Clinical course and cardiovascular outcomes in patients with the long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency

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Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency (LCHADD) is a rare inborn metabolic disease with the significant cardiac involvement, but remains without an established frequency of its occurrence. Its pathophysiology has not been fully understood or explained until now [1–3]. In the literature, there are sparse reports about cardiac symptoms in LCHADD [4–7]. Inborn errors of metabolism could often present with cardiomyopathy as it does with other diseases such as mitochondrial and lysosomal storage [8, 9].

Seventeen children with LCHADD confirmed genetically at the average age of 6 months (range, 0.1–13.0 years) were admitted and were under regular follow-up. They were all from 15 unrelated families in the Kashubian area of Poland (Table 1). Molecular analysis of gene coding for mitochondrial trifunctional protein revealed 1528G>C mutation of the HADHA gene (locus 2p23) in all of them. Two cases (patients 10, 11) were detected through newborn screening by tandem mass spectrometry. In the cases of two other children (patients 7, 8), the suspicion of LCHADD was established because of the positive family history. The other patients were diagnosed after the first episode of clinical decompensation. Cardiac abnormalities were detected in 15 of 17 (88.2%) patients (Table 1). Cardiomyopathy was diagnosed in 11 (64.7%) children. In 2 cases (patients 9, 16), both types of cardiomyopathies, dilated cardiomyopathy (DCM) followed by hypertrophic cardiomyopathy, were disclosed in the follow-up period [5]. One initially healthy child (patient 11) with no echocardiographic evidence of any type of cardiomyopathy, developed an acute DCM and died a few hours later after the first symptoms of decompensation; DCM was confirmed by autopsy. Four children (patients 10, 12, 14, 15), with detected DCM at the time of diagnosis of LCHADD, manifested the normalization of echocardiographic image during the follow-up. Seven other patients (patients 2, 4, 6, 7, 8, 11, 17) from this study group had no echocardiographical evidence of any type of cardiomyopathy up to their final follow-up visit at the end of the study. The cardiomyopathies were not the only cardiac anomalies observed in these patients. One child (patient 7) was diagnosed with intermittent ventricular preexcitation on 24 h Holter-electrocardiography monitoring and one girl (patient 1) with prolongation of QTc. In the other 8 children (patients 2, 6, 8, 9, 12, 14, 15, 16) unspecific repolarization abnormalities were identified during the follow-up period. Additionally, in one child (patient 13) coarctation of the aorta was diagnosed. All children maintained a low-fat diet with medium-chain triglycerides (MCTs) supplementation (compliance 95–100%) and standard heart failure treatment if necessary.

As it can be seen only 4 patients were diagnosed directly after screening or after positive family history (patients 7, 8, 10, 11). The remain-
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<td>3.65</td>
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*Death; NBS+ — diagnosis through newborn screening; GA — gestational age; M — male; F — female; FH — family history; N — normal heart; NA — non-applicable; EOS — end of study (last follow-up visit or death; LQTc — long QTc; NE — normal ECG for age; UR — unspecific repolarization abnormalities; I–WPW — intermittent Wolff-Parkinson-White; NG — nasogastric tube

Cardiomyopathy type: dilated (DCM); hypertrophic (HCM)

DCM — dilated cardiomyopathy in patients 2, 3, 5, 9, 10, 12, 14, 15, 16 is defined as ejection fraction (EF) < 50%

DCM/HCM/N — dilated cardiomyopathy at the diagnosis converted to hypertrophic cardiomyopathy and then to the normal heart in follow-up in patients 9 and 16

DCM/N — dilated cardiomyopathy at the diagnosis converted to the normal heart in follow-up in patients 10, 12, 14, 15

Summary of the 17 LCHADD patients

6 F/11 M
1/17 preeclampsia preterm
1/17 tween pregnancy

Median: 3000
Range: 1350–3500
Median: 0.5
Range: 0.1–13.0

5/17 deaths
4/5 autopsies confirmation of DCM

Median: 9.02
Range: 0.48–29.78

11/17 DCM
2 transition DCM/HCM/N
4 transition DCM/N
5 DCM from the begining to the EOS
6/17 N from the begining to the EOS

4/17 carnitine intake
8/17 UR
11/17 LQTc
1/17 I–WPW

6/17 normal
1/17 NG
Cardiac abnormalities in LCHADD

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Conflict of interest: None declared

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References


