

Biotinidase Deficiency Presenting in Newborn Period: A Case Report

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Abstract: Background: Biotinidase deficiency is a rare metabolic disorder with presentation at 3 to 6 months of life with encephalopathy, alopecia, dermatitis. It rarely manifests in newborn period. Case: A male newborn with similar presentation. Enzyme assay confirmed profound deficiency in the Biotinidase enzyme activity. Intervention: Baby's encephalopathy and dermatitis improved on addition of Biotin. Message: Biotinidase deficiency has favorable outcome in when prompt treatment is instituted.

Keywords: Biotinidases deficiency, Encephalopathy, Dermatitis, Newborn

1. Introduction

Multiple carboxylase deficiency (MCD) are rare metabolic disorder with decreased or absent activity of mitochondrial carboxylases namely Methyl coA carboxylase, Propionyl carboxylase, Methyl crotonyl CoA carboxylase and Acetyl CoA carboxylase and cytosolic acetyl coA carboxylase¹. The two enzymatic causes of MCD are Holocarboxylase deficiency and Biotinidase deficiency (BD)¹. Holocarboxylase synthetase covalently links biotin to the five biotin dependent carboxylases. Biotin is a coenzyme composed of for the carboxylases². It is a coenzyme in amino acid catabolism, fatty acid synthesis, and gluconeogenesis². Biotinidase recycles the vitamin biotin². The incidence of partial BD is reported as 1 per 60,089 and profound has been reported as 1 per 112,271 of live births, respectively³. Both respond well to Biotin replacement therapy¹. Biotinidase deficiency is more common and is a benign and has late presentation as compared to Holocarboxylase deficiency¹. The early presentation with severe clinical manifestation of Biotinidase deficiency which responded to biotin has been described in this report.

2. Case report

A male newborn infant with 38 weeks gestation and birth weight of 3000 gm presented at 17th day of life with features of poor feeding, lethargy and fast breathing for 3 days. He was born to 29 year old second gravida mother as product of 3rd degree consanguineous union. Mothers antenatal period were unremarkable. Previous obstetric history revealed death of a term good size, three years back, on day 5 of life. The baby was well baby with onset poor feeding and lethargy on day 5 of life and died on day 6 of life. The index case had uneventful intranatal period with no significant event in first two weeks of postnatal life. Baby was exclusively breast fed and was well for initial first two weeks of life. At admission baby presented with acidotic breathing, stupor with intermittent tonic posturing of limbs, poor neonatal reflexes and firm hepatomegaly. Perfusion was well maintained during the hospital stay and hair were easily pluckable leading to zone of alopecia. He was found to have severe metabolic acidosis, normoglycemia, and ketonuria increased serum lactate (71mg/dl) with normal levels of blood ammonia (51 mmol/L). Urine Gas Chromatography Mass Spectrometry revealed raised lactic acid, 3 OH Isovaleric acid, 3OH butyric acid, 2OH butyric acid, 3 methycrotonylglycine, β -methycrotonylglycine,

Isovaleric glycine, Isobutyryl glycine, s/o Holocarboxylase or Biotinidase deficiency. Tandem Mass Spectrometry suggestive of raised C5 OH acyl Carnitine. Ultrasonography brain was suggestive of mild cerebral edema. On day two of admission baby developed rashes over temporal and in perioral region. Baby was managed conservatively with intravenous fluids, Sodium bicarbonate, Carnitine 300 mg and Biotin 10 mg twice a day. By 48 hrs of admission there was improvement in sensorium, rashes, metabolic acidosis with normalization of serum lactate. Baby was started on enteral feeds on day 3 of admission switching to exclusive breast feeding by day 5 of admission. Further diagnosis was confirmed by Biotinidase activity levels of 0.38 nmol/L/min (normal > 5nmol/L/min), which was less than 10%. Baby was discharged on day ten of admission on breastfeeds and 10 mg twice a day of oral Biotin. On follow up on day 35 and at two months of life baby was neurologically normal on breastfeeds and gaining weight with improvement of facial rashes.

3. Discussion

Our patient had the classical presentations of defect in organic acid metabolism. The history of consanguinity and the unexplained death of sibling pointed towards a metabolic disorder. Clinical features, metabolic acidosis with ketosis, increased lactate, and Biotinidase deficiency confirmed the diagnosis. Early Biotin therapy was followed by clinical recovery in the present case.

Biotinidase deficiency does not manifest in the newborn period². In India only few case reports of Biotinidase deficiency with early presentation have been reported but they were in the postneonatal age group^{4,5,6} but not in newborn period. Clinical presentation depends on the severity of enzymatic defect. Profound defects usually manifest between 3-6 months of age with neurological manifestations like seizures, hypotonia, and developmental delay^{4,7}. Presence of rash differentiates this condition from other organic acidemias. Skin manifestations like eczematous skin rash, seborrheic dermatitis and alopecia are common⁷. Respiratory problems like hyperventilation, laryngeal stridor and apnea. Patients can have abnormalities in cellular immunity⁷. The cost of treatment is low and prognosis is good⁸.

Biotin is a water-soluble vitamin that serves as an essential coenzyme for carboxylases that catalyzes the fixation of

bicarbonate in organic acids and play crucial roles in the metabolism of fatty acids, amino acids and glucose. Biotin deficiency is either due to Holocarboxylase or due to Biotinidase deficiency. Biotinidase enzyme, is present in high levels in the serum, liver, and kidneys and its function is to cleave the vitamin biotin from the organic compound Biocytin. Biotin is recycled in the body when Biotinidase liberates biotin from endogenous and dietary proteins and maintains a pool of Biotin⁹.

Biochemical findings include elevated lactic acid, and a specific pattern in urine organic acids including elevations of 3-OH-propionic acid, lactate, and 3-methylcrotonylglycine¹. 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 therapy¹⁰. Diagnosis can be suggested by abnormal level of C5OH acyl carnitine in the tandem mass spectroscopy and

established with decreased activity level of Biotinidase enzyme of the serum¹⁰, as was done in our case.

Mendelian inheritance is autosomal recessive. The gene that encodes biotinidase, called BTBD, is cytogenetically located on the short arm (p) of chromosome 3, band 25 (3p25)⁵. Most cases respond to oral Biotin therapy. Treatment with biotin doses ranging between 3 and 200 mg per day has been reported¹¹. Outcome was favorable in cases where early diagnosis was made and prompt treatment was instituted⁶. If detected late babies have gross developmental delay. Thus early diagnosis and treatment improves the outcome.

In conclusion, profound Biotinidase deficiency presenting in newborn period is a rarely reported presentation which our patient had making this case worth reporting.



Figure: Picture showing dermatitis and alopecia in our baby

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