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Case Report

A Boy with Hypertrophic Cardiomyopathy and Liver Dysfunction

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Abstract

Danon disease cause hypertrophic cardiomyopathy (HCM), proximal-limb muscle weakness, muscular atrophy, high levels of creatine kinase (CK) and hepatic enzymes, ophthalmologic involvement and learning problems.

Molecular genetics studies showed mutations in the *LAMP2* gene. This gene is located on the X chromosome.

We present a case of a 13 years old boy with HCM and liver dysfunction. His mother also showed mild HCM during an observation.

This case was confirmed by positive *LAMP2* gene: the c.1003C>T (p.Gln335*) variant in the *LAMP2*:NM_013995.2 gene results in a premature (stop) codon and is therefore predicted to be pathogenic.

Genetic counseling and prenatal diagnosis were offered to the parents.

Keywords: *Hypertrophic Cardiomyopathy; Liver Dysfunction; LAMP2 Gene; Danon Disease*

Introduction

Danon disease is a glycogen-storage disease different from the previously described Pompe disease.

The mainly symptom is hypertrophic cardiomyopathy (HCM). Others symptoms include proximal-limb muscle weakness, high level of CK, eyes involvement, learning disabilities and increase of hepatic enzyme values.

Is an X-linked dominant trait, with spontaneous mutations in several families.

The age at presentation is between infancy to the second decade in males.

Female patients have a mild form of the disease, with the age at presentation in the third decade.

Male can present with palpitations, chest pain, 'Wolff-Parkinson-White' syndrome, prolonged QRS complex, atrioventricular block, including third-degree block, left bundle-branch block, bradycardia, intra-atrial re-entrant tachycardia and ventricular tachycardia.Weakness are usually progressive of the proximal extremities and neck muscles in the pattern of a limb-girdle muscular dystrophy.

Female patients present with dilated cardiomyopathy, but less or no weakness. Ophthalmologic findings showed depigmentation of the peripheral retina or diffuse choriocapillary atrophy.

Other findings included: hepatomegaly, splenomegaly, foot deformities [1,2].

Mutations in the *LAMP2* gene are responsible for Danon disease. Electromyography reveals myopathic pattern in male patients.

Case Report

A 13 years old boy, was observed when he was 8 y of age in pediatric outpatient because of obesity. His BMI was 25.2%, > 95, with blood pressure normal. He was diagnosed speech delay since young (5y). At 9 years old, he started to have bilateral myopia and astigmatism.

On physical examination, he was obese, without any other sign, like acanthosis nigricans, cyanosis, clubbing, hepatosplenomegaly, or heart murmur. The blood test showed liver dysfunction with aspartate transaminase (AST) and alanine aminotransferase (ALT) elevated: 439 (n:10-48) and 401 (N: 5-40) U/L respectively. We also found high level of CK- 1804 U/L (n: until 190). Others blood tests were all normal for: ammonia, alpha-fetoprotein, alpha 1 antitrypsin, hepatitis, cytomegalovirus, toxoplasmosis, infectious mononucleosis, amino-acids, organic acids, carnitine pattern, insulin, copper and ceruloplasmin. We also excluded Pompe disease, Duchene Muscular dystrophy and Familial Hypertrophic cardiomyopathy. Abdominal ultrasound was normal. During one of is follow-up consultation when he was 13y of age, we found a strong first sound on heart pulmonary focus and was sent to pediatric cardiology for evaluation. ECG revealed 'Wolff-Parkinson-White' syndrome (Figure 1). Heart echo showed severe bilateral hypertrophic cardiomyopathy, mainly very thickened muscle in left ventricular lateral view 3.74 cm, apex, septal 1.78, left ventricle inside volume very small, diastolic 50 ml/systolic only 20 ml, Ejection Fraction: 76%. Right ventricle also thickened in bottom of the heart (Figure 2). These changes were confirmed by MRI of the heart. DNA study showed positive *LAMP2* gene. The c.1003C>T (p.Gln335*) variant in the *LAMP2*:NM_013995.2 gene results in a premature (stop) codon and is therefore predicted to be pathogenic.

