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Primary carnitine deficiency as a cause of metabolic leukoencephalopathy: Report of one case

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Full Text

Sir,

Mitochondrial beta-oxidation of fatty acids provides the essential energy during increased metabolic demands. Carnitine is required in the transfer of long-chain fatty acids across the inner mitochondrial membrane for beta-oxidation in tissues like the liver, the skeletal muscles, and the cardiac muscles.[1] Carnitine deficiency impairs the mitochondrial beta-oxidation of fatty acids, causing acute metabolic decompensation along with hepatic encephalopathy, hypoketotic hypoglycemia, and cardiomyopathy. The brain magnetic resonance imaging (MRI) findings in primary carnitine deficiency (PCD) have not been reported. We report the case of an 8-month-old baby girl who presented with acute gastroenteritis and encephalopathy. Brain MRI showed diffusion restriction in bilateral frontal subcortical and periventricular white matter, anterior corpus callosum, bilateral head of the caudate nucleus, and corona radiata. Plasma free carnitine level was below the normal range, suggesting the presence of PCD.

An 8-month-old baby girl born out of consanguineous parentage with normal perinatal history presented with a history of fever for 3 days, loose stools for 2 days, and excessive irritability along with lethargy for 1 day. Fever was continuous and high grade associated with 10–15 episodes of small-quantity of loose stools per day. There was no history of seizures. Her development was normal for her age. On examination, her heart rate was 140 beats per minute, respiratory rate was 38 per minute, and oxygen saturation was 96%. The anterior fontanel was depressed. Hepatomegaly was present. The baby was drowsy and moving her

limbs to pain. The deep tendon reflexes were brisk, and the plantars were bilaterally extensor. There was no neck stiffness. On the second day of admission, she was put on mechanical ventilator in view of her worsening sensorium. Her total leukocyte count was high, with mild thrombocytopenia. Her blood glucose level was low (52 mg/dl). There was mild hyponatremia (129 mEq/L), hypokalemia (3.0 mEq/L), and metabolic acidosis (pH 7.26). The renal and thyroid functions were normal. Her liver transaminase levels were elevated (aspartate aminotransferase, 64 IU/L; alanine aminotransferase, 86 IU/L) and plasma ammonia level was high (76 μmol/L). The blood, urine, and stool cultures were sterile. Her abdomen ultrasonography and chest radiograph were normal. Computed tomography of the brain showed prominent subarachnoid spaces in bilateral frontal and anterior temporal lobes. Brain MRI showed diffusion restriction in bilateral frontal subcortical and periventricular white matter, anterior corpus callosum, bilateral head of the caudate nucleus and corona radiata, as well as prominent subarachnoid spaces around bilateral frontal and anterior temporal lobes [Figure 1] and [Figure 2]. The cerebrospinal fluid examination was normal. Tandem mass spectroscopy showed a normal amino acid and organic acid profile, and also a normal profile of urea cycle intermediates. However, the fatty acid oxidation profile was abnormal in the form of very low free carnitine (2.6 mM/l), with a normal acylcarnitine profile. She was treated with intravenous fluids, antibiotics, and levocarnitine (100 mg/kg/day in divided doses). She gradually improved in sensorium and was extubated.{Figure 1}{Figure 2}

Carnitine (3-hydroxy-4-trimethyl aminobutyric acid) is derived from dietary sources as well as following its endogenous synthesis from lysine and methionine in the liver and kidney. During the periods of fasting, fatty acids are the chief sources of energy production, and beta-oxidation of fatty acids provides the necessary energy. Carnitine is required in the transfer of long-chain fatty acids across the inner mitochondrial membrane for beta-oxidation. Carnitine deficiency causes defective fatty acid oxidation and utilization for energy production. When fatty acids cannot be utilized, glucose is consumed without regeneration via gluconeogenesis, resulting in hypoglycemia.[2] Carnitine deficiency can be primary or secondary. PCD is an autosomal recessive disorder of fatty acid oxidation caused by a defect in OCTN2, a plasma membrane carnitine transporter, due to the SLC22A5 gene mutation.[3] The clinical manifestations of primary carnitine deficiency include hypoketotic hypoglycemic encephalopathy, hepatomegaly, elevated liver transaminases, hyperammonemia, cardiomyopathy, pericardial effusion, and skeletal muscle weakness. [4] Carnitine deficiency has been associated with cerebral arterial infarcts in infants and intractable seizures. [5] It is diagnosed by estimating the plasma carnitine levels. Further confirmation of PCD is by the molecular genetic testing of the SLC22A5 gene.

Secondary causes of carnitine deficiency include organic acidemias; fatty acid oxidation defects such as very-long-chain acyl-CoA dehydrogenase (VLCAD), medium-chain acyl-CoA dehydrogenase (MCAD), long-chain hydroxyacyl-CoA dehydrogenase (LCHAD), and carnitine palmitoyltransferase II (CPT II) deficiencies; drugs like cyclosporine and valproate; renal tubular dysfunction; malnutrition; and total parenteral nutrition. The management of PCD involves supplementation of levocarnitine in the form of intravenous therapy at 100–400 mg/kg/day during life-threatening events and oral therapy at 100–300 mg/kg/day for chronic cases,[6] prevention of hypoglycemic episodes by frequent feeding, avoidance of fasting, and prompt institution of intravenous dextrose during a febrile illness.

There are few reports on the brain MRI findings in patients with PCD. Yilmaz et al., (2015) reported the brain MRI features in a 12-year-old boy with PCD who manifested with hypoketotic hypoglycemic encephalopathy. MRI showed T2 hyperintensity and diffusion restriction bilaterally in the corona radiata, cerebral white matter, deep white matter of the cerebellum, and ascending (inferior cerebellar peduncle) and descending tracts (corticospinal and corticobulbar tracts) of the brain stem.[7] Our patient had similar MRI features, but brain stem and cerebellar MRI abnormalities were lacking. Frontotemporal atrophy with subcortical white matter abnormalities have been reported in glutaric acidurias. Brain MRI in infantile Alexander disease shows symmetric white matter abnormalities in bilateral frontal cortex, caudate nuclei, and genu of the internal capsule, with relative sparing of the temporo-occipital lobes.

The present case reports the novel MRI features in an infant with PCD who had an encephalopathy following gastroenteritis. Carnitine deficiency has a good prognosis if recognized early and managed with carnitine

supplementation.

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Conflicts of interest

There are no conflicts of interest.

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