A 26-year-old man was referred for family screening and cardiologic workup by the Institute of Legal Medicine. His mother recently succumbed to sudden cardiac death at work at 49 years of age. Her macroscopic and microscopic autopsy revealed arrhythmogenic right ventricular (RV) cardiomyopathy/dysplasia (ARVC/D) with diffuse left ventricular (LV) involvement (Figure 1). The 26-year-old patient, who has never engaged in competitive sports, reported a history of syncope without injury while playing leisure soccer 7 years ago. Since then, he has rarely felt palpitations. There was no history of infection within the last 12 months before the cardiologic workup. Clinical findings were normal. A 12-lead-surface ECG demonstrated notched early repolarization in the inferior leads and QRS fragmentation in aVL but no ECG criteria according to the 2010 ARVC/D Task Force (Figure 2). Signal-averaged ECG was unremarkable, and 24-hour Holter ECG revealed >1000 premature ventricular contractions with 3 different morphologies. Laboratory parameters were within the normal range, particularly for C-reactive protein, brain natriuretic peptide, and troponin T. Transthoracic 2- and 3-dimensional echocardiography (transthoracic echocardiography), RV angiography, and 3-D electroanatomical endocardial RV voltage mapping were unremarkable. Cardiac magnetic resonance imaging confirmed the absence of RV structural abnormalities but revealed diffuse fibrofatty infiltration (late gadolinium enhancement) within the LV wall, involving primarily the epicardial and midmyocardial layers of the inferolateral, anterolateral, and septal edge, has not yet been reported.

Finally, arrhythmogenic LV cardiomyopathy without RV involvement was diagnosed. Accordingly, the patient fulfilled only a borderline diagnosis of ARVC/D according to the 2010 Task Force criteria with 1 major criterion (family history) and 1 minor criterion (>500 premature ventricular contractions per 24 hours on Holter ECG). The compound mutation status may help to explain early LV involvement in the absence of gross RV abnormalities in her son. Because of his history of syncope during effort, >1000 premature ventricular contractions with different morphologies per 24 hours, positive family history of sudden cardiac death, and diffuse LV involvement, the patient received a submuscular single-chamber implantable cardioverter-defibrillator with dual-chamber sensing (VDD) for primary prophylaxis. The postoperative follow-up was uneventful.

Usually, arrhythmogenic cardiomyopathy presents in its right-dominant form, commonly referred to as ARVC/D, involving the LV in up to 70% of cases at later stages, as seen in the mother of the reported patient. The diagnostic criteria of ARVC/D are well established, whereas the diagnostic criteria of left-dominant arrhythmogenic cardiomyopathy or isolated arrhythmogenic LV cardiomyopathy are less well defined. Arrhythmogenic LV cardiomyopathy can be difficult to differentiate from dilated cardiomyopathy but manifests primarily with arrhythmias and frequent premature ventricular contractions rather than heart failure. Genetic testing, family history, and ventricular arrhythmias, as shown in this case, can help to distinguish between these 2 sometimes overlapping entities and other differential diagnoses such as infiltrative diseases or cardiac sarcoid. The diagnosis of arrhythmogenic LV cardiomyopathy is challenging, and its prevalence is likely to be underestimated. As in this case, it can often be missed by echocardiography in its early stages. In addition to arrhythmia
monitoring, genetic testing and cardiac magnetic resonance imaging constitute valuable tools in the diagnostic workup.

Disclosures

None.

References


Figure 1. Macroscopic (left) and microscopic (middle and right) autopsy heart specimen of the patient’s mother, who suffered from arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D). Genetic screening identified a novel pathogenic variant in plakophilin-2 (c.2392A>G, p.T798A). The images show a significant amount of fibrous (black arrows) and fatty (yellow arrows) tissue surrounded by residual cardiac myocytes (green arrows) in the thinned right ventricular (RV) outflow tract, subtricuspid region, and left ventricular (LV) wall (left), macroscopic specimen visualizing the RV inflow and RV outflow tract; middle, histology [Elastica van Gieson stain] from the LV, magnification ×20; right, histology [Elastica van Gieson stain] from the RV revealing <50% residual cardiomyocytes, thus fulfilling a major ARVC/D criterion according to the 2010 task force criteria, magnification x100). PV indicates pulmonary valve; and TV, tricuspid valve.

Figure 2. The 12-lead ECG (25 mm/s, 1 mm/mV) of a patient with arrhythmogenic left ventricular cardiomyopathy (ALVC) does not fulfill any diagnostic ECG criteria for arrhythmogenic right ventricular cardiomyopathy/dysplasia or ALVC. Of note, notched early repolarization in the inferior leads (II, III, and aVF; arrowhead in lead II) and QRS fragmentation in aVL (arrow) are visible, but the significance of these findings remains unclear.
Figure 3. Cardiac magnetic resonance imaging of the patient reveals late gadolinium enhancement (left to right: apical, midventricular, basal), mainly within the epicardial and midmyocardial layers of the left ventricle (LV), compatible with fibrofatty infiltration involving primarily the inferolateral, anterolateral, and septal LV segments (thin arrows). Note that right ventricular (RV) dimensions are normal, and no late gadolinium enhancement is visible within the RV wall (bold arrow). Biventricular function is preserved (see Movies I–III in the online-only Data Supplement).
Arrhythmogenic Left Ventricular Cardiomyopathy: Suspected by Cardiac Magnetic Resonance Imaging, Confirmed by Identification of a Novel Plakophilin-2 Variant
Ardan M. Saguner, Beate Buchmann, Daniel Wyler, Robert Manka, Alexander Gotschy, Argelia Medeiros-Domingo, Corinna Brunckhorst, Firat Duru and Kurt A. Mayer

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Movie Legend

Movie 1. Cardiac magnetic resonance imaging in the three-chamber view shows normal chamber dimensions and ventricular systolic function. No regional wall motion abnormalities are visible. Best viewed with Windows Media Player.

Movie 2. Cardiac magnetic resonance imaging in the four-chamber view shows normal chamber dimensions and ventricular systolic function. No regional wall motion abnormalities are visible. Best viewed with Windows Media Player.

Movie 3. Cardiac magnetic resonance imaging in the short axis view shows normal biventricular dimensions and systolic function. No regional wall motion abnormalities are visible. Best viewed with Windows Media Player.