Case Series

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Three Patients with CPT1A Deficiency: Literature Review and Case Series

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ABSTRACT

Background: Carnitine palmitoyltransferase 1A deficiency is a rare genetic disorder with autosomal recessive inheritance pattern of fatty acid metabolism secondary to CPT1A mutation. Several dozen infants and children have been described with a deficiency of the liver and kidney CPT1 isoenzyme (CPT1-A). Clinical manifestation includes fasting-induced hypoketotic hypoglycemia, occasionally with extremely abnormal liver function test (LFT) and rarely with renal tubular acidosis. Acyl carnitine analysis has been the main method for the diagnosis of CPT1A deficiency. Prompt treatment of hypoglycemia includes intravenous fluid containing 10% dextrose. To prevent hypoglycemia, infants should eat frequently during the day and have cornstarch continuously at night. Fasting should not last more than 12 hours during illness, surgery, or medical procedures.

Case Presentation: We reported three patients with CPT1A deficiency presented with hypoglycemia and Reye like syndrome in early childhood that with early diagnosis and treatment they are well in follow-up.

Conclusion: Prognosis of this genetic disorder will be good with appropriate treatment.

Introduction

Carnitine palmitoyltransferase 1A (CPT1A) is a hepatic isoform of CPT1, which is located in the outer mitochondrial membrane and is important for mitochondrial fatty acid oxidation (FAO).[1] CPT1 is the rate-limiting enzyme for the transport of long-chain fatty acids into the mitochondria.CPT1-A is expressed in the liver and kidney.[2] In CPT1-A deficiency long-chain fatty acids don't enter the liver mitochondria, therefore, can't make ketone bodies from this source.[3] Fatty acids that are released during the normal physiologic lipolysis phase are converted in the liver to triglycerides resulting in hepatic steatosis.[4]

It is characterized by severe episodes of hypoketotic hypoglycemia usually occur after fasting or illness and begin in early childhood.[5] It usually presents in infancy with fasting-induced hepatic encephalopathy leading to hyperammonemia, coagulopathy, elevated liver function tests, hypoketotic hypoglycemia. Lethargy progresses to coma if catabolism isn't reversed. The phenotype is similar to that described in Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency and Reye syndrome.[4] Although the condition can be fatal without treatment and recurrent events can result in neurologic sequelae.[6]

During periods of wellbeing, patients with CPT1-A deficiency appear normal on physical examination. The only biochemical abnormality may be an elevated total serum carnitine level.[7]

A low level of long-chain acylcarnitine (C16, C18) might be the predominant finding. During periods of metabolic decompensation, the phenotype can resemble that seen in Reye syndrome with rapidly deteriorating liver function, hyperammonemia, coagulopathy and profound hypoglycemia with hypoketonemia and hypoketonuria.

Urine organic acid analysis may reveal massively increased excretion of medium-chain dicarboxylic acids (C6-C12).

CPT1-A enzyme activity can be measured in cultured skin fibroblasts, white blood cells and the liver.[8]

The human CPT1-A gene is located on chromosome 11 ($q_{13.3} - q_{13.5}$).[4] Diagnosis is established by corresponding biochemical profile and confirmed with molecular sequencing of the CPT1A gene.[9]

The mainstay is the prevention of fasting and catabolic states. A low-fat diet (with 10% of calories from essential fatty acids and 25% from MCT) is usually recommended. 10%-20% of calories should come from protein with the remainder of carbohydrates. Uncooked corn starch at bedtime may be helpful in older children (more than 1 year of age).[4]

Case Presentation

Case 1: A 3.5-year-old girl was admitted to Shahid Sadoughi hospital with progressive impaired mental status due to gastroenteritis. She had two hypoglycemic episodes in the past 16 months. Her parents had consanguineous marriage. In her physical examination, hepatomegaly was detected.in the laboratory test she had low blood sugar (25mg/dl), negative urine ketones, uric acid: 13.8 mg/dl, Creatine phosphokinase: 2240 U/L, Ammonia: 731µg/dl. Plasma acylcarnitine profiles were in favor of CPT1 enzyme deficiency [concentration of free carnitine was clearly elevated: 202 µmol/L (normal: 20-80 µmol/L), the long chain acyl carnitines were decreased, the ratio carnitine/ C16+C18: 851(normal<47)]. She was treated with dextrose water 10% 1.5*maintenance. Because of high ammonia and impaired mental status, peritoneal dialysis was done. She also received sodium benzoate. In the long term, she was treated with raw corn starch (1gr/kg every night) and low fat diet by a nutritionist and prevention of long fasting. She is well at 3 years' follow up.

Case 2: The nephew of the above mentioned patient whose parents had consanguineous marriage was 4 months old with a history of hospitalization at birth due to apnea and cyanosis following fasting. He was treated with tablet phenobarbital 15 mg half daily. In his physical examination, he had hepatomegaly. The head circumference size was small (microcephaly due to craniosynostosis). In acylcarnitine profile high free carnitine was detected (C0/C16+C18: 2558). The diagnosis of CPT1 deficiency was established. He is under the treatment of this disease and he is well at 18 months' follow up.

Case 3: A 20-month-old child presented with repeated lethargy after long fasting and infections. He had hepatomegaly and biopsy showing steatosis. The parents had consanguinity. Optic atrophy was detected. Signs of rising intracranial pressure in brain CT scan were seen. Cerebrospinal fluid pressure was 25 mmHg. Treatment of high

intracranial pressure with the puncture of cerebrospinal fluid and tablet acetazolamide was done. According to acylcarnitine profile, CPT1 deficiency was diagnosed. The patient recommended to prevent long fasting and use of raw corn starch every night and is well at 3 years' follow up.

Discussion

CPT1A deficiency is a rare disorder of mitochondrial fatty acid oxidation inherited as an autosomal recessive trait.[10] Patients usually present between birth and 18 months of age following an illness with various symptoms including hypoketotic hypoglycemia, lethargy, and seizures. Diagnosis can be achieved through newborn metabolic screening.[11] Symptomatology comprises attacks of hypoketotic hypoglycemia with risk of sudden death or neurological sequelae.[10] We reported three patients with CPT1A deficiency presented with hypoglycemia and Reye like syndrome in early childhood that with early diagnosis and treatment they are well in follow-up.

Conclusion

In the few available studies, the outcome of patients with CPT1A deficiency appears good if catabolic events can be prevented during infancy[4], so prognosis of this disease is good with appropriate diagnosis and treatment.

Conflict of Interests

Authors have no conflict of interests.

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