



Carnitine Palmitoyltransferase Type 1 Deficiency: A Case Report of Fatty Acid Oxidation Disorder Encephalopathy



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ABSTRACT

Background: Carnitine palmitoyltransferase-1 (CPT-1) deficiency is a rare autosomal recessive disorder of mitochondrial long-chain fatty acid oxidation with fewer than 30 case reports.

Case report: A 30-month-old child with fever and loss of consciousness was referred to our hospital. She had symptoms of colds for three days that were treated, but she had anorexia. Her abdomen was soft and hepatomegaly 5 cm below the edge of the rib was detected. According to a neurological consultation, with the probability of a seizure, the patient began to receive levetiracetam. The patient was treated with sodium benzoate due to her decreased level of consciousness and increased blood ammonia (300). In the acylcarnitine profile, mildly elevated levels of single acylcarnitine were seen to confirm the diagnosis of CPT-1 deficiency.

Conclusions: CPT-1 deficiency is a rare autosomal recessive defect of mitochondrial long-chain fatty acid oxidation that presents as an acute "Reye-like" hepatic encephalopathy and non-ketotic hypoglycemia, developmental delay, and hepatomegaly.

Introduction

Fatty acid oxidation disorder is one of the 20 types of fatty acid transport that is inherited as autosomal recessive disorder and could manifest as elevated levels of ammonia in the neonate period, metabolic acidosis, cardiomyopathy, and sudden death or delayed myopathy retinopathy and encephalopathy [1].

Carnitine palmitoyltransferase-1 (CPT-1) deficiency is a rare autosomal recessive disorder of mitochondrial long-chain fatty acid oxidation with fewer than 30 case reports. The CPT contains enzyme and transporter functions that transport long-chain fatty acyl groups from the cytosol into the mitochondrial matrix that is the site of fatty acid β oxidation. The first component of the system, CPT-1, an integral mitochondrial outer membrane protein, acts on cytosolic long-chain acyl-CoA, catalyz-

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ing the transfer of the acyl group to carnitine¹ [2]. Mutation in the CPT-1A gene causes CPT-1 deficiency [3].

Symptoms of “Reye-like” syndrome are seen in children with metabolic disorders, central nervous system, infections, and poisoning, and drug use. Although its manifestations are sometimes treated as meningitis. Children with CPT-1 deficiency usually presents as an acute “Reye-like” hepatic encephalopathy and non-ketotic hypoglycemia, developmental delay, and hepatomegaly [4]. Our patient was a 30-month-old child who had symptoms of encephalopathy and loss of consciousness with a “Reye-like” presentation.

Case Presentation

A 30-month-old child with fever and loss of consciousness was admitted to our hospital. She had symptoms of colds for three days and was treated for them, but she had anorexia. In the examination of the head and neck, the pharynx and left ear were erythematous without lymphadenopathy. The lung was clear and heart examination was normal.

The abdomen was soft and hepatomegaly 5 cm below the edge of the rib was detected. The extremity was normal and on the examination of the nervous system, the pupils were bilaterally dilated and non-responsive to light. Deep tendon reflexes were decreased. Bobinsky was downward and her GCS was 10. The examinations of other organs were normal and did not have a positive point. She was admitted to the intensive care unit.

Lab data were collected (Table 1). Venous blood gas was shown no acidosis or alkalosis. The lumbar puncture was done with these results: WBC: 1; RBC: 5; protein: 37; glucose: 13. After 48 hours, the lumbar puncture was repeated with these results: WBC: 2; RBC:

1800; glucose: 85; protein: 50. The ammoniac level was 300. Uric acid was raised to 10 and liver enzymes were high, but other liver function tests (PT, PTT, INR) were normal. The first blood glucose was 25, but ketone was negative in the urine test.

Brain CT scan and MRI were normal. An ultrasound was performed and the liver was 86 mm and the spleen was 68 mm. Doppler ultrasound was normal and only the gallbladder stone was seen at 5 mm. Liver biopsy was done and micro- and macro-vesicular fatty changes were seen. The patient with suspected encephalitis was treated with cefotaxime, vancomycin, and acyclovir and after 48 hours due to the normality of the second LP test, acyclovir, vancomycin, and cefotaxime were discontinued. Because of the gallbladder stone, the patient was treated with Ursobil.

According to a neurological consultation, with the probability of a seizure, the patient began to receive levetiracetam. The patient was treated with sodium benzoate due to a decreased level of consciousness and increased blood ammonia (300), which became clearer and so the drug was repeated for the patient on the following days. We started for the patient cocktail therapy with B complex syrup, L-carnitine, Mct oil, vitamin B6, E, A, D, K, and biotin.

