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Case report

Atypical form of arrhythmogenic cardiomyopathy

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ABSTRACT

A case of a family suffering from arrhythmogenic cardiomyopathy affecting dominantly the left ventricle of the heart was diagnosed in our hospital. A forty-six-year-old man was admitted to the emergency room because of a collapse with both respiratory and circulatory arrest during a sport activity. Fibrillation of the ventricles was initially registered upon electrocardiography, and there had been several sudden deaths at a young age in the patient's family. There was no significant stenosis of his coronary arteries and because of the electrocardiographic and echocardiographic findings, cardiac magnetic resonance was indicated. The cardiac magnetic resonance finding on the patient's heart probably corresponds to a less frequent type of arrhythmogenic cardiomyopathy with dominant left ventricular involvement. The patient's first-degree relatives underwent comprehensive examinations at our cardiology department, and a similar cardiac magnetic resonance finding concerning the heart was made in the younger brother of the proband. Both brothers had an implantable cardioverter-defibrillator implanted and the whole family remains subject to regular follow-ups at our department.

Introduction

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD) is a hereditary disease caused by progressive replacement of the right ventricle (RV) myocardium by fibro-fatty tissue manifesting with life-threatening ventricular arrhythmias and slowly progressing ventricular dysfunction [1]. It is mostly an autosomal dominant hereditary disease with variable expressivity and penetrance [2]. This disease is not very common, with an estimated prevalence of 1:5000. Patients suffering from ARVD manifest with the first symptoms (palpitations, pre-syncope, syncope or sudden cardiac death) within the second to fifth decade of their life [3].

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Case report

A forty-six-year-old man was admitted to the hospital because of a collapse with respiratory and circulatory arrest during a sport activity. Cardiopulmonary resuscitation (CPR) was immediately started and an ambulance arrived within 5 min. Ventricular fibrillation was registered on the initial electrocardiography (ECG). The CPR took 10 min altogether and during this time the patient was defibrillated three times and then taken to the emergency room of our hospital.

The ECG upon admission registered sinus rhythm with ST segment depressions and negative T waves in leads I, II, aV3–V6 and Rsr' morphology of the QRS complex in leads I, II, aVL, aVF, V5 and V6. Sinus rhythm without any malignant arrhythmia persisted during the whole hospitalization. There was significant positivity of Troponin T (0.078 μg/l; range 0–0.014 μg/l). The echocardiography found akinesis of the apex and adjacent part of the septum and apical part of the left ventricular (LV) anterior wall with global ejection fraction (EF) of 30%. The patient negated any typical chest pain; he felt only a certain discomfort in the chest while moving or taking a deep breath as a result of the resuscitation.

While taking down the family history, several sudden deaths at a young age were mentioned – the patient's father and brother had died of ventricular fibrillation aged 43 and 33 respectively. Several female relatives from the father's side died suddenly at a young age. The patient now has three living relatives – a 35-year-old brother and two daughters aged 10 and 18, who feel subjectively healthy.

The patient was treated for arterial hypertension, hyperlipoproteinemia and thrombophilia (homozygote for the gene PAI – 1 encoding platelet activation inhibitor, heterozygote for the gene P1A2 – GP IIIa encoding platelet surface adhesive glycoprotein IIIa). He has undergone follow-ups at the cardiology department since 2004, when the first coronary angiography was performed after a bicycle stress test with frequent ventricular extrasystoles – there was no stenosis on the coronary arteries, and EF was 72%. Then patient underwent annual cardiology examinations with an echocardiography registering the impairment of EF. In 2011 the bicycle stress test was repeated with frequent ventricular extrasystoles during resting and restitution, which disappeared during exercise. A repeat coronary angiography was indicated, and akinesis of the apex, hypokinesis of part of the anterior LV wall with LVEF 37%; and left anterior descending artery (LAD) stenosis of less than 40% were found.

During this hospitalization, following an ECG and echocardiographic finding after admission to emergency, acute coronary angiography was indicated – 20% and 40% stenoses of the LAD (speculation about spontaneous opening of the arterial closure) and haemodynamically insignificant stenoses on the circumflex artery and the right coronary artery with LVEF 30% were described.

A cardiac magnetic resonance (CMR) was performed. Mild dilatation of the left cardiac cavities, borderline dimensions of the right ventricle (RV) and global EF 41% were reported. Akinesis of the lateral LV wall and apex (Fig. 1) and minor akinesis of part of the RV inferior wall (Fig. 2) were described on native cine sequences. Subepicardial, locally transmural,

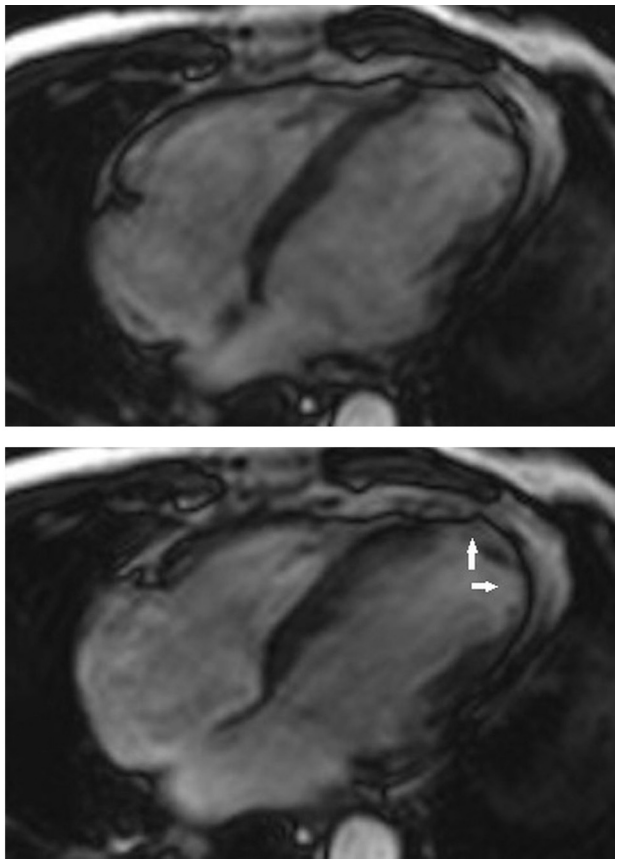

Fig. 1 – (a and b) Cardiac magnetic resonance. Cine sequences (TRUE FISP CINE) of 4-chamber view in diastole (a) and systole (b) showing impaired systolic function and regional akinesis of the apex and anterolateral free wall of the left ventricle (arrows).

lipomatosis of the LV lateral wall and apex was described on T1-weighted sequences (Fig. 3). Late gadolinium enhancement (LGE) was described in the same areas and in the akinetic part of the RV inferior wall after gadolinium contrast agent administration (Figs. 4 and 5).

A genetic examination and DNA analysis of the RYR2 gene was performed, and sequence changes in exons 95, 98 and 102 were found. RYR2 gene mutations are sometimes associated with ARVD and changes in these exons are registered in mutation database [4]. However, these sequence changes are so frequent that we cannot exclude the possibility that it is just a polymorphism. Later new generation sequencing (NGS) of 46 genes associated with cardiomyopathies was performed, and two potentially pathogenic mutations were found. The first one was in the DSG2 gene encoding desmosomal protein desmoglein, and the other one was in the DES gene encoding cytoskeletal protein desmin, which is linked to desmosomes.

After evaluation of all the examinations undertaken, a secondary preventive implantable cardioverter-defibrillator (ICD) implantation was indicated and chronic medication was modified (a higher dose of beta blocker, and clopidogrel was added due to the thrombophilia). A comprehensive cardiology