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CASE REPORT

A case of biotinidase deficiency with unchanged basal ganglia lesions in MRI during an eight year follow-up

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ABSTRACT

Biotinidase deficiency is an autosomal recessive disorder that is presented with dermatitis and neurologic manifestations such as seizure, ataxia, hypotonia, mental retardation and autistic behavior. Basal ganglia lesions in magnetic resonance imaging (MRI) in biotin deficiency was reported and we report a ten year old girl with biotinidase deficiency and basal ganglia lesions in MRI. She is a 10-year-old girl with attacks of seizure from the age of two years. In the first admission, she had mild metabolic acidosis and her brain MRI showed multiple lesions in the basal ganglia and enzyme assay revealed partial biotinidase enzyme deficiency. Treatment with 10 mg daily biotin was started and rapid and good control over seizures was seen. She had episodes of seizure at the ages of four, six and nine years with fever and upper respiratory infection for which biotin dosage was increased. Now and in the last follow up, she is a student of fourth grade of primary school and academic performance is partially favorable and has some residual neurological dysfunction on examination such as dysarthria, ataxia ,and tremor, dystonia of the left hand and mild stiffness of lower extremities. The new brain MRI showed severe degeneration of the caudate nucleus and the putamen that unchanged during the eight year follow-up.

Key words: biotin, biotinidase deficiency, basal ganglia lesions, MRI

INTRODUCTION

Biotin, as a member of the B complex group of vitamins, covalently binds to five carboxylases which are essential in metabolism of proteins, fats and carbohydrates. This attachment is catalyzed by holocarboxylase synthetase enzyme, but finally covalently bound biotin should be released from carboxylases by biotinidase to make free biotin available for utility in the cellular needs. Biotinidase enzyme is essential for biotin recycling. Biotinidase deficiency (BD) is an autosomal recessive disorder with an estimated worldwide incidence of one in 60,089 live births. Clinical manifestations of BD include periorificial cracking and perioral stomatitis, conjunctivitis, hearing loss, alopecia ,ataxia, hypotonia, seizure, impairment of immune function, mental retardation, autistic behavior, episodes of acidosis, ketosis and organic aciduria which can be presented at any time from one week to as late as 10 years of age. Asymptomatic children and adults with biotinidase deficiency have been recognized in screening programs.[1]

Severity and time of clinical presentation depends on the severity of enzyme deficiency. Patients with profound BD possess less than 10% of normal serum biotinidase activity and partial BD patients have 10-30% of normal enzyme level. Early diagnosis by neonatal screening is possible and timely administration of 5-20 mg of daily biotin can cause rapid improvement of clinical symptoms and biotin therapy should be continued lifelong. However, residual neurological damage is seen in some patients.[2]

Neuroimaging findings of children with biotinidase deficiency include cerebral edema, attenuated white matter signal, cerebral atrophy and compensatory ventricular enlargement. Neuroimaging features may improve or become normal after biotin treatment.[3]

Biotin deficiency with basal ganglia lesions and bilateral hyperintensities of the caudate and putamen in magnetic resonance imaging (MRI) or biotin-responsive basal ganglia disease were reported previously.[4-8]

We report a case of partial biotinidase deficiency with symmetric basal ganglia lesions that MRI findings remained unchanged during follow-up of 8 years.

CASE REPORT

The patient is a ten-year-old girl with a history of seizure from two years of age. She is the only child and product of the first pregnancy of non-consanguineous parents that was born by cesarean section for maternal pregnancy-induced hypertension at 33 weeks. Her birth weight was 760 grams and she was admitted to the neonatal intensive-care unit for 73 days after birth in view of prematurity and respiratory distress. The

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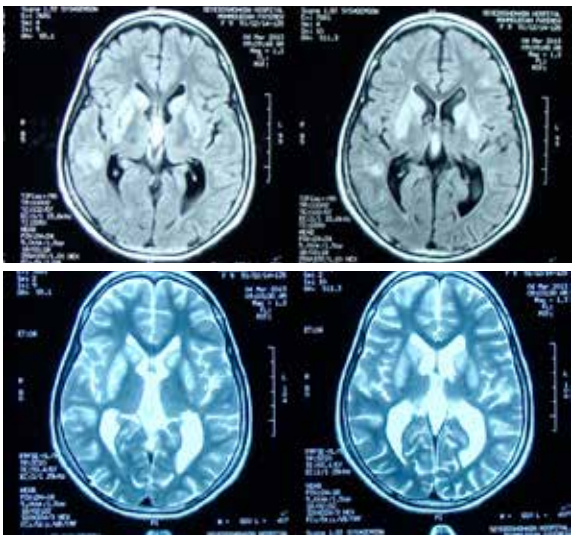

Figure 1, Bilateral symmetric lesions of the caudate nucleus and the putamen in brain MRI

family history of epilepsy, metabolic disorders and other hereditary diseases were negative.

