Case Report

MRI Findings in Encephalopathy with Primary Carnitine Deficiency: A Case Report

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ABSTRACT

BACKGROUND AND PURPOSE

We presented MRI and DWI findings of a 12-year-old boy with primary carnitine deficiency, manifested with hypoglycemic hypoketotic encephalopathy.

METHODS

Magnetic resonance imaging (MRI) and diffusion weighted imaging (DWI) were performed to the patient.

RESULTS

In our case, T2 hyperintensity and diffusion restriction were noted bilaterally in the corona radiate, cerebral white matter, deep white matter of cerebellum, ascending (inferior cerebellar peduncle) and descending tracts (corticospinal and corticobulbar tracts) of brainstem.

CONCLUSIONS

MRI and DWI are helpful in the diagnosis, therapy planning and follow up of encephalopathic cases with carnitine deficiency.

Keywords: MRI, encephalopathy, primary carnitine deficiency.

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Introduction

Carnitine is an essential cofactor synthesized in liver and kidney cells from lysine and methionine. It is essential for the transfer of long-chain fatty acids from the cytosol to mitochondria and for subsequent beta-oxidation.[1] Primary carnitine deficiency is an autosomal recessive disorder of the carnitine cycle that results in defective fatty acid oxidation. It is caused by defective activity of the novel organic cation/carnitine transporter OCTN2 resulting in urinary carnitine wasting, low serum carnitine levels, and decreased intracellular carnitine accumulation. It has a frequency of about 1 in 40,000 newborns. The lack of carnitine impairs the ability to use fat as fuel during periods of fasting or stress. This can result in an acute metabolic decompensation early in life with hypoketotic hypoglycemia, encephalopathy and coma, Reye like syndrome, and sudden infant death, or in a more insidious presentation, later in life, with skeletal or cardiac myopathy.[2] We presented MRI and DWI findings of a 12-year-old boy with primary carnitine deficiency, manifested with hypoglycemic hypoketotic encephalopathy.

Case Report

A 12-year-old male patient was referred to our pediatric neurology department for muscle weakness and gait disturbance. A week previously he had been admitted to another hospital suffering from hypoglycemia symptoms such as sweating, confusion, and tremor. On physical examination, the patient was afebrile with normal vital signs. He was 24 kg in weight, and 138 cm in height. He had noted prominent fatigue since the fourth year of his life. His family history had third-degree relationship between his mother and father. On neurological examination, he was conscious, and perception of time and location was normal. Muscle strength of his upper extremity was decreased (proximal 4/5 and distal 3/5). Deep tendon reflexes were decreased. Serum glucose and ketone levels were normal due to hypoglycemia theraphy in the other hospital. C3 propionil carnitine .07 μmol/L (*N*: .28-2.9) and free carnitine 2.75 μmol/L (*N*:10-60) levels were low. Free carnitine level in urine was increased (936 μmol). Decreased plasma free carnitine level and increased urine free carnitine level suggested the diagnosis of primary systemic carnitine deficiency, resulting from impaired tubular reabsorbtion of carnitine. The cardiothoracic ratio was increased (57%), and pulmonary conus and vascular signs were normal on telecardiogram. ECG demonstrated left ventricular hypertrophy and echocardiography revealed dilated cardiomyopathy, consistent with congestive heart failure.

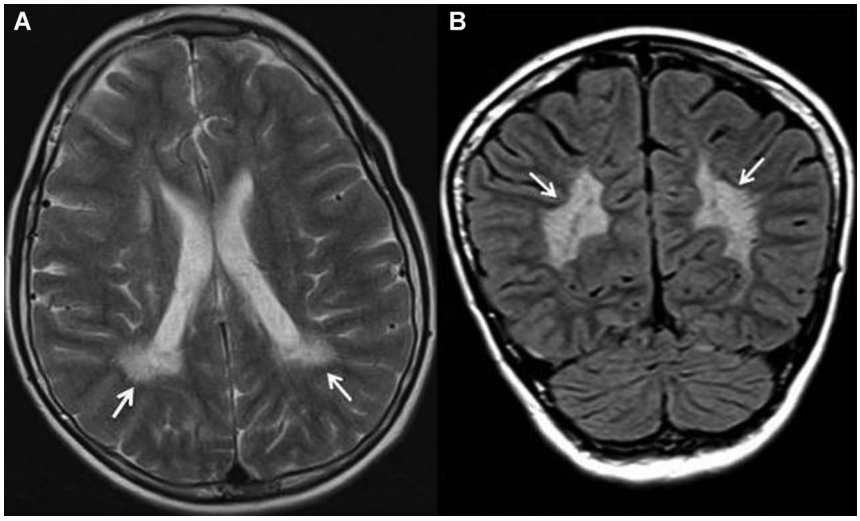

Fig 1. T2 W (A) axial and FLAIR (B) coronal images show symmetric hyperintense changes in supratentorial periventricular and deep white matter.

