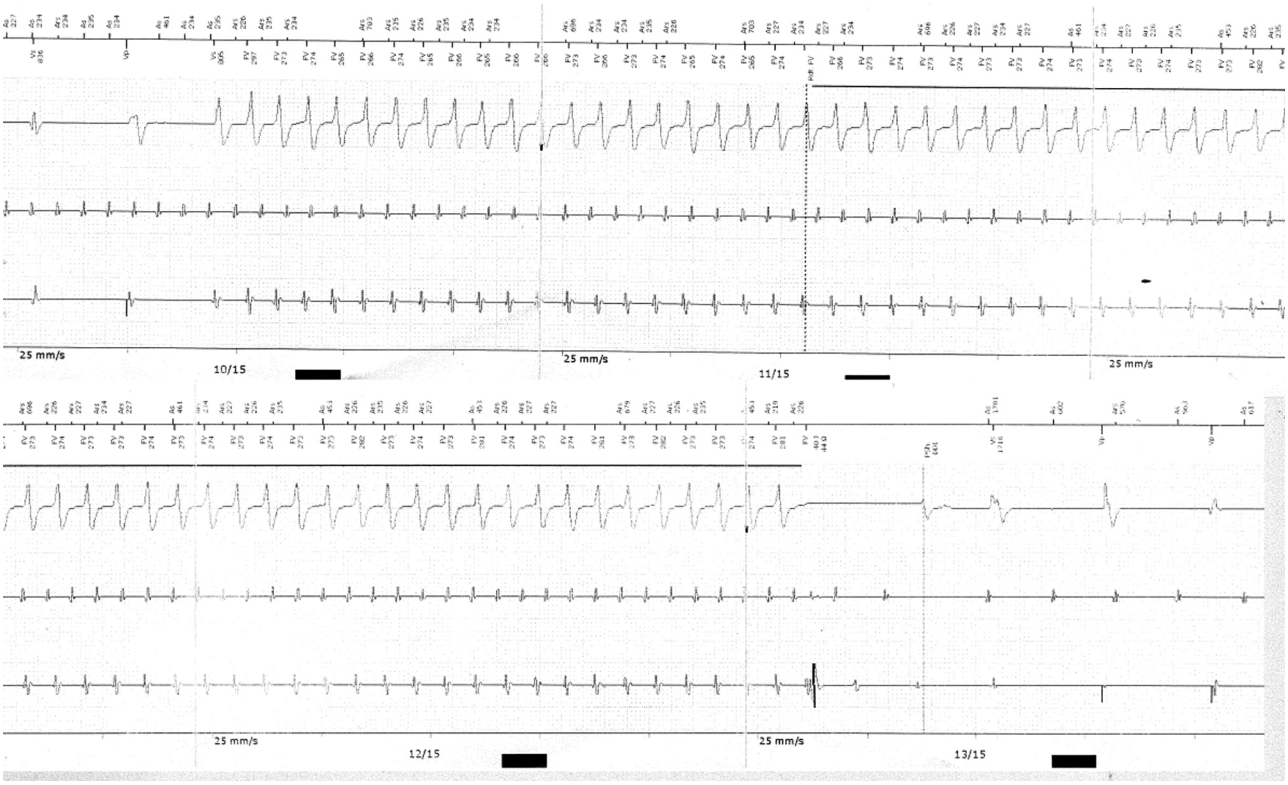

Figure 2. Electrogram showing appropriate discharge that interrupts ventricular tachycardia.

Arrhythmogenic right ventricular dysplasia is an autosomal-dominant disease that mainly affects genes responsible for cell-to-cell binding (plakoglobin or desmoplakin). The pathogenic hypothesis suggests that cell death occurs as a result of variations in the desmosomes, with fibrofatty tissue replacement of the myocardium, creating a substrate for ventricular arrhythmias. These changes take place predominantly in the RV, although the left ventricle may also be affected.[1] Clinical symptoms are usually seen in adolescence and adulthood, although some individuals may remain asymptomatic. The first manifestation may be sudden death or progressive heart failure due to contractile dysfunction. In advanced disease stages, biventricular dilatation may resemble dilated cardiomyopathy. The diagnosis is based on the presence of several validated criteria. Patients require individualized treatment.[2]

Fibrofatty infiltration of the bundle of His has been found in pathology studies in more than 60% of patients with ARVD,[3] but this histologic evidence does not correlate with conduction abnormalities. Few cases of ARVD with conduction abnormalities have been described in the literature.[4,5] Peters et al.[6] studied the electrocardiograms of 376 patients with ARVD and found conduction abnormalities (including complete right bundle branch block and any degree of atrioventricular block) in only 6% of patients. Our case presentation is interesting for 2 reasons: first, because of its rare presentation and second, because of the patient's history of life-threatening arrhythmias. Fortunately, these arrhythmias began only after ICD implantation, which was not clearly indicated in our patient according to his initial manifestations. Although we cannot completely rule out the ICD ventricular discharges as a trigger of the arrhythmias, atrial tachyarrhythmia may play a role in the onset of the SVT episodes because of the new source of ventricular activation (discharges instead of conduction) in a patient with an arrhythmogenic substrate and heart disease.

A consensus statement has recently been published for the treatment of ARVD and it includes an algorithm to identify patients who will derive the greatest benefit from ICD implantation. Patients at high risk are well identified but those at intermediate risk, such as our patient, are poorly identified. This stratification highlights the importance of individualizing the management of patients with ARVD and the indication for ICD implantation.