In the course of admission, the patient’s clinical situation and the level of consciousness improved. Her pupils showed normal and responsive to light from the third day of hospitalization, and the tests also showed a satisfactory improvement. The patient was discharged in a good physical condition with drug orders, vitamins, and supportive care. Based on the total symptoms of the patient, i.e., hypoglycemia following illness, low appetite, negative urine ketone, decreased consciousness, abnormal hepatic enzymes, as well as the biopsy results of liver and evidence from previous studies of metabolic

Table 1. Lab test results

WBC: 10*1000/mm³	K: 3.9 meq/L	Triglyceride: 800 mg/dL
HCT: 33%	Uric acid: 10.2.3 mg/dL	Cholesterol: 120 mg/dL
Platelet: 346*1000/mm ³	Creatine phosphokinase: 350 U/L	AST: 65.1148 U/L
Albumine: 4.1 g/dL	Bilirubin Total: 0.7 mg/dL	ALT: 35.900 U/L
Total protein: 6.4 g/dL	Bilirubin Direct: 0.3 mg/dL	ALP: 456.620 U/L
Mg: 2.7 meq/L	Blood urea nitrogen: 47.7mg/dL	Blood sugar: 20.57.202 mg/dL
Na: 138 meq/L	Creatine: 0.3 mg/dL	Ldh: 870.3365 U/L

study, and despite no assessment of CPT-I activity in cultured fibroblast in this country, the mildly elevated levels of single acylcarnitine in the patient guide us to diagnose encephalopathy caused by a fatty acid oxidation disorder and a CPT-1 deficiency

Discussion

Fatty acids are an important source of energy in situations where the body encounters metabolic stress, such as increased muscle activity, fasting, or fever, and provides 80% of the energy needed for the heart, liver, and musculoskeletal system [5]. Because the neonate has limited glycogen reserves and high metabolism, fatty acids play an important role in their energy supply. When glycogen is stored, acid oxidation causes the formation of acyl-CoA that transfers stored energy to tissues. Short and medium fatty acids are transmitted directly to cytosol and mitochondria.

Long-chain fatty acids are transmitted to the carnitine from the mitochondrial membrane and released as acyl-CoA, which is used in the oxidation pathway [5]. The CPT contains an enzyme and a transmitter structure that transmits long-chain fatty acid groups from cytosol to the mitochondrial matrix. The mitochondrial outer membrane protein, which is the first component of the CPT-1 system, affects long-chain fatty acids by catalyzing the transfer of the acyl-CoA group to carnitine [6]. CPT-1 deficiency is a rare autosomal recessively inherited defect of mitochondrial long-chain fatty acid oxidation. Children with CPT-1 usually show acute hepatic encephalopathy symptoms that are due to fasting, illness, or stress.

Significant laboratory symptoms include hypoglycemia, loss of ketone urine or its absence, increased levels of liver enzymes, increased serum ammonium concentration, increased total carnitine plasma, increased ratio of free carnitine to the sum of palmitoylcarnitine and stearyl carnitine (C0/[C16+18]), and reduced activity of the enzyme that can be assessed on cultured skin fibroblasts [7]. In our country, evaluation of CPT activity in fibroblast culture is not available, but in the profile of acylcarnitine, which was performed for the patient, mildly elevated levels of single acylcarnitine were observed that is highly specific for the diagnosis of CPT-I deficiency.

After detecting this impairment, the symptoms should be prevented by fasting and the use of fatty acids as a source of energy during fever or digestive diseases [7, 8]. Besides, fat restriction and the use of medium-chain triglycerides can be useful by the bypass of the acylcarnitine cycle [9]. To provide energy during the disease, a high-fat

and low-fat diet could prevent the early manifestations of the disease [10, 11]. To prevent the loss of sugar during sleep, the frequent feeding of corn starch infants is a good source of supply for slow release carbonates [7].

In conclusion, based on the clinical, laboratory, and pathology symptoms, our patient was treated with a diagnosis of encephalopathy caused by low acid oxidation due to CPT-1 deficiency.

Ethical Considerations

Compliance with ethical guidelines

The study was conducted with permission of the patient's family and under the supervision of the Ethics Committee of Amir Al-Momenin Hospital in Semnan.

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Conflict of interest

The authors declared no conflict of interest.

Authors' contribution

All authors contributed in preparing this article.

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