ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 01 | January - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CARNITINE UPTAKE DEFICIENCY- A RARE CASE REPORT

Paediatrics

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ABSTRACT

Systemic primary carnitine deficiency (CDSP) is a rare metabolic disorder in which the body cannot properly process fats into energy. A deficiency of carnitine results in accumulation of fats in the liver, muscle, and heart. Symptoms of CDSP in infants can include poor feeding, tiredness, irritability and low blood sugar [1,2,3.]

KEYWORDS

CDSP (Systemic primary carnitine deficiency)

INTRODUCTION

Systemic primary carnitine deficiency (CDSP) is a rare metabolic disorder in which the body cannot properly process fats into energy. Carnitine functions to carry fatty acids obtained through diet to the energy centers in muscle cells (mitochondria). A deficiency of carnitine results in accumulation of fats in the liver, muscle, and heart. Symptoms of CDSP in infants can include poor feeding, tiredness, irritability and low blood sugar 1,2,3(hypoglycemia) but CDSP can also present later in childhood with heart and muscle abnormalities. Some people with CDSP are diagnosed as adults and have mild or no symptoms. CDSP is caused by mutations in the CLC22A5 gene 4,5, resulting in absent or dysfunctional OCTN2 protein. Normally, this protein functions to reabsorb carnitine in kidneys and transport carnitine inside cells. If the protein is absent or abnormal, there is a shortage of carnitine in cells.

CDSP is inherited as an autosomal recessive genetic trait. Recessive genetic disorders occur when an individual inherits two copies of an abnormal gene for the same trait, one from each parent. If an individual inherits one normal gene and one gene for the disease, the person will be a carrier for the disease but will not show symptoms. The risk for two carrier parents to both pass the altered gene and have an affected child is 25% with each pregnancy. The risk to have a child who is a carrier like the parents is 50% with each pregnancy. The chance for a child to receive normal genes from both parents is 25%. The risk is the same for males and females.All individuals carry 4-5 abnormal genes. Parents who are close relatives (consanguineous) have a higher chance than unrelated parents to both carry the same abnormal gene, which increases the risk to have children with a recessive genetic disorder.

CDSP is treatable by the daily use of L-carnitine supplements.

CASE SUMMARY

A 8 month old female child ,3rd by birth order and born by 3rd degree consanguineous marriage was admitted to our hospital with complaints of fever and cough for 4 days , excessive sleepiness for one day , decreased urine output since one day .She was born by normal vaginal delivery ,cried immediately after birth, birth weight - 2.6kg and had no history of NICU stay. Mother also complained of development delay as there was no neck holding and she had only cooing .On examination she had high philtrum (Figure 1), depressed nasal bridge ,no organomegaly .She was drowsy and had feeble pulses ,blood sugar was normal .Symptomatic treatment was given. All the necessary investigations were sent. Chest x-ray showed bilateral pneumonia . ABG showed metabolic acidosis . She had hypoglycemia and generalized tonic clonic seizures for which symptomatic treatment was given. Metabolic cause was suspected. GCMS TMS was sent and it showed carnitine uptake deficiency.

Figure-1

The child was then started on L-carnitine at 200mg/kg/day. There were no further episodes of seizures and hypoglycemia.

CONCLUSION AND DISCUSSION

Newborns are not routinely screened for PCD ,meaning that diagnosis are often missed or delayed. The presence of low levels of carnitine and short acylcarnitines in blood plasma is a clue that an underlying metabolic disorder associated with primary or secondary carnitine deficiency should be suspected. However, it is important to note that the transport of maternal carnitine through the placenta can lead to false negatives in newborns and exclusively breastfed infants in the first days of life.Mitochondrial β-oxidation of fatty acids is an essential energy-producing pathway during times of increased metabolic demand. Carnitine plays an important role in the transfer of long-chain fatty acids into the mitochondria for β-oxidation, especially in tissues like the liver, skeletal muscles, and cardiac muscles.[6,7,8]

Abolished or reduced carnitine transporter activity impairs the proper use of fatty acids as an energy source during periods of fasting or stress. Very few studies have performed brain MRIs in patients with PCD; however the brains of infants with PCD show symmetric white matter abnormalities in the bilateral frontal cortex, caudate nuclei, and genus of the internal capsule, leaving the temporal–occipital lobes relatively unaffected .T2-weighted hyperintensity and decreased diffusion at the level of corona radiata, cerebral and cerebellar white matter, cerebellar peduncles, and corticospinal and corticobulbar brainstem tracts have been reported in severe cases of PCD with hypoglycemic hypoketotic encephalopathy.[9,10]

According to international guidelines, patients with PCD must receive carnitine administration and an adequate dietary intake of carnitine (mainly from meat). Theoretically, carnitine administration should start before irreversible organ damage occurs. Although we observed a low to moderate clinical improvement in our patient, the lack of full

reversal of the symptoms after two years of carnitine treatment might be secondary to permanent brain structure or brain circuit alterations.

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