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Metabolic Stroke in Biotinidase Deficiency: A Case Report

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Abstract

An apparently normal infant born out of non-consanguineous marriage presented with abnormal movements, seizures, respiratory failure and coma at 3 months of age. MRI Brain revealed bilateral corona radiata and internal capsule acute ischemic insult with supra-tentorial early brain shrinkage. Multiple carboxylase deficiency was suspected clinically in view of erythematous skin rash, alopecia, seborrhoea and metabolic acidosis. Biotin was started and baby showed dramatic clinical improvement. Screening for inborn errors of metabolism from blood spot was positive for biotinidase deficiency and biotinidase enzyme activity in serum was low (0.17nmol/min/ml) confirming the diagnosis. The baby was treated with Biotin supplementation and on follow up at 30 months of age baby had minimal developmental delay and normal MRI of Brain.

Key words Biotinidase Deficiency, stroke, multiple carboxylase deficiency

INTRODUCTION

Biotinidase deficiency is a rare metabolic disorder with an estimated incidence of 1:61,067, though, severe or profound disease is much rarer.[1-2] Deficiency of biotinidase enzyme results in biotin deficiency which is a cofactor for all four carboxylase enzymes responsible for metabolic pathways of leucine, isoleucine and valine. Clinical manifestations include atopic or seborrheic dermatitis, alopecia, ataxia, myoclonic seizures, hypotonia, developmental delay and sensorineural hearing loss. Neonatal screening is available and diagnosis can be established by measