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Case Report

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

Cheruku Rajesh, N. Shivaramakrishna Babji, Mohammed Ashraf Mohiddin Siddiq*

Department of Pediatrics, Mamata Medical College and Hospital, Khammam, Telangana, India

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***Correspondence:**
Dr. Mohammed Ashraf Mohiddin Siddiq,
E-mail: drashrafped@gmail.com

ABSTRACT

Early biotinidase deficiency is an inherited form of multiple carboxylase deficiency leading to increased accumulation of biocytin and decreased biotin, predominantly effecting the central nervous system and skin. The symptoms can be reversed by early biotin supplementation.

Keywords: Biotinidase deficiency, Seizures, Skin rash, Developmental delay, Alopecia

INTRODUCTION

Biotin responsive multiple carboxylase deficiency is a metabolic disorder effecting 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 SpO_2-80% with 2 litres of O_2 with nasal prongs, pulse rate-202 bpm, CRT <3 seconds, pallor was present, no bulging of anterior fontanelle. Baby was started on anticonvulsants levipil, 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, PCO_2 20 mmHg, HCO_3 6.6 mmol/lit. As child didn't respond to loading dose of levipil, 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.

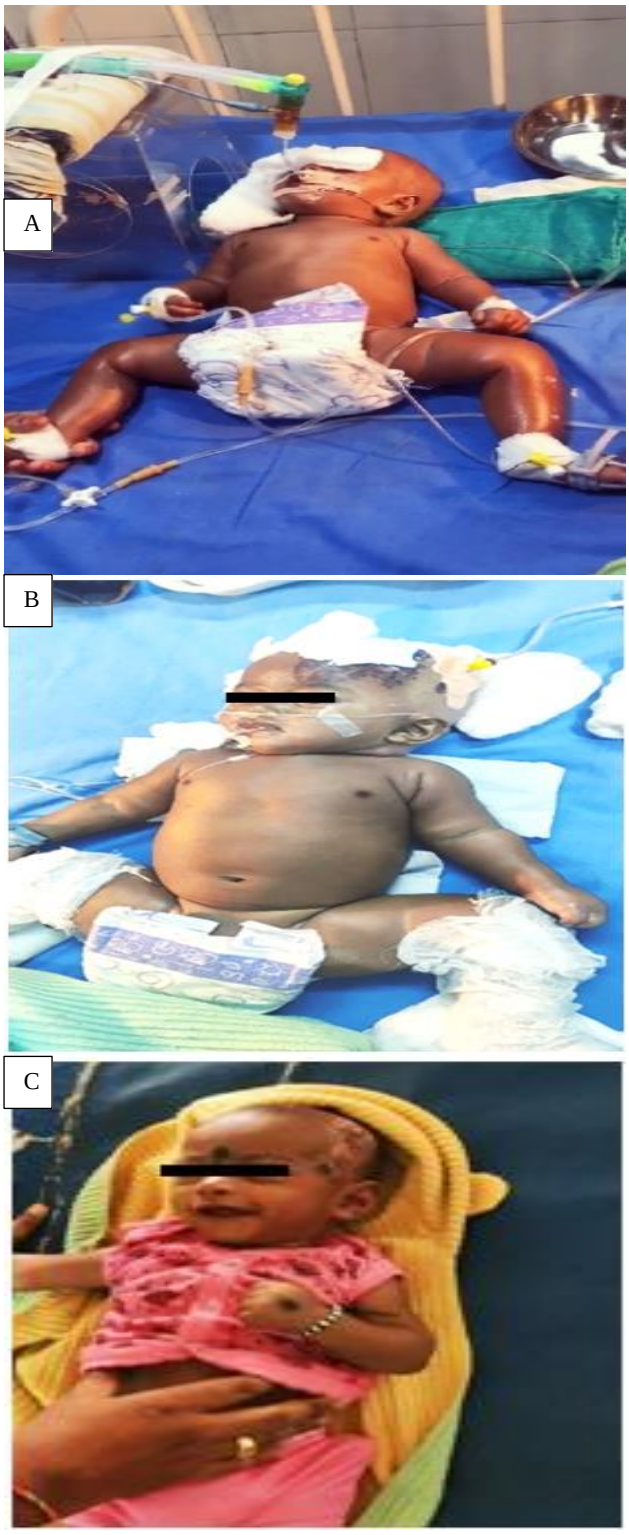

Figure 1 (A, B and C): At admission, 3 days before discharge and follow up visit (1 month).

In view of suspicion of Inborn error metabolism, tandom mass spectroscopy (TMS) of blood sample was sent. On 2nd day of admission, baby condition deteriorated and was in shock. Hence treated with normal saline boluses and inotropes. Baby continued to have persistent metabolic acidosis, being treated with sodium bicarbonate infusions. In spite of all the measures baby continued to have seizures albeit the number of episodes decreased. Here is a 4 months old baby born to a 3rd degree consanguineous couple with recurrent seizures, persistent vomiting, developmental delay, persistent metabolic acidosis, loss of scalp hair with thinning and TMS report done, was suggestive of biotinidase deficiency with biotinidase level of 24 IU (normal >50 IU) and elevated levels of hydroxyisovaleryl carnitine (C5-OH). A diagnosis of early infant biotinidase deficiency, a type of multiple carboxylase deficiency was made. Child was started on 30 mg/day biotin following which the seizure episodes decreased and stopped within 3 days of starting biotin. Phenytoin was weaned off gradually and stopped. Baby general condition improved gradually and was extubated after 2 more days. Baby started taking breastfeeds, doing well and hence discharged with advice to continue biotin and syrup levipil till further advice. On follow up visit after 1 month and 2 months, baby was active, taking direct breastfeeds and developed social smile, recognizing mother and no seizures. Marked improvement in baby's condition following biotin supplementation confirms diagnosis.

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.[7] 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.[8] 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.[9] Children with partial deficiency of biotinidase enzyme may be asymptomatic or presents with intractable seborrheic dermatitis.[10] 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.[7] Respiratory distress can occur in the form of hyperventilation, laryngeal stridor, and apnea.[11] 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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