

Restrictive cardiomyopathy due to novel desmin gene mutation

Kardiomiopatia restrykcyjna — nowa mutacja desminy

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Desminopathies are a heterogeneous group of diseases characterised by the presence of desmin-positive aggregates in muscle tissue and most commonly caused by desmin gene (*DES*) mutations. There are nearly 70 mutations known, and most of them are localised in coil 2B [Cepetanaki Y et al., *Curr Opin Cell Biol.* 2015; 32: 113–120]. Desminopathies manifest as cardiomyopathy and/or myopathy. In a patient with restrictive cardiomyopathy we found novel *DES* mutation (735+1G>T) predicted to cause altered splicing. This mutation has not been previously reported. The proband was a 62-year-old woman with progressive skeletal muscle weakness, who was wheel-chair bound at the time of diagnosis.

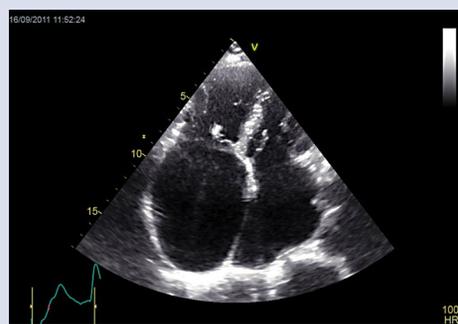


Figure 1. Echocardiography: markedly enlarged atria

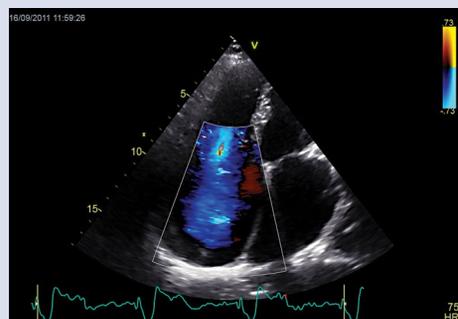


Figure 2. Echocardiography: severe tricuspid insufficiency

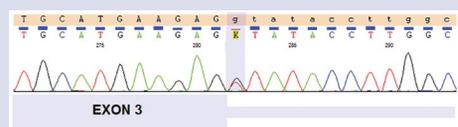


Figure 3. Chromatogram from direct Sanger sequencing showing novel *DES* mutation (735+1G>T)

First cardiological symptoms (syncopal episodes) led to VVI pacemaker implantation at the age of 46 years. With time she had progressive heart failure symptoms, New York Heart Association III, permanent atrial fibrillation, and episodes of sustained ventricular tachycardia, which prompted an upgrade of VVI to ICD-VR — at the time she was pacing-dependent. Neurological assessment showed severe myopathy of the inferior extremities. In 12-lead electrocardiogram: atrial fibrillation, ventricular pacing, rate 77 bpm. Two-dimensional echocardiographic study showed small well contracting left ventricle (left ventricular end-diastolic diameter: 35 mm, left ventricular ejection fraction: 55%) with markedly enlarged atria, restrictive pattern of mitral inflow, and severe tricuspid insufficiency (Figs. 1, 2). Laboratory assessment revealed increased level of N-terminal pro B-type natriuretic peptide (NT-proBNP; 1564; normal range: 0–125 pg/mL). Creatine kinase activity (maximal value: 423; normal range: 26–192 U/L) and troponin I levels (maximal value: 0.035; normal range: < 0.01 ng/mL) were increased. She died at the age of 65 years at home. Her son was diagnosed to have restrictive cardiomyopathy and died after heart transplantation at the age of 23 years. Her grandson was healthy at the age of 17 years. Only the proband was genetically tested. Genetic testing was performed using direct Sanger sequencing of the entire coding region of *DES* including splice sites (ABI 3130 Genetic Analyser). We identified novel splice variant IVS3+1G>T (735+1G>T) (Fig. 3). In the same nucleotide other splice variants have been described previously. The IVS3+1G>A variant disrupting exon 3 has been reported in a patient with unclassified cardiomyopathy, which evolved from hypertrophic to restrictive cardiomyopathy and later to dilated cardiomyopathy [Gudkova A et al., *Pediatr Cardiol.* 2013; 34(2): 467–470]. Another *DES* variant affecting the same splice site, IVS3+3A>G, has been previously reported in a patient with skeletal muscle weakness and complete atrioventricular block [Park KY et al., *J Med Genet.* 2000; 37(11): 851–857]. This particular case highlights the importance of genetic testing in rare familial cardiac diseases.

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Conflict of interest: none declared

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