Cardiac Myotonic Dystrophy Mimicking Arrhythmogenic Right Ventricular Cardiomyopathy in a Young Sudden Cardiac Death Victim

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An 11-year-old girl sitting in the kitchen suddenly complained of dizziness. Seconds later, she collapsed and had cardiac arrest. Cardiopulmonary resuscitation was initiated immediately but was unsuccessful, despite prolonged efforts. The girl was previously healthy and had never experienced any cardiac or muscular symptoms.

At autopsy, the gross examination was normal. The heart weighed 230 g; the chamber sizes, wall thicknesses, and myocardial appearance were normal. Microscopic examination of the right ventricular myocardium showed marked fibrofatty replacement (Figures 1 and 2). No replacements were found in the left ventricular myocardium or in the skeletal musculature. On this basis, it was concluded that the cause of death was arrhythmogenic right ventricular cardiomyopathy (ARVC).

The patient’s relatives (Figure 3) were referred for clinical and genetic counseling because of presumed ARVC-related death in the family. At the interview, it was revealed that an aunt had a child with severe myotonic dystrophy type 1 (DM1). Careful examination revealed that the patient’s brother and father had vague muscular symptoms and that the father previously had cataract surgery. It was hypothesized that the cause of death was unrecognized cardiac DM1 instead of ARVC. Genetic testing of the patient, her brother, and her father revealed a high number of CTG repeats in the dystrophia myotonica protein kinase (DMPK) gene, diagnostic of DM1. Screening of the ARVC-related genes plakophilin-2 (PKP2) and desmoglein-2 (DSG2) were negative. The likely cause of death was revised to cardiac DM1. Because of conduction defects, the brother and father were fitted with prophylactic implantable cardioverter-defibrillators.

The histopathologic hallmark of ARVC is fibrofatty replacement. It is a common cause of sudden cardiac death in the young.1 The diagnosis, which is based on a set of criteria, is often challenging. Differential diagnoses include right ventricular outflow tract tachycardia, cardiac sarcoidosis, myocarditis, Uhl anomaly, idiopathic dilated cardiomyopathy, and other inherited cardiac arrhythmia syndromes. An implantable cardioverter-defibrillator is often recommended for treatment of ARVC.

Approximately 30% of patients with DM1 experience cardiac involvement at some stage. The risk of cardiac involvement may correlate with the number of CTG repeats.2 The most common feature is conduction defects, but ventricular tacharyrhythmias and ventricular function impairment are also seen. Electroanatomic mapping of the right cardiac chambers in patients with DM1 have shown widespread alterations, consistent with a generalized myocardial affection.3 Endomyocardial biopsies from patients with DM1 may show a variety of nonspecific findings, including fibrosis, fatty infiltrations, hypertrophy, and inflammation.4

To exclude cardiac DM1 as a frequent cause of misdiagnosis of ARVC, we screened our cohort of 63 unrelated patients with ARVC and ARVC-like diseases for an expanded number of CTG repeats. All had a normal number of CTG repeats. As no confirmatory test exists for ARVC, it cannot completely be ruled out that the patient had both DM1 and ARVC. We think that all the characteristic findings of the patient and her family can be explained by DM1, and the statistical probability of coincidence of ARVC and DM1 is extremely low. We conclude that cardiac DM1 may mimic ARVC, and this should be considered in patient handling and in family screening.

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Figure 1. Biopsy from the right ventricular free wall showing fibrofatty replacement. Hematoxylin-eosin stain, magnification ×25.
Figure 2. Biopsy from the right ventricular free wall showing fibrofatty replacement. Van Gieson stain, magnification $\times 100$. 
References

Figure 3. Pedigree. Individuals with myotonic dystrophy type 1 are marked in gray and the proband is marked with an arrow. The top numbers refer to the approximate number of CTG repeats in the 3’ untranslated region of the DMPK gene, and the bottom numbers refer to the age (in years) at the time of diagnosis. Unaffected individuals have between 5 and 35 copies.
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