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Prospective Validation of the Redin-SCORE to Predict the Risk of Rehospitalization for Heart Failure in a Contemporary Cohort of Outpatients

Validación prospectiva del Redin-SCORE para predecir el riesgo de reingreso por insuficiencia cardiaca en una cohorte actual de pacientes ambulatorios

To the Editor,

The natural history of heart failure (HF) is marked by decompensations, which usually require hospitalization. In Spain, the number of hospital admissions for HF has increased in recent decades.[1,2] In addition to the inherent cost, in-hospital mortality is also high.[3] Prevention of readmission should therefore be one of the main objectives of the treatment of outpatients with HF. Most models for predicting readmission are based on data from hospitalized patients and so they do not reliably reflect the clinical condition of outpatients. Recently, our group has developed a new tool, the Redin-SCORE,[4] to calculate the risk of readmission due to HF in the short- and long-term for outpatients. The score is easy to calculate and uses 6 parameters regularly monitored in patients with HF: presence of signs of left HF (paroxysmal nocturnal dyspnea, orthopnea, third heart sounds or crackles); heart rate $>$ 70 bpm; anemia (hemoglobin $<$ 130 g/L in men and $<$ 120 g/L in women); N-terminal fraction of brain natriuretic peptide $>$ 1000 ng/L; glomerular filtration rate $<$ 60 mL/min/1.73 m^2; and dilated left atrium in the echocardiogram ($>$ 26 mm/m^2). However, one of the limitations inherent in any score is the need of validation in other populations and, in our particular case, the low incidence of events (17%) recorded in the original sample. Therefore, to extend the validity of this new risk scale, it was decided to assess its predictive and discriminatory capacity in a contemporary cohort of outpatients with heart failure.

To this end, a prospective study was undertaken with patients referred for the first time to the HF unit of our hospital between June 2012 and December 2014 (n = 237). Follow-up was performed by a trained group of cardiologists and nursing staff through review of medical records and telephone calls to register data on hospitalization for HF during the following year. The discriminatory capacity was calculated using the C statistic. The calibration, slope, and intersection of the model were assessed using the Hosmer-Lemeshow goodness-of-fit test. The decision curves were analyzed to determine when application of the Redin-SCORE increased the number of true positives without increasing the number of false negatives.[5,6]

Of the 237 patients included, 5.4% (13 patients) required admission for HF during the first month and 29.5% (70 patients) during the first year. The main characteristics of the cohort according to the presence of events at follow-up are shown in the Table. The patients who were admitted for HF were older and a higher proportion had ischemic heart disease. They were also in a more advanced functional class. In the laboratory tests, these

Table
Baseline Characteristics of the Population According to Risk of Heart Failure at 1 Year

	No admission (n = 167)	Admission for HF (n = 70)	*P*
Men	114 (68)	50 (71)	.630
Age, y	65 ± 14	70 ± 11	.008
Atrial fibrillation	60 (36)	29 (41)	.425
Ischemic origin	44 (26)	32 (46)	.004
Diabetes mellitus	53 (32)	30 (43)	.102
Hypertension	118 (71)	55 (79)	.211
Dyslipidemia	73 (44)	46 (66)	.002
History of smoking	115 (69)	44 (63)	.369
NYHA III-IV	53 (32)	46 (66)	<.001
COPD	40 (27)	20 (31)	.557
SBP, mmHg	126 ± 21	120 ± 22	.085
LVEF, %	40 ± 17	41 ± 18	.651
NT-proBNP, ng/L	2.968 ± 5.481	6.143 ± 7.679	.002
GFR (CKD-EPI, mL/min/1.73 m^2	62 ± 20	53 ± 19	.001
Hemoglobin, g/L	134 ± 18	126 ± 18	.002
β-blockers	146 (87)	56 (80)	.142
ACEI/ARA-II	147 (88)	60 (86)	.626
Furosemide	129 (77)	65 (93)	.004
Aldosterone antagonists	75 (45)	38 (54)	.187
Pacemaker	19 (13)	15 (23)	.057
Resynchronization	13 (8)	8 (11)	.368
ICD	29 (17)	14 (20)	.631
Heart transplant	3 (2)	5 (7)	.038
Signs of left HF	25 (15)	22 (31)	.004
HR > 70 bpm	89 (53)	37 (53)	.951
Anemia	51 (31)	36 (51)	.002
NT-proBNP > 1000 ng/L	94 (56)	58 (83)	<.001
GFR < 60 mL/min/1.73 m^2	60 (36)	44 (63)	<.001
LA > 26 mm/m^2	77 (46)	44 (63)	.019
Overall mortality, %	4 (2)	22 (31)	< .001

Discrimination and calibration in the overall population	C statistic	*P* value: Hosmer-Lemershow	Slope	Intersection
Readmission for HF at 1 mo	0.67	.458	0.54	−1.23
Readmission for HF at 1 y	0.71	.601	1.05	0.05

ACEI, angiotensin converting enzyme inhibitor; ARA-II, angiotensin II receptor antagonist; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; HF, heart failure; HR, heart rate; ICD, implantable cardioverter device; LA, left atrium; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class; SBP, systolic blood pressure.
Data are expressed as No. (%) or mean ± standard deviation.