A Treatable Refractory Epilepsy: A Case Report

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Abstract

Introduction:
Biotinidase deficiency is a life threatening inborn error of metabolism specially when delayed in diagnosis.
We report a 2-month-old male infant that presented with refractory infantile spasm, alopecia and seborrheic dermatitis. With a high suspicion of the biotinidase deficiency we started biotin 10 mg daily orally before definite diagnosis was made. Rapid treatment was life-saving and all complications disappeared rapidly.
With this report we tried to explain the clinical manifestations of biotinidase deficiency and show the importance of early diagnosis and treatment in resolving the complications.

Keyword:
Biotinidase deficiency, Biotin, Refractory epilepsy, Inborn error of metabolism.

Introduction

Biotinidase deficiency is a treatable inborn error of metabolism with autosomal recessive inheritance and its prevalence is 1/60000 in normal population (1). Clinical manifestations of this disease often develop during infancy but it can starts from first week of age or when the child is several years old. It usually presents with wide variety of symptoms and signs that divided into different groups. Neurological complications like intractable myoclonic seizure, hypotonia, ataxia, hearing loss and developmental delay are common features. Cutaneous manifestations such as skin rash, alopecia and seborrheic dermatitis may occur (1-2). During investigations we can see metabolic acidosis, hyperammonemia and ketonuria. Diagnosis is confirmed by measurement of enzyme activity in the serum. Early diagnosis and therapy with biotin 10 mg daily can dramatically resolve all complications (1-3).

Case Report

Our patient was a male infant who presented at the age of 2 months with infantile spasm to our center. Perinatal history was normal; he was term and product of vaginal delivery, APGAR score was 9-10. He had birth weight of 3500 gr and his head circumference was 36cm.

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Family history was negative for similar problems and all of family members were healthy.

Repeated episodes of seizures typed infantile spasm (flexion type) started at 50th day of life that was uncontrolled despite use of phenobarbital and clonazepam. Seborrheic dermatitis and alopecia started since 20th day of life. When he admitted to the hospital with infantile spasm, vital signs were normal. He had weight of 2 kg, anterior fontanel 2x2 cm and head circumference of 42 cm. There was seborrheic dermatitis and alopecia of the scalp and eyebrow (figure 1). He was slightly hypoton but deep tendon reflexes were normal. Laboratory findings included normal levels of calcium, magnesium, blood sugar, creatinine, blood gas, sodium and potassium. Sepsis screen was negative. EEG showed paroxysms of sharp & slow waves and also spike & waves (figure 2).

Fig. 1: Before treatment: seborrheic dermatitis and alopecia of the scalp and eyebrow

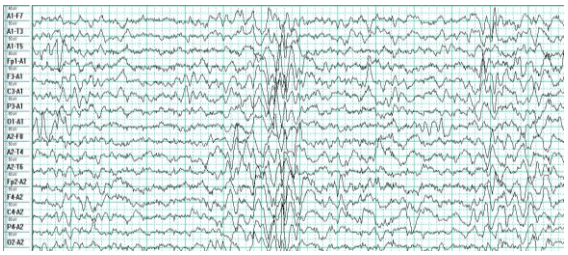

Fig. 2: Paroxysms of sharp & slow waves and also spike & waves

Brain CT scan was normal. According to the clinical manifestations, treatment with biotin tablet 10 mg daily started empirically, and there was dramatic response: seizures and hypotonia disappeared in one week, anti convulsant drugs were tapered during 2 months without any recurrence of seizure and EEG became normal. Skin rash resolved in 10 days and hairs grown on the scalp (figure 3).

Fig. 3: After treatment: Healthy baby (all of cutaneous and neurologic complications resolved).

Now he is healthy after 1 year of follow up. The diagnosis was suggested by abnormal level of C5OH acyl carnitine in the tandem mass spectroscopy and confirmed with decreased activity level of biotinidase enzyme of the serum.

Discussion

In born error of metabolism is called to the group of disorders that usually cause by gene mutations. These mutations can change protein structure or synthesis. Children with inherited error of metabolism have variety of symptoms and signs. They are usually normal at birth and symptoms appear later in life. In the severe forms patients become symptomatic during neonatal period and can be lethal if untreated. Inborn error of metabolism should be suspected in any child with unexplained mental retardation, mental deterioration, developmental delay, motor deficit, seizure, vomiting or acidosis (4).

Biotin is a water soluble vitamin that is a cofactor for carboxylase enzymes that are involved in metabolism of some amino acids like Lucine and Isolucine. Deficiency in biotinidase results in biotin deficiency,

dysfunction of carboxylase enzymes and organic acidemia (1,2).

Symptoms appear when the child is several months or years old but it may develop during neonatal period. CNS involvement presents with infantile spasm, intractable myoclonic seizure (5-7), hypotonia, developmental delay, ataxia, irritability, lethargy, coma and sensory neural hearing loss (8-10,11-13). Cutaneous manifestations include atopic or seborrheic dermatitis, generalized erythematous rash and partial or total alopecia. Presence of rash differentiates this condition from other organic acidemias. Feeding problems, vomiting and failure to thrive may occur. Immune deficiency from T-cell abnormalities can present with susceptibility to different infections (1,2). If there is partial deficiency of biotinidase enzyme (when activity is 15-30% of normal) patient may have refractory seborrheic dermatitis that resolved only with biotin therapy (1,2,14). Some children with partial biotinidase deficiency are asymptomatic and identified during screening programs. Diagnosis can be suggested by abnormal level of C_5OH acyl carnitine in the tandem mass spectroscopy and established with decreased activity level of biotinidase enzyme of the serum. It can be diagnosed with mass screening test of the newborn (Tandem Mass) (1,2,15).

Prenatal diagnosis is achieved by the measurement of enzyme activity in the amniotic cells or by identification of the mutant gene in suspected cases (1,16).

Treatment with biotin 5-20 mg/24h orally results in a dramatic response and improves clinical manifestation and normalizes biochemical abnormalities. Biotin therapy needs to be continued throughout the patient's life (1-2,17-18).

Our case presented with neurological and cutaneous manifestations (seizure, hypotonia, alopecia and seborrheic dermatitis) in early infancy. With a high suspicion of the biotinidase deficiency we started biotin tablets with the dose of 10 mg daily that led to rapid clinical response and all symptoms disappeared. He is healthy now without any complications.

Conclusion

Biotinidase deficiency should be suspected in any child with progressive neurological deterioration (e.g. seizure, hypotonia, neurodevelopmental delay) with or without cutaneous involvement (e.g. Skin rash, seborrheic dermatitis and alopecia). An early diagnosis is very important; therefore a high suspicion is the best clue. Diagnostic confirmation test of this disease is now available. Early diagnosis and therapy can significantly reduce their complications and prognosis will be excellent.

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