Danon disease: Rare cause of cardiomyopathy

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Danon disease is the only X-linked dominant storage disease and is one of the few glycogenoses concerning cardiac muscle. It is caused by a mutation that impairs autophagocytosis and accumulates glycogen in cells [1, 2]. Symptoms manifest earlier and more severely in men, very often in adolescence [2]. Cardiomyopathy often coexists with myopathy and mental retardation [1].

A 9-year-old male patient with palpitations was admitted to the Department of Pediatric Cardiology due to suspected paroxysmal tachyarrhythmia. In the patient's family history, there was a grandmother's heart transplantation (HTx) due to unknown cardiomyopathy, which had been performed 23 years earlier. Laboratory tests showed elevated levels of N-terminal pro-B-type natriuretic peptide (8396 pg/ml [reference range <83 pg/ml]), hs-TnI (257.5 ng/l [reference range <52 ng/l]), and creatine kinase (CK of 563 U/l [reference range <137 U/l]). Electrocardiogram was indicative of left ventricular hypertrophy: the Sokolow-Lyon index was78 mm (norm 37 mm), inverted T wave in V5-V6, and shortened PR were 100 ms, prolonged QRS was 140 ms, with characteristic slurring in II, aVF, and V2–V6 suggestive of ventricular pre-excitation.

The latest data showed that in Danon disease these ECG features may occur in the absence of an additional conduction pathway and they can mimic Wolff-Parkinson-White syndrome; therefore, an invasive electrophysiological procedure was not performed [4]. Twenty-four-hour Holter monitoring showed 17 episodes of supraventricular tachycardia (max. 170/min; up to 23 consecutive heartbeats). Transthoracic echocardiography revealed features of left ventricular hypertrophy and overload (Figure 1A, 1B). Cardiac magnetic resonance imaging (MRI) showed myocardial fibrosis. Hypertrophic cardiomyopathy was diagnosed, and antiarrhythmic treatment was initiated (metoprolol succinate ER 2 mg/kg *per os*). During the following hospitalization, a full diagnostic panel was performed. Congenital metabolic diseases (including Pompe disease) were excluded, and Gas chromatography–mass spectrometry urine and tandem mass spectrometry blood tests were correct. A genetic test was performed and confirmed a pathogenic mutation in the LAMP-2(Xq24) gene [1, 3]. The presence of this mutation confirmed Danon disease. In addition, the genetic test revealed the same gene mutation in the patient's two-year-old brother despite a lack of symptoms.

During the next few months, subsequent hospital admissions due to progressing heart failure occurred. Ultrasonography showed fluid accumulation in the pleural and peritoneal cavity. Moreover, a single episode of atrial fibrillation was observed with signs of clinical deterioration. The patient underwent electrical cardioversion (Figure 1C) with 50J, and sinus rhythm was restored. However, severe hypotension occurred, and the patient was transferred to the Intensive Care Department, where he was treated with constant infusion of dopamine and dobutamine. Due to inadequate SVT control and disqualification from ablation, treatment was changed to HTx. Cardiac catheterization before HTx showed characteristics of glycogen storage disease i.e. post- and pre-capillary pulmonary hypertension (mPAP: 42 mm Hg, PCWP: 19 mm Hg, PVR: 6.4 WU, PVRI: 8.8 WU/m^2) with negative vasoreactivity testing with epoprostenol (12 ng/kg/min +100% oxygen), with a significant decrease in pulmonary resistance (<3 WU) and increased PCPW (mPAP: 39 mm

