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A CASE REPORT OF BIOTINIDASE DEFICIENCY

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ABSTRACT

Background: Biotinidase deficiency is an autosomal recessive inborn error of metabolism, characterized by neurological and cutaneous symptoms. Eventhough the prevalence is 1 in 60089 live births, the diagnosis of this rare condition should not be missed since there is dramatic response to oral therapy if diagnosed earlier. The aim of the report is to share the classical presentation of biotinidase deficiency and its dramatic response to oral biotin supplementation. C**haracteristics:** 2 month old baby with multiple episodes of seizures, skin and hair changes. Investigations revealed the diagnosis of biotinidase deficiency. The baby was started on oral biotin therapy. **Outcome:** Responded dramatically to treatment with control of seizures, skin and hair changes. **Message:** Biotinidase deficiency is a rare and curable disorder and the diagnosis should not be missed.

KEYWORDS: biotinidase, hypomyelination, acyl carnitine, refractory seizures.

INTRODUCTION

The enzyme biotinidase is required for the restoration of free biotin from biocytin after it has activated various carboxylases in the biotin cycle.[1,2] Absence of biotinidase results in biotin deficiency, resulting in a wide spectrum of neurological, dermatological and immunological abnormalities.[3] Biotinidase deficieny is an autosomal recessive inborn error of metabolism. Eventhough the prevalence is 1 in 60089 live births[4], the diagnosis of this

rare condition should not be missed since there is dramatic response to oral therapy if diagnosed earlier.

The aim of the report is to share the classical presentation of biotinidase deficiency and its dramatic response to oral biotin supplementation.

CASE PRESENTATION

A 2 month old girl baby born out of non consanguinous marriage presented with multiple episodes of convulsions, each lasting for few seconds and the baby regained basal level of consciousness in between the episodes. There was no history of fever, vomiting, lethargy, incessant cry, recent vaccination or head trauma. Past history was insignificant. Social smile was not attained by the baby. The mother had history of 2 abortions inbetween two live births.

On examination, child was awake, lethargic, not interested in surroundings, not interacting with mother, had round dull facies, sebborreic dermatitis of scalp, alopecia, madarosis, bilateral conjunctivitis, open mouth, dry skin, generalised hypotonia, did not fix and follow light, reflexes were brisk, no organomegaly.

Fundus showed no optic atropy. Behavioral observed audiometry was normal for age. MRI brain showed mild hypomyelination of white mater.

Complete blood count, renal function tests, serum electrolytes, CSF analysis were performed and results were found to be normal.

Even with two doses of anti epileptics, seizures were persistent and refractory. Due to refractory seizures we proceeded with serum ammonia, pyruvate, lactate, urine metabolic screening, all came to be normal.

Tandem mass spectrometry showed elevated acyl carnitine levels C5OH and C4DC, suggesting a differential diagnosis of biotinidase deficieny, holocarboxylase deficiency, HMG Co A lyase deficiency or methyl malonic acidemia. Serum was sent for analysis of biotinidase analysis sent, value came to be very low 1.50 nmoles/ml/min (20.35 – 37.58 nmoes/ml/min). Thereby, the final diagnosis of biotinidase deficiency was made.

Baby was started on T. Biotin 10 mg OD and showed dramatic improvement with the first dose of biotin. On follow up, no further seizures were reported. The baby's activity improved, attained social smile, skin lesions and alopecia resolved.

DISCUSSION

Biotin is a water soluble vitamin, a cofactor for enzymes involved in carboxylation. These biotin dependent carboxyases catalyse key reactions in gluconeogenesis, fatty acid metabolism and amino acid catabolism. Although individual deficiencies of all four carboxylases have been reported, the clinical spectrum varies widely from a severe form, presenting early (multiple carboxylase deficiency, holocarboxylase synthase deficiency) to milder varieties presenting late (biotinidase deficiency).[5,6] Dietary biotin is bound to proteins, free biotin is generated in the intestine by the action of digestive enzymes , by intestinal bacteria, also by biotinidase. Biotinidase enzyme is found in serum and most tissues of the body. It is essential for the recycling of biotin by releasing it from the apoenzymes. Free biotin must form a covalent bond with the apoprotein of 4 carboxylases to form the activated enzyme.

Biotinidase deficieny is an autosomal recessive condition. The prevalence is 1 in 60089 live births.[4] The gene for biotinidase is located in chromosome 3p25.1. The absence of biotinidase result in biotin deficiency. Symptoms appear later when the child is several months or years old, delay may be due maternally derived biotin. Deficiency can be profound with < 10 % of enzyme activity or partial with 15 -20% of activity The

clinical findings of biotin deficiency include atopic or seborrheic dermatitis, conjunctivitis, thinning of hair, alopecia, lethargy, hypotonia, seizure, ataxia, developmental delay, optic atrophy, sensorineural hearing loss and withdrawn behavior. Some older children present with progressive spastic quadriparesis and hearing and visual impairment.[7] The seizures in biotinidase deficiency are considered to be unresponsive to conventional antiepileptic drugs.[8]

Diagnosis can be established by measuring the enzyme activity in the serum. Treatment is with oral biotin at a dose of 10mg/day which is adequate to treat even profound deficiency, thus biotinidase deficiency is included in the universal newborn screening programmes. The prognosis is good if treatment is initiated early and continued lifelong.[9]

Biotinidase deficiency may be detected on newborn screening[10] or by prenatal molecular diagnosis for mutations, recommended in case of previous affected child in the family. Recently, molecular genetic tests have been used for detection of carrier state.[11]

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