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Case Report

Biotinidase Deficiency: A Treatable Neurometabolic Disorder- A Case Report

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Abstract

Biotinidase deficiency is an rare autosomal recessive disorder with a wide-spectrum of neurological, dermatological, and immunological dysfunction. Identification of this disorder is important as it is easily treatable and the patients show dramatic response to therapy, besides the fact that it can prove fatal if not diagnosed. We report a case of two and half months old female child of biotinidase deficiency who presented with repeated attack of convulsion for 7 days, seborrheic dermatitis, alopecia and angular stomatitis for 15 days. Her perinatal period was uneventful and no consanguinity between parents. On admission she was hypotonic, reflex exaggerated, plantar extensor. She had mild metabolic acidosis, CT Scan of brain shows mild generalized atrophy of brain with bifronto-parietal craniocortical subarachnoid collection, TMS-increased C5OHcarnitine and enzyme assay revealed profound biotinidase deficiency. Treatment with 02 mg daily biotin was started and rapid and good control over seizures was seen.

Key words: Biotin, biotinidase

Introduction

Biotin also called vitamin B-7 which is a member of the B-vitamin family and good sources are found in egg yolk, milk, soya, barley, Brewer's yeast and royal jelly[1]. Biotin is a water-soluble vitamin that is a cofactor for all 4 carboxylase enzymes in humans: pyruvate carboxylase, acetyl CoA carboxylase, propionyl CoA carboxylase, and 3methylcrotonyl CoA carboxylase. Dietary biotin is bound to proteins; free biotin is generated in the intestine by the action of digestive enzymes, by intestinal bacteria, and perhaps by biotinidase. The gene for biotinidase is located on chromosome 3p25 and many disease-causing mutations have been identified in different families[2]. Biotinidase deficiency is a rare metabolic disease with estimated incidence of approximately 1:60089.Absence of biotinidase results in biotin deficiency, which results in a wide spectrum of neurological, dermatological, and immunological abnormalities[3].

Symptoms may appear later, when the child is several months or several years old; symptoms may develop as early as 1 week of age. Severity and time of clinical presentation depends on the severity of enzyme deficiency. Patients with profound biotinidase deficiency possess less than 10% of normal serum biotinidase activity and partial deficiency patients have 10-30% of normal enzyme level.[1,4] Atopic or seborrheic dermatitis, alopecia, ataxia, myoclonic seizures, hypotonia, developmental delay, sensorineural hearing loss, and immunodeficiency may occur. Most of these individuals have shown to have partial deficiency of the enzyme activity[5].

Asymptomatic children and adults with biotinidase deficiency have been recognized in screening programs. Biotinidase is an essential enzyme required for recycling biotin by lysing lysine moiety from biocytin. Prenatal diagnosis is possible by the measurement of the enzyme activity in the amniotic cells or by identification of the mutant gene[4,6]. A simplified method for mass screening of newborn infants is now available and is in use in the USA and around the world. Diagnosis can be established by measurement of the enzyme activity in the serum. Treatment with free biotin (5-20 mg/24 hr) results in a dramatic clinical and biochemical response Children with untreated profound biotinidase deficiency usually have one or more of the following features- seizures, hypotonia, eczematous skin rash and alopecia. Biotinidase deficiency is an important cause of preventable neurological impairment[5,7].

Case Report

A two and half months old female child admitted into Combined Military Hospital, Dhaka on 22nd March 2015 with the complaints of repeated attack of convulsion for last 7 days, Oral ulcer, alopecia and skin lesion for last 15 days. No history of fever. No significant past illness. Her perinatal period was uneventful, birth weight was 3000g. The baby was on breast milk and formula milk. Only issue, no consanguinity between parents. On examinations the baby was conscious, fair complexion,

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alopecia, lethargic, seborrheic dermatitis, angular stomatitis, anterior fontanelle not bulged, vital signs normal, no neck stiffness, muscle bulk normal, hypotonic, reflex exaggerated, plantar extensor, ankle clonus present, liver 3 cm firm nontender, spleen just palpable, other system reveals normal.

Picture shows alopecia, seborrheic dermatitis, angular stomatitis

A complete blood picture shows microcytic hypochromic anaemia, serum chemistries including serum electrolytes, sugar, urea, creatinine, calcium, magnesium, liver enzymes, thyroid hormone were within normal limits. ABG-mild metabolic acidosis , CSF study-normal except reduced sugar, CT Scan of brain-mild generalized atrophy of brain with bifronto-parietal cranio-cortical subarachnoid collection, EEG - consistent with localized centro-temporal spike activity, Serum ammonia and lactate raised, Biotinidaseassay- 0.63 nmol/min/ml (reduced), TMS-Children with biotinidase deficiency have increased C50H,Urinary ketone body- absent, echo cardiography and opthalmoscopy- normal, audiometry- outer hair cells are not functioning in both ear.

The parents were counselled about the case and prenatal diagnosis in a subsequent pregnancy. The baby was started on daily oral biotin 600mg 8 hourly and Levetiracetam 100mg 12 hourly and made significant recovery.

Discussion

Symptoms may appear later, when the child is several months or several years old; symptoms may develop as early as 1 week of age. Most of these individuals have shown to have partial deficiency of the enzyme activity[1]. In this case symptoms appeared more or less earlier.

Free biotin is generated in the intestine by the action of digestive enzymes, by intestinal bacteria, and perhaps by biotinidase[2]. Seborrheic dermatitis, alopecia and candidal infections are due to immunological dysfunction are the predominant skin manifestations[3] and the patient had most of these features.

Seizures occur in more than 50% of patients and they may be frequent or intermittent.[4] The neurological symptoms may be secondary to accumulation of lactic acid in the brain. Biotinidase deficiency or the late onset or infantile form of multiple carboxylase deficiency has an autosomal recessive mode of inheritance and was first described by Wolf and colleagues in 1985[5]. In this case seizures occurs intermittently.

Biotinidase is an essential enzyme required for recycling biotin by lysing lysine moiety from biocytin, as elucidated in the biotin cycle. Deficiency of biotinidase results in the deficiency of biotin, which is required as a catalyst for the carboxylase systems in the body[6].

Children with untreated profound biotinidase deficiency usually have one or more of the following features-seizures, hypotonia, eczematous skin rash and alopecia as was seen in this patient. Other features include conjunctivitis, candidiasis and ataxia[7].

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[8] in this case mild generalized atrophy of brain with bifronto-parietal craniocortical subarachnoid collection were seen.

Conclusion

Since neonatal biotinidase deficiency screening programs are not available in Bangladesh. Increased awareness with early detection of the disorder and timely administration of adequate doses of biotin, symptoms of the disorder can be successfully treated or prevented.

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