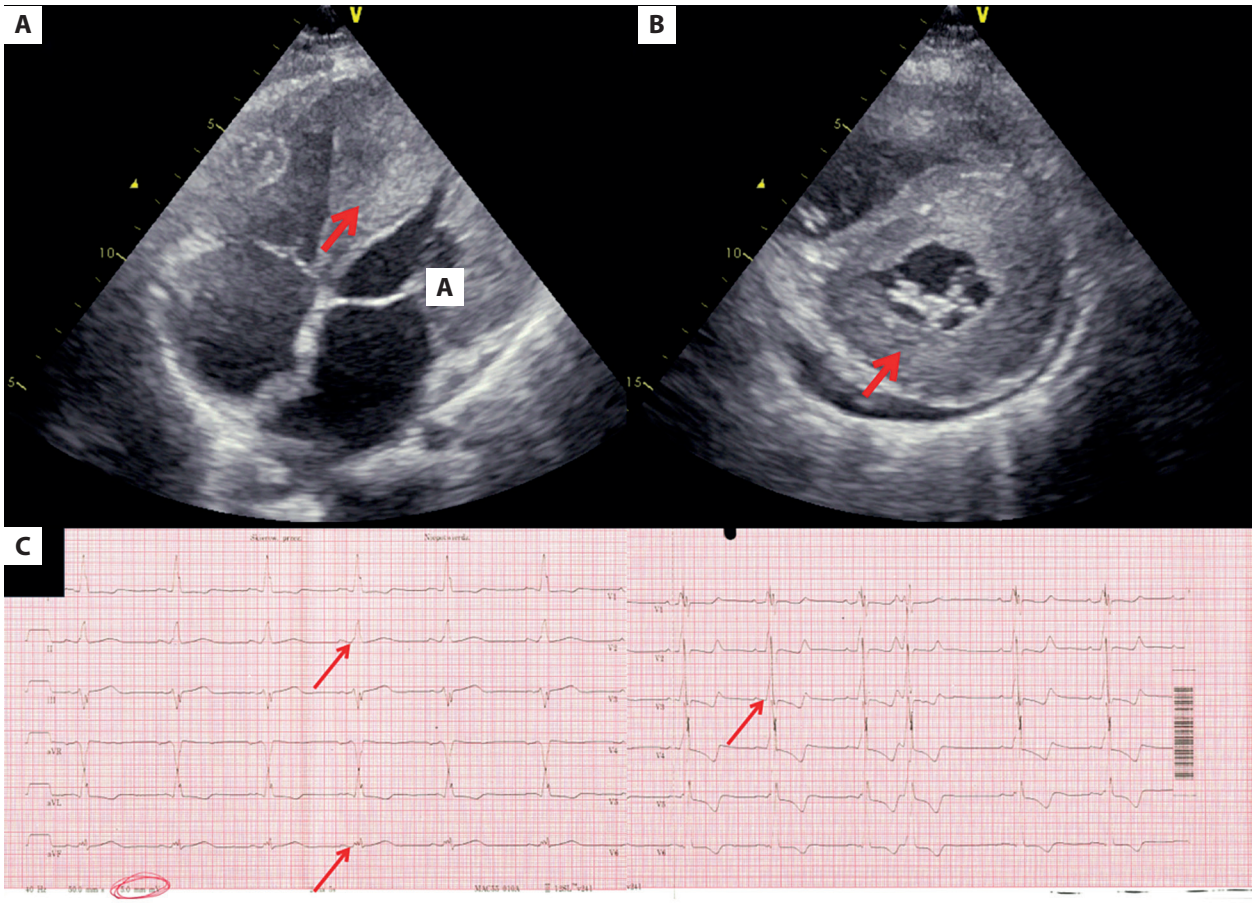

Figure 1. A. Echocardiography — apical four-chamber view: left ventricular hypertrophy: 3.3/1.9 cm, asymmetric hypertrophy of intraventricular septum (red arrow): 2.6 cm (Z score: 21.67), and left ventricular ejection fraction: 78%. **B.** Echocardiography — parasternal short axis — mitral valve: hypertrophy of the left ventricular posterior wall (red arrow): 2.1 cm (Z score: 11.08), presence of trace amounts of fluid. **C.** 12-lead electrocardiogram with signs of left ventricular hypertrophy and characteristic slurring of the upstroke of the QRS complex in II, aVF, V2–V6 (red arrows) mimicking ventricular pre-excitation

Hg, PCWP: 27 mm Hg, PVR: 2.86 WU, PVRI: 3.94 WU/m^2) [5]. Rapid progression of cardiomyopathy resulted in urgent qualification for HTx. Multicenter cooperation enabled efficient transfer to a transplant center, and transplantation was performed seven months after the diagnosis of Danon disease. The surgery was successful, but one month later, severe Ebstein–Barr virus infection caused the patient's death.

Article information

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