She had delay in motor and was able to walk by two years and could speak two word sentences by three years. At the age of two years, she had seizure and fever for which was admitted for ten days. In laboratory evaluation, complete blood count (CBC), serum glucose, calcium, sodium, potassium, blood urea nitrogen and creatinine level, liver function test, cerebrospinal fluid examination and serum ammonia and lactate level were normal. Blood and cerebrospinal fluid cultures were negative. Blood gas analysis showed mild metabolic acidosis (pH= 7.31, HCO3= 16, BE= -5 and PCO2=29.6).

In electroencephalography, multi-focal spike discharges were seen. Brain MRI showed multiple lesions in the basal ganglia with hyper intensity on T2W and hypo intensity on T1W sequence.

She was being treated with sodium valproate but seizures were not controlled. Based on these clinical and paraclinical finding, biotinidase deficiency was suspected and enzyme assay revealed partial biotinidase enzyme deficiency with enzyme activity 15% of normal enzyme level. Treatment with 10 mg biotin daily was started and rapid and good control over seizures were seen.

Sodium valporate and biotin therapy were continued. The patient had episodes of seizure at the ages of four, six and nine years with fever and upper respiratory infection for which biotin dosage increased to 20 mg daily.

Now and in the last follow up, she is 10 years old and is a student of fourth grade of primary school and academic performance is partially favorable. On examination, she had 37 kilograms weight(10th percentile), 145 centimeters height (10th percentile) and 52 centimeters head circumference (50th percentile), skin and hair were normal and she had dysarthria, ataxia ,tremor, dystonia of the left hand and mild stiffness of lower extremities. The new brain MRI showed severe degeneration of the caudate nucleus and the putamen (Fig. 1).

DISCUSSION

Biotinidase deficiency is a form of multiple carboxylase deficiency with defect in biotin recycling. Sei zures occur in more than 50% of patients and they may be frequent or intermittent or they may occur only with fever 9 and in our case, seizures occur only with fever.

Avidin is a glycoprotein that is found in raw egg white and binds to dietary biotin and prevents its absorption. Adhisivam et al. reported an Indian ten year old boy with acute quadriplegia and multiple symmetric basal ganglia lesions whom had biotin deficiency due to prolonged raw egg consumption. (4 Debs et al. reported two European cases (a 33 years man and his 29-year-old sister) with generalized dystonia, epilepsy, attacks of encephalopathy and bilateral lesions of caudate nucleus and putamen in both of whom high doses of biotin or combination of biotin and thiamine caused significant clinical and MRI findings improvement.[5]

Ozand et al. reported ten cases of biotin-responsive basal ganglia disease in Saudi Arabia. Subacute encephalopathy, with confusion, dysarthria and dysphagia with occasional supranuclear facial nerve palsy or external ophthalmoplegia, and progressing to severe cogwheel rigidity, dystonia and quadriparesis were the first manifestations in these patients. Bilateral necrosis of head of the caudate nucleus and complete, or partial, involvement of the putamen were detected in their brain MRI that during a follow-up of 3^{-10} years, remained unchanged. Treatment with biotin in dosage of 5^{-10} mg/kg/day disappeared the symptoms within a few days without neurological squeal. Those who have had repeated episodes or were diagnosed late, suffered from residual symptoms such as paraparesis, mild mental retardation or dystonia. Absence of symptoms such as dry skin, seborrheic dermatitis, fungal infections and erythematous periorifacial macular rashes in their patients might be suggested that sufficient biotin is available in all regions except the brain and showed susceptibility of the striatal neurons to a lack of adequate biotin. [6]

El-Hajj et al. reported a case of a biotin-responsive basal ganglia disease in Beirut, Lebanon that, compared to the Ozand et al. cases, 7) presented much earlier and was milder and better responded to lower doses of biotin.

In a study in Mumbai, Indi, MRI findings of four patients with biotinidase deficiency included cerebral atrophy, encephalopathy, ventriculomegaly and widened extracerebral CSF spaces. Uncommon findings were caudate involvement, parieto-occipital cortical abnormalities and one patient with restricted diffusion. Two patients had subdural effusions and Fol-

low-up studies revealed complete reversal of imaging findings in two patients.[10]

Subcortical cysts of brain 11 and symmetrical changes in the medial thalamus, dorsal brainstem, medulla and spinal cord 12 were reported in MRI of patients with biotinidase deficiency.

Leukoencephalopathy, widening of the ventricles and extra-cerebral CSF spaces, delayed myelination and subtle subcortical changes were reported in brain MRI of five patients with biotinidase deficiency in Germany that biotin therapy improved myelination and normalized the CSF spaces in one case, but one case had progressive atrophy and cystic degeneration.[13]

Today, newborn biotinidase deficiency screening programs are carried in the United States and in many other countries. With early detection of the disorder and timely administration of adequate doses of biotin , symptoms of the disorder can be successfully treated or prevented.[14]

CONCLUSION

Since neonatal biotinidase deficiency screening programs are not available in Iran, increased awareness of the disorder and biotinidase deficiency recognition which is a cause of basal ganglia lesions in MRI similar to our patient, would ease timely diagnosis and many of neurological squeals which are associated with missing the condition can be prevented.

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