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Case report

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Carnitine Palmitoyl Tranferase Type 1 Deficiency in Fatty acid oxidation disorder: A Case report

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Abstract

Carnitine palmitoyltransferase 1(CPT-1) catalyzes the formation of acylcarnitine, which is the first step in the oxidation of long chain fatty acid in the mitochondria. CPT-1 deficiency is an inborn error of metabolism. Reported patient with CPT -1 deficiency was a 16 months old boy present with hypoketotic hypoglycaemia, hepatomegaly with raised liver transaminases, hyperamminaemia, convulsion and unconsciousness. Diagnosis was established by IMD panel study. Treatment was done by correction of hypoglycemia, avoidance of hypoglycemia by ensuring frequent feeding, avoidance of prolonged fasting, treatment of infection & other supportive measures. [J Shaheed Suhrawardy Med Coll, 2014;6(1):38-40]

Key Words: Carnitine palmitoyltranferase 1, inborn error of metabolism

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Introduction

The carnitine palmitoyl tranferase (CPT) encompasses enzyme and transporter functions that affect the net transport of long chain fatty acyl groups from the cytosol into the mitochondrial matrix, 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, catalyzing the transfer of the acyl group to carnitine[1]. CPT-1 deficiency is a rare autosomal recessively inherited defect of mitochondrial long chain fatty acid oxidation with fewer than 30 reported cases[2]. Mutation in the CPT1A gene causes carnitine palmitoyltransferase I deficiency[3]. It was first described by Bougneres and colleagues[4]. Children with CPT-1 deficiency usually presents as an acute "Reye-like" hepatic encephalopathy precipitated by fasting or the stress of an intercurrent illness. Typical features include altered consciousness, hepatomegaly, with life threatening attacks of hypoketotic hypoglycemia and coma during the first 2 years of life. These children usually do not have cardiac or skeletal muscle involvement[2, 5].

The rarity of the disease may limit the experience of clinicians in its diagnosis and management. Though many conditions mimic CPT-1 deficiency, everybody should keep in mind if any children presents with hypoketotic hypoglycemia, coma and hepatomegaly it may be a case of CPT-1 deficiency. If early pick up of disease is possible and proper counseling of parents or caregiver can be provided for avoidance of prolonged fasting then permanent neurological damage from hypoglycemia can be prevented. This case is therefore reported to create an awareness of CPT -1 deficiency among the paediatrician.

Case Report

A 16 months old male child hailing from Chittagong only issue of non-consanguineous parents was admitted in the Department of Pediatrics of Apollo Hospitals, Dhaka with

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intermittent fever for 2 weeks associated with poor oral intake, loose motion and vomiting and history of one episode of convulsion followed by unconsciousness 2 weeks back. Initially the patient was admitted in a local hospital where meningoencephalitis was excluded by CSF study and was treated with different antibiotics, antiviral, anti-malarial, and anticonvulsant. The patient had been healthy up to 5-6 months of age; meanwhile the patient's mother noticed that the child occasionally became drowsy and lethargic especially during any illness. Since then the patient also had poor weight gain. On physical examination, the patient was conscious, febrile, moderately pale, icteric, lethargic, slightly hypotonic, no signs of meningism, severely wasted; however, not stunted. Vital parameters of the patient were normal; anthropometric measurement was revealed and was found that weight was 7.18 Kg, length was 78 cm (Z score of weight for age: <-3, weight for height: <-3), milestones of development was normal. Abdomen was distended; liver was firm and enlarged to 11 cm below the costal margin. Other systemic examination was normal. Investigations showed hypoglycaemia (RBS-1.6 mmol/L), decreased haemoglobin (7.8 g/dL) and white cell count was 11.1 with normal differential count and platelet count. CRP was 1.2 mg/dl; serum ammonia was high (342 mcg/dL) with normal serum electrolytes, urea, creatinine and cholesterol. ABG revealed compensated metabolic acidosis. Liver function test revealed hyperbilirubinaemia (Serum bilirubin-4.3 mg/dl), raised transaminases (SGPT-157, SGOT-340, GGT-262), hypoalbuminaemia (S. albumin: 3.1 g/dl), prothombin time was 14.3. ICT for malaria and kala-azar was negative. Viral markers were negative. Chest radiography revealed normal sized heart. Ultrasonography of whole abdomen revealed hepatomegaly. Urine ketones were negative. Blood, urine and stool cultures revealed no growth. Blood quantitative IMD panel showed raised free carnitine (190 µmol/L) and C0/(C16+C18) [1357µmol/L]. The patient was finally diagnosed as a case of Carnitine Palmotoyltransferase I deficiency with failure to thrive. The patient was treated with intravenous glucose and fluids, antibiotics for sepsis, packed red cell transfusion for anaemia. Parents of the patient were given instructions to avoid prolonged fasting. Gradually the fever subsided, appetite improved, hypoglycaemia, anaemia, hyperammonaemia and altered liver function test was improved. Discharged had given with proper dietary advice and need for follow up but unfortunately he didn't return for follow up.

Discussion

Carnitine palmotoyltransferase I deficiency is very rare in general population; however, improved detection in newborn period may increase the detection rate for the disorder[3,6]. Three CPT I isoforms with differential tissue distribution have been identified, viz. liver-type (LCPT-I or CPT IA), muscle-type (M-CPT I or CPT IB), and brain (CPT IC) isoforms[7]. CPT I A is the only isoform for which human deficiency has been recognized. In contrast to most other inborn errors of fatty acid oxidation, free carnitine concentration is increased rather than decreased in CPT I deficiency[2]. Typical laboratory features include hypoglycaemia, absent or low levels of ketones, elevated liver transaminases, raised serum ammonia concentration, elevated total carnitine , elevated ratio of free carnitine to the sum of palmitoylcarnitine and stearoylcarnitine [C0/(C16+18)] and reduced CPT I enzyme activity can be assessed on cultured skin fibroblasts[3].

This patient presented with fever, poor oral intake, loose motion, vomiting and history of convulsion and unconscious and the laboratory features revealed hypoglycaemia with absent of urinary ketone, hyper-ammonaemia, altered liver function test, raised total carnitine and ratio of C0/(C16+18). Though assessment of CPT I activity in cultured fibroblast is not available in this country; however, Fingerhut et al[5] showed that increased ratio of C0/ (C16+18) is highly specific for presyptomatic diagnosis of CPT I deficiency.

After diagnosis, prevention of any period of fasting is the main mode of treatment which requires the use of fatty acids as an energy source especially during a febrile or gastrointestinal illness[3,5]. In addition, as medium chain fatty acids bypass the carnitine cycle, dietary restriction of fat intake associated with supplementation with medium chain triglyceroles (MCTs) is considered to be helpful[6]. Primary manifestations can be prevented by high carbohydrate diet (70% of calories) with low fat (<20% of calories) diet for providing constant supply of carbohydrate energy, especially during illness[7-8]. Frequent feeding especially in infants with corn starch overnight provide a constant source of slow release carbohydrate to prevent hypoglycemia during sleep[3]. This patient was also treated by correction of hypoglycaemia and other supportive management as well as counseling which had done regarding avoidance of prolonged fasting. Dietary counseling, importance of prevention of hypoglycaemia for prevention of permanent neurological damage, genetic counseling also had been done.

Conclusion

Carnitine palmotoyltransferase I deficiency is included in the category of disorder of mitochondrial fatty acid oxidation. With prompt and careful treatment, children with CPT I deficiency often live healthy lives with near normal growth and development. After 5 years of age, metabolic crises tend to happen less often and are not as severe as earlier. If repeated episodes of metabolic crisis occur, there is a chance for permanent learning disabilities or mental retardation.

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