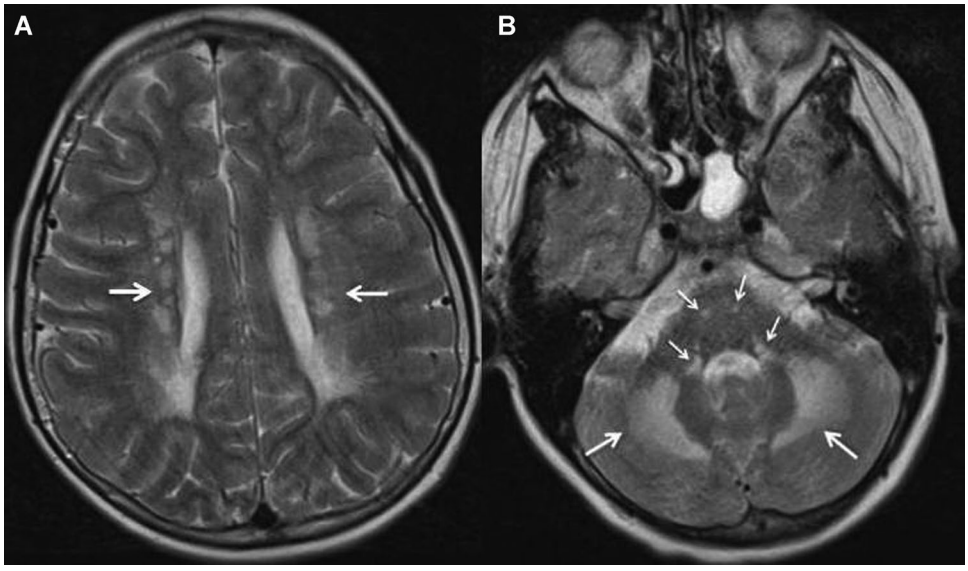

Fig 2. (A, B): T2 W axial images demonstrate symmetric hyperintensity in corona radiata, cerebellar deep white matter, ascending and descending tracts of brainstem.

On T2-weighted, FLAIR, and DWI brain MRI there were various degrees of hyperintense changes and diffusion restriction in the supratentorial periventricular and deep white matter of the hemispheres, cerebellar deep white matter, and ascending and descending tracts of brainstem (Figs 1–3), as well as atrophy of the posterior part of corpus callosum (Fig 1). These MRI findings were consistent with hypoglycemic hypoketotic encephalopathy secondary to primary carnitine deficiency. An SLC22A5 gene mutation was found. Heart failure ceased on oral carnitine therapy.

Discussion

Primary or secondary carnitine deficiencies cause mitochondiral dysfunction due to a disruption of oxidative metabolism. The resulting energy depletion may lead to neuronal cell death in brain, as it is highly dependent on oxidative metabolism and sensitive to secondary accumulation of toxic metabolites within the organelles. Mitochondrial dysfunction leads to swelling of astrocytes and damage in myelin sheath in white matter.[3]

Kim H et al reported MRI of a 47-year-old women who has acquired encephalopathy associated with carnitine deficiency. They found subtle hyperintense lesion in the right occipital lobe and mildly diffusion restriction and focal hyperintense lesion in the rigth occipital subcortex in T2-weighted images and symmetric hyperintense lesions in basal ganglia bilaterally on T1-weighted images.[3] Thompson et al presented MRI of five children who have different MRI findings such as increased T1 signal intensity in the right perirolandic region presumed to be a hemorrhagic infarction, increased T2 signal intensity involving the distribution of the left middle cerebral artery including the

