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Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency: Case Report

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Abstract

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency is a rare metabolic disorder that prevents the body from converting long chain fats to energy. Signs and symptoms of LCHAD deficiency typically appear during infancy or early childhood and can include feeding difficulties, lack of energy, low blood sugar (hypoglycemia), weak muscle tone (hypotonia), liver problems, and abnormalities in retina. Individuals with LCHAD deficiency are at risk for breakdown of muscle tissue in case of hyperthermia, severe physical activity, infectious diseases, fasting. We present a case of acute rhabdomyolysis in 3 years old patient with LCHAD deficiency.

Keywords: LCHAD; metabolic disorder; non-diabetic hypoglycemia; long chain fatty acids.

1. Introduction

LCHAD deficiency is an autosomal recessive metabolic disorder, inborn error of fatty acid oxidation [1]. Estimated incidence is 1:50 000 in Sweden, 1: 91 700 in Estonia and 1: 170,000 in Germany [2, 3]. The mutation is localized in 2nd chromosome gene HADHA [4]. LCHAD is enzyme that ensures long chain fatty acids' degradation in organism. Deficiency of this enzyme leads to impair of the Krebs cycle and ATP synthesis, which leads to a metabolic crisis (non-diabetic hypoglycemia) [5].

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The most frequently affected organs are heart, muscles, liver, eyes (toxic acylcarnitine accumulation) [6]. Laboratory findings can be hypoglycemia, creatinine kinase and liver transaminase elevations. Symptoms - poor weight gain, drowsiness, vomiting, hypoglycemia, hypotonia, cardiomyopathy, abnormal vision, hepatopathy. Trigger factor is hyperthermia (above 38 degrees), severe physical activity, infectious diseases, skip of meal/starvation that can lead to cardiomyopathy, acute liver failure, rhabdomyolysis, acute renal failure, hypoglycemia and death [2 ,4, 7].

2. Case report

Patient, 3 years 5 months old, admitted to pediatric care unit due to complaints about the temperature 38.5 degree during last week, pain in the legs, painful dry cough, decreased appetite.

From patient history is known that the girl was born from second pregnancy, first delivery, 39/40 gestation week, and weight at birth 3080 g, congenital intrauterine pneumonia (discharged at 7th day of life). The first pregnancy was miscarriage. During the first months baby had poor weight gain (400g per month). At age of 4.5 months the patient presented with complaints about poor appetite, repeated vomiting, loose stools, fatigue. An examination revealed apathy, drowsiness, hypoglycemia (2,3mmol/l), metabolic acidosis, hypotonia, hepatomegaly (+ 3,5 cm). The patient was hospitalized in intensive care unit. Laboratory abnormalities – elevated liver transaminases, elevated ammonia and lactate, urine organic acid changes. DNA mutation analysis approved homozygous 1528G> C mutation.

Laboratory finding at the day of presentation: glucose-6,3 mmol/l, CRP-33,95 mg/l, LDH-609 U/l, ALAT-92.3 U/l, ASAT-169.8 U/l, ammonia-70,44 umol/l, lactate-3,1 mmol /l. Two days later: ALAT-566,18 U/l, CPK-1280,74 U/l, CRP-19,36 mg/l, Three days later: ALAT-474,7 U/l, ASAT-674,8 U/l, LDH-2232 U/l, CPK-15318 U/l, ammonia-62,17 umol/l. Five days later: ALAT-316,8 U/l, ASAT-190, 1 U/l, LDH-1746 U/l, CPK-3534 U/l, ammonia-66,03 umol/l. X-ray: right-side pneumonia.

3. Discussion

LCHAD deficiency is a rare disease that can have many faces, varying from sudden infant death to milder cases. Mortality mainly caused by cardiac decompensation and liver failure may be as high as 80% in the first years of life [8, 9]. The death rate in study of 50 LCHADD patients was 38 % before or within 3 months after diagnosis [10]. Therefore it is important to recognize the condition early and to start correct treatment. The aim of the treatment is to minimize the necessity of energy production from long-chain fatty acids of both exogenous and endogenous origin, and thereby avoid accumulation of toxic intermediates of the defective b-oxidation. The diet, low in fat content and hence long chain fatty acids from normal food, is supplemented with medium-chain triglycerides and thereby bypasses the enzymatic defect. To inhibit lipolysis, frequent feeds are necessary. During catabolic events such as febrile infections, anabolic treatment with an intravenous glucose infusion may be necessary. Even after the diagnosis has been established and treatment started, the patients may have episodes of metabolic decompensation, especially during infections or fasting as in this case, with muscle pain, muscular hypotonia, and rhabdomyolysis [11, 12]. Rhabdomyolysis is characterized by severe acute muscle

injury resulting in muscle pain, weakness, and/or swelling with release of myofiber contents into the bloodstream. Symptoms develop over hours to days following an inciting factor and may be associated with dark pigmentation of the urine. Serum creatine kinase and urine myoglobin levels are markedly elevated [13]. In presented patient creatine kinase level was six times greater than normal level. If next child is planned in the family, genetics consultation is necessary [4].

4. Conclusion

LCHAD deficiency patients should be identified as soon as possible in early childhood. They should receive appropriate diet and medical advice. In case of hyperthermia and/or infectious diseases antipyretic and antimicrobial therapy should be given immediately, due to probability of rapid decompensation. In case of decompensation, intravenous glucose should be given.

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