BIOTINIDASE DEFICIENCY

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INTRODUCTION

- *Biotinidase deficiency is an inherited disorder in which the body is unable to recycle the vitamin biotin. Mutations in the BTD gene cause biotinidase deficiency.*
- *Biotinidase removes biotin that is bound to proteins in food, leaving the vitamin in its free (unbound) state which acts as a co-factor for carboxylation in gluconeogenesis, fatty acid synthesis and fatty acid oxidation.*
- *Symptoms of profound biotinidase deficiency (<10% serum activity) usually appear between ages 1 week and 10 years, typically with optic atrophy, hypotonia, seizures, hair loss and skin rash along with ataxia and developmental delay. Individuals with partial biotinidase deficiency (10%-30% serum biotinidase activity) may develop symptoms only when stressed, such as during infection.*

CASE REPORT

Our case is of a 4-month-old baby from Kodagu district, Karnataka, was born from a consanguineous marriage. The antenatal history was uneventful. The parents have two older sons, aged 10 and 7, who are healthy. However, their third child, a daughter born last year, exhibited symptoms of decreased feeding and poor activity by the 20th day of life. She developed status epilepticus seizures and was admitted to the PICU.

Her EEG showed diffuse encephalopathy and CECT suggested bilateral fronto-temporo-parietal subdural hemorrhage and subdural effusion along with hydrocephalus. She was on a ventilator for one month and was discharged against medical advice, shortly after wich she passed away. Given these past events, newborn screening was conducted for the our child in the on her first day of life, which showed Fatty acid oxidation defect and organic aciduria. Her immunization history and arthropometric findings were normal, developmentally only social smile was present at 2 months and general examination showed a depressed epicanthal fold at the root of nose and sparse eyelashes. Systemic examination was normal.

Following NBS reports, Blood Tandom mass spectrometry and Urine Gas Chromatography Mass Spectrometry were done followed by Singleton exome sequencing which showed a Missense variant, c.416G>A in exon: 4 of BTD gene. On segregation, the variant was present in heterozygous state in her mother and father.

MANAGEMENT

Initially child was started on metabolic cocktail including thiamine, riboflavin and biotin.

• After genetic reports confirmed Biotinidase deficiency, thiamine and riboflavin were discontinued and Biotin supplementation was started at 10mg OD (1ml=10mg)

• The parents were informed about sick day rules and the 25% recurrence risk of the disease in future pregnancies.

• The child is currently on regular follow up with strict compliance to prescribed medications

DISCUSSION

All individuals with profound and partial biotinidase deficiencies should be treated with oral biotin, therapy is lifelong. Targeted therapy: Oral biotin of 5-10 mg/day for those who have <10% mean normal serum enzyme activity and 2.5-10 mg/day in those who have 10%-30% of mean normal serum enzyme activity. Supportive care in symptomatic individuals: Hydration and bicarbonate in those with metabolic decompensation and acidosis, supportive developmental therapies and educational resources for those with developmental delay; subspecialist ophthalmologic care for those with optic atrophy; hearing aids and, if severe, consideration of cochlear implants for those with hearing loss.

CONCLUSION

- *This case highlights on how Newborn screening for common metabolic and genetic disorders should be an integral part of neonatal care as early detection and treatment can help prevent intellectual and physical defects and life threatening illnesses*