Case Report

Case report of early biotinidase deficiency, a type of multiple carboxylase deficiency

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INTRODUCTION

Biotin responsive multiple carboxylase deficiency is a metabolic disorder affecting the metabolism due to deficiency of propionyl Co-A, 3-methylcrotonyl co-A enzyme and pyruvate carboxylase.1 It is an inherited disorder that responds to large doses of biotin supplementation. Early infantile form of this disease is due to deficiency of holocarboxylasesynthetase enzyme which following attachment to biotin transforms inactive apocarboxylase to active forms.1 Clinical manifestations appear as early as within 1 week of life up to 10 years with mean age of presentation is around 3.5 months.2 Child presents with vomiting, lethargy, hypotonia, skin rashes, seizures, developmental delay, alopecia.3-6

CASE REPORT

A 4 months old boy presented with seizures, vomiting, poor weight gain and loss of scalp hair for 1 month. He was delivered by LSCS. He is 2nd child born to parents with 3rd degree consanguineous marriage with birth weight 2500 gm. The child was on breastfeeding and doing well till 3 months of age, after which the child started having a many episode of generalized seizures, each episode lasting for approximately 3-5 min. For this complaint child was put on syrup phenobarbitone, maintenance dose after pediatric out patient consultation. Baby developed frequent episodes of vomiting, continues to have seizures and developmental delay as noted in the form of not attaining social smile, recognizing mother and head control. Also developed diffuse thinning of scalp hair with loss of hair. No family history of epilepsy and similar complaints. Elder sibling is 3-year-old and developmentally normal.

Baby developed repeated seizures on the day of admission sometimes focal and generalized seizures, most of the time with decreased activity, refusal of feeds, impaired consciousness and severe respiratory distress in the form of subcostal and intercostal retractions. There was no regaining of consciousness between seizures episodes. On examination the baby was convulsing with vitals SpO2-80% with 2 litres of O2 with nasal prongs, pulse rate-202 bpm, CRT <3 seconds, pallor was present, no bulging of anterior fontanelle. Baby was started on anticonvulsants levpil, intubated and was started on mechanical ventilation. Investigation reveals Hb-8.8 gm%, GRBS-117 mg/dl, chest x-ray was normal. LFT and RFT, Serum electrolytes were within normal limits. Arterial blood gas analysis reveals severe metabolic acidosis pH 7.05, PCO2 20 mmHg, HCO3 6.6 mmol/lit. As child didn’t respond to loading dose of levpil, phenytoin was also loaded and maintenance dose of both
anticonvulsants were continued. PRBC transfusion was given in view of anemia. As baby continued to have seizures in spite adequate doses of levipil and phenytoin, midazolam infusion was started.

**DISCUSSION**

Biotin is an important water-soluble vitamin, it acts as a cofactor for all four carboxylase enzymes in human body namely propionyl Co-A carboxylase, acetyl Co-A carboxylase, pyruvate carboxylase and 3-methylcrotony Co-A carboxylase. Propionyl Co-A carboxylase and methylcrotonyl Co-A carboxylase involved in catabolic pathways of leucine, isoleucine and valine. Biotinidase converts the precursor of biocytin to biotin. Biotin is an essential co factor for carboxylase enzyme which have important role in fatty acid synthesis, gluconeogenesis and catabolism of branched chain amino acids. Biotinidase deficiency is a classic example of vitamin responsive disease. The age of presentation varies, ranges from few weeks after birth up to the age of 8 years depending on whether the deficiency of biotinidase is partial or total. CNS manifestations are due to accumulation of biocytin and biotinyl peptides and lactate in the cerebrospinal fluid. Children with partial deficiency of biotinidase enzyme may be asymptomatic or presents with intractable seborrheic dermatitis. Clinical manifestations predominantly involve the skin and central nervous system. Child usually presents with alopecia, seizures, hypotonia, developmental delay, candidiasis, ataxia, optic nerve atrophy, sensorineural hearing loss and seborrheic dermatitis. T cell dysfunction can also occur, which may lead to immune deficiency resulting in opportunistic infections. Respiratory distress can occur in the form of hyperventilation, laryngeal stridor, and apnea. Treatment is by supplementation of free biotin 5-20 mg, per day leads to dramatic clinical and
biochemical improvements. Some children might require higher doses of biotin 30-60 mg per day.

**CONCLUSION**

Early biotidinase deficiency should be suspected in infancy whenever an infant presents with clinical manifestations of recurrent difficult to control seizures, persistent vomiting, alopecia, developmental delay and failure to thrive. Recognition of this condition is important as it is a treatable condition and symptoms are well controlled by biotin supplementation.

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**REFERENCES**


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