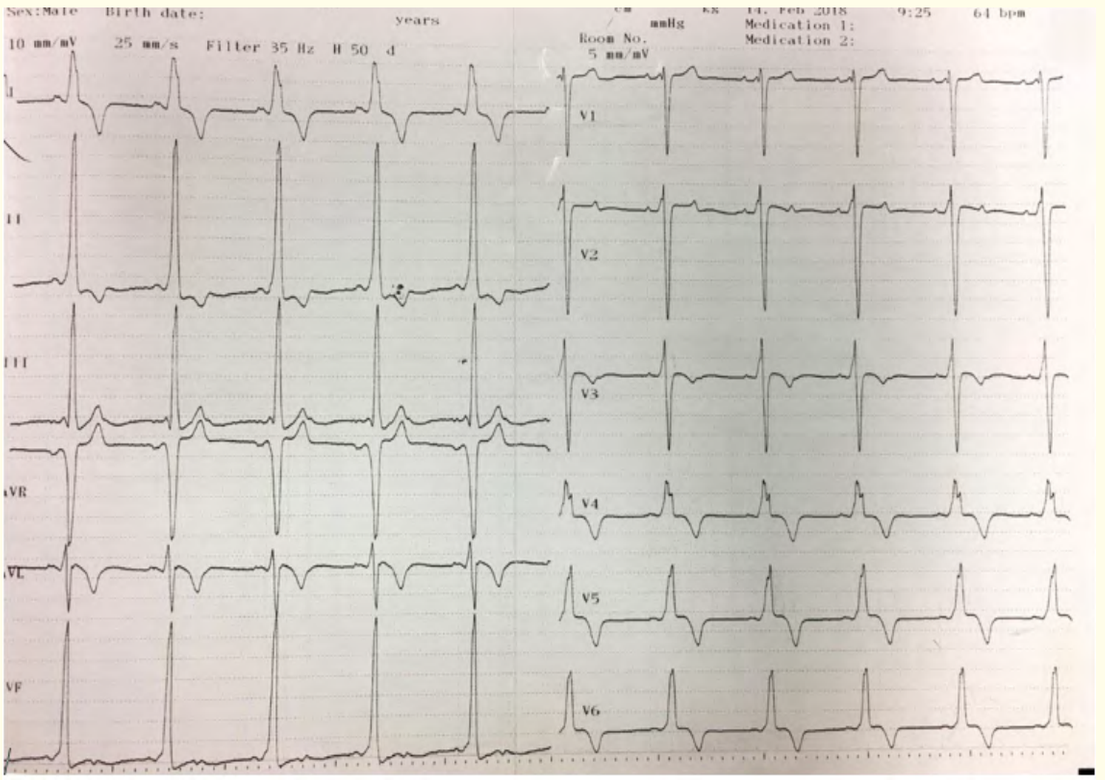

Figure 1: *'Wolff-Parkinson-White' syndrome.*

His parents are young and unrelated. He has a younger sister that is healthy. He has on his past history, an uncle, mother side, that die of unknown cardiac arrest when he was 20 years old. Mother heart ultrasound showed mild left ventricular hypertrophy during an observation.

Discussion

Danon disease is an X-linked dominant inheritance pattern. Males are more affected than females. In males, the key features are HCM, weakness and intellectual disability [1-5]. In many males, the disease progresses until a heart transplant is required or death. Females are also affected, although usually more mildly, and often onset is delayed until they reach adulthood. Female patients present with dilated cardiomyopathy [6]. Other features include heart arrhythmias and eye disease affecting the retina. Danon disease is not usually evident at

birth unless blood tests are done in a suspected case (i.e. a son born to a mother known to have the disease). Cardiac MRI may be useful for assessing hypertrophy [7].

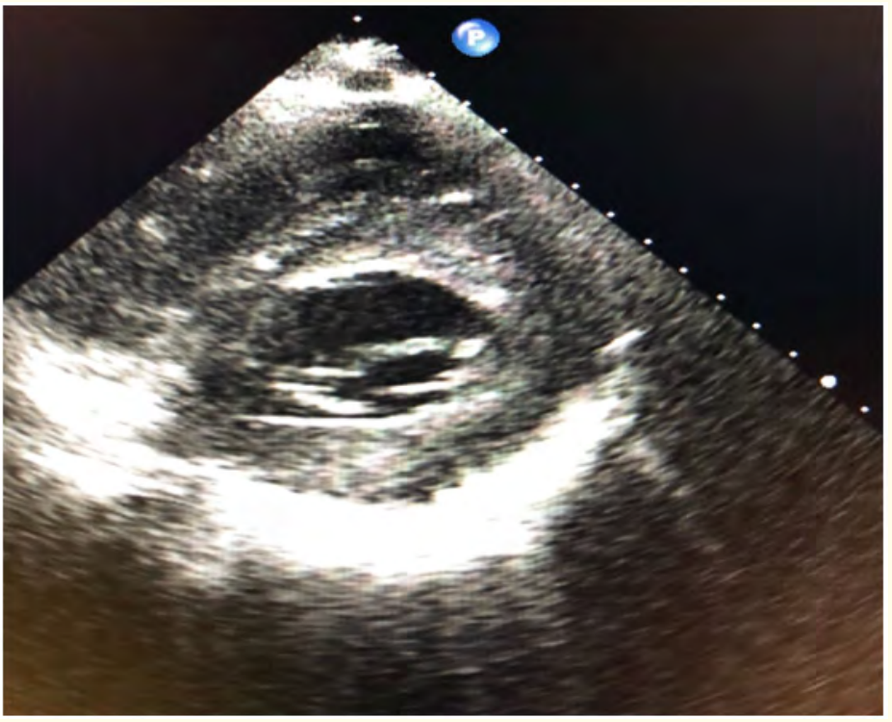

Figure 2: *Severe bilateral hypertrophic cardiomyopathy, mainly very thickened muscle in left ventricular lateral view.*

Serum CK levels are increased 2 - 3 times in male patients.

Liver enzymes are elevated in one half of patients, but liver dysfunction does not occur.

Differential diagnosis are with: X-linked myopathy with excessive autophagy (XMEA), infantile autophagic vacuolar myopathy, Pompe disease, *PRKAG2* mutation form of hypertrophic cardiomyopathy, Wolff-Parkinson-White syndrome, Becker muscular dystrophy and limb-girdle muscular dystrophies.

Our case, the cardiomyopathy was diagnosed at 13 years old, when we found a loudly first sound at heart auscultation. Until them all study was focus on the cause of liver dysfunction. The gene study confirm the diagnosis of Danon disease. At this moment, the patient no need any treatment. Sooner or later will need to do a heart transplant.

These parents have the risk of 50% to have another child with Danon disease because this is a x-linked disorder. We can offer prenatal diagnosis for the next pregnancy with DNA study.

Conclusion

When we have a patient with cardiomyopathy, particularly hypertrophic type, associated with liver dysfunction, the diagnosis of Danon disease must be considered.

Conflict of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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