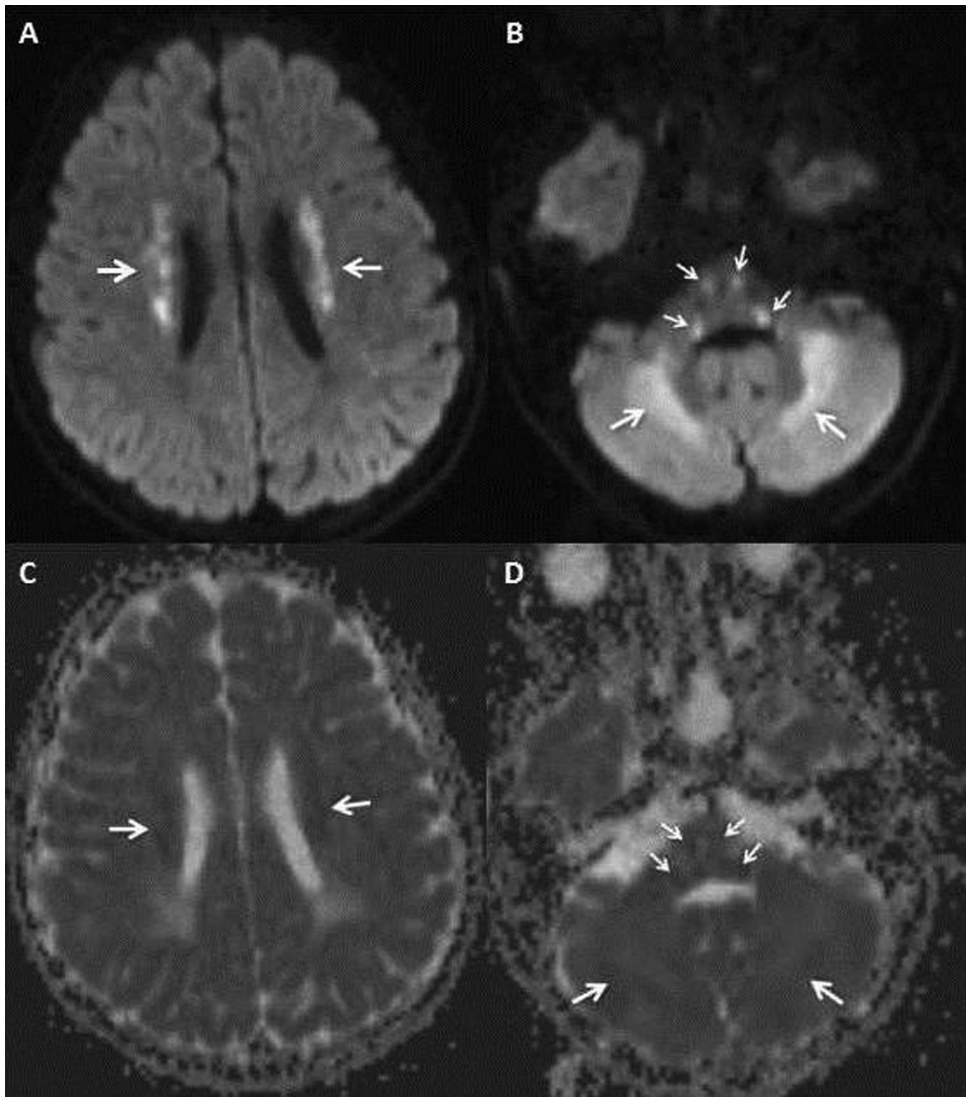

Fig 3. DWI shows symmetric diffusion restriction in corona radiata (A, C) and cerebellar deep white matter, ascending and descending tracts of brain stem (B, D).

basal ganglia, a right parietal infarct with surrounding edema, increased T2 signal intensity in the right calcarine cortex, and nonspecific periventricular white matter T2 hyperintensities.[4] The main cause of MRI findings and encephalopathy in carnitine deficiency is probably hypoglycemia. In hypoglycemia of adult patients, brain injury MRI findings are limited, but typically the most involved regions are the cerebral cortex, basal ganglia, splenium of the corpus callosum, hippocampus internal capsule, and cerebral white matter. The parietal and occipital regions are more vulnerable to hypoglycemia in neonates.[5]

In our case, T2 signal changes with diffusion restriction were noted bilaterally in the corona radiate, cerebral white matter, deep white matter of cerebellum, ascending (inferior cerebellar peduncle) and descending tracts (corticospinal and corticobulbar tracts) of brainstem. This type of involvement is different from those described in previous studies.

DWI is a useful technique for visualizing the regional mobilities of protons in the brain, and it has been recently used as a diagnostic tool in patients with mitochondrial encephalopathy, demyelinating disease, and ischemic disease. It probes the local tissue microstructure, allowing measurement of axon and myelin loss as well as the differentiation of cytotoxic and vasogenic edema. In our case, DWI ($b = 1{,}000$ s/mm^2) and corresponding ADC maps showed diffusion restriction in the cerebral and cerebellar white matter, as well as the long tracts of brain stem, consistent with cytotoxic edema.

In conclusion, carnitine deficiency is a rare clinical entity, which may manifest in children as hypoglycemic hypoketotic encephalopathy. Because carnitine and related metabolites can be quantitated in plasma, it should be added to the list of metabolic disorders especially in children who present with stroke. Hypoglycemic hypoketotic encephalopathy caused by carnitine deficiency should be considered during the radiological diagnosis of encephalopathies. MRI is helpful in the diagnosis, therapy planning, and follow-up of encephalopathic cases with carnitine deficiency.

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