CASE REPORT

Carnitine-Acylcarnitine Translocase Deficiency (CACTD) in an Infant who Presented with Convulsions in the Pediatrics Department of Punjab Rangers Teaching Hospital (PRTH), Lahore

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ABSTRACT

Carnitine-Acylcarnitine translocase deficiency (CACTD) is an autosomal disorder affecting mitochondrial oxidation of fatty acids, caused by a mutation in the SLC25A20 gene. This deficiency disrupts the carnitine cycle, which is essential for providing energy during fasting states and periods of high energy expenditure. Its deficiency leads to hypoglycemia and hyperammonemia, impacting the brain, liver, and heart functions, resulting in muscle weakness. An 8-month-old baby girl presented with complaints of two episodes of generalized tonic-clonic convulsions, each lasting 5-10 seconds, self-resolving, without cyanosis or frothing at the mouth. There was also a complaint of loose stools. Upon detailed examination and laboratory diagnosis, it was confirmed that the patient had CACTD. The patient was given cornita syrup, a carnitine supplement, along with an iron supplement. Additionally, the mother was counseled to feed the baby frequently and not to let her go hungry for more than 4 hours.

Key Words: *Carnitine-Acylcarnitine translocase deficiency (CACTD), carnitine cycle, Consanguineous marriage, Convulsions, Fatty acid oxidation, Genetic studies*

INTRODUCTION

Carnitine-acylcarnitine translocase deficiency (CACTD) is identified as a rare but lethal autosomal recessive disorder due to fatty acid oxidation in the mitochondria, which is described as the defect in the transport of acylcarnitine over the mitochondrial membrane of the cell.[1] This disorder primarily results from a mutation in the SLC25A20 gene located on chromosome 3p21.31.[2] Carnitine acyl-carnitine is an essential part of the carnitine cycle.[3] It is a major source of energy during states of fasting and increased energy expenditure. Therefore, CACTD presents with nonketotic hypoglycemia, hyperammonemia, neurologic damage, liver dysfunction, cardiomyopathy, and muscle weakness. This is because the enzyme is present in the mitochondria of all tissues, especially the liver, heart, and skeletal muscles.[4]

This case report describes the data of a CACTD patient who had a history of the death of an elder sibling from the same disease.

CASE REPORT

An 8-month-old female presented at our hospital with two episodes of generalized tonic-clonic convulsions, lasting 5-10 seconds and resolving spontaneously. No cyanosis or frothing from the mouth was observed during the convulsions. Additionally, the patient had loose stools,

approximately 5-6 episodes daily, consisting of small amounts that were yellow and did not contain blood or mucus. There was a history of the death of an elder sibling at 1 year of age due to a similar disease. She was born via emergency lower uterine segment caesarean section (LSCS) at 34 + 1 weeks under general anesthesia (GA). The procedure was indicated due to gestational diabetes, premature rupture of membranes, and a history of four previous C- sections. She remained hospitalized in the nursery for 5 days and was managed for early-onset sepsis. During the history taking, it was noted that the case was a product of a consanguineous marriage. Clinical examination revealed a weight of 7 kg (10^{th} percentile), height of 67 cm (25^{th} percentile), and occipitofrontal circumference (OFC) of 41cm, along with pallor, jaundice, abdominal distension, and a liver palpable 4 cm below the right costal margin. Laboratory tests were conducted with results as follows: serum total bilirubin (STB) 19 µmol/L (normal range: 0- 17 µmol/L), ALT 194 U/L (normal range: 0-42 U/L), AST 238 U/L (normal range: up to 32), ALP 535 U/L (normal range: 53-240), Hb 10. 2 g/dl (normal range: 12-15 g/dl), TLC 8. 4 x 10 ^ 9/L (normal range: 4- 10 x 10 ^ 9/L), Plt 379 x 10 ^ 9/L (normal range: 150- 400 x 10 ^ 9/L), random glucose 5. 0 mmol/L (normal range: 3. 3- 5. 6 mmol/L), serum cholesterol 2. 5 mmol/L (normal range < 5. 2 mmol/L), serum sodium 137 mmol/L (normal range: 135- 150 mmol/L), potassium 4. 9 mmol/L (normal range: 3. 5- 5. 0 mmol/L), chloride 101 mmol/L (normal range: 97- 106 mmol/L), uric acid 189 µmol/L (normal range: 150- 340 µmol/L), urea 5. 2 mmol/L (normal range: 2. 1-7. 1 mmol/L), and creatinine 51 µmol/L (normal range: 4- 40 µmol/L). Genetic studies were done, revealing CACTD deficiency. She was advised to take oral carnitine supplements and to eat meals at intervals no longer than 4 to 5 hours to prevent hypoglycemia. The patient was given Cornita syrup (carnitine supplement) along with an iron supplement. The patient's mother was advised not to let the baby go hungry for more than 4 hours, as the liver is responsible for glucose formation.

DISCUSSION

Fatty acid oxidation defects are a group of inborn errors of metabolism. The pathogenesis of these disorders is related to the oxidation of fatty acids, which is an essential source of energy in infants, especially newborns, due to low glycogen stores.[5] The previous studies have shown that the expanded carrier screening (ECS) about whole exome sequencing (WES) is required to overcome the issue of limited ECS limitation. It is further recommended to avoid consanguineous marriages.[6] A case of neonate was reported by Chen et al. in 2020. According to this case, there was late-onset CACTD due to a homozygous mutation in the SLC25A20 gene. The symptoms appeared in the patient after 61 days, the latest onset reported for this mutation, resulting in respiratory insufficiency and cardiac arrest. The liver biopsy showed an accumulation of lipid droplets and iron deposition, specifying metabolic dysfunction. This case highlights the significance of early recognition and management in CACTD, especially in populations with high rates of blood kinships, to enhance the prognosis in this lethal condition.[7]

While viewing the literature, it was seen that few other studies also included the molecular characteristics of the disease.[1,8-9] Berrak et. al. noticed a mutation in c.270delC along with the detection of a novel c.408C>A variant. Despite intense therapy, all three cases had poor prognosis and died. Hence, genetic counselling and parents' guidance to cater to future pregnancies can be helpful.[1] Moreover, Zhang et. al. further comprehended the molecular concepts of mitochondrial carnitine/acylcarnitine carrier (CAC) structure and mechanism for its transport.[8] Andres et. al. summed up that the ACADVL, CPT2, and TANGO2 genes are responsible for causing very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency, Carnitine palmitoyltransferase II (CPT II) deficiency, and TANGO2-related metabolic encephalopathy and arrhythmias, respectively.[9] These studies provided a strong ground to further review the molecular and genetic aspects of the disease.

Conflicts of Interest: No conflict of interest to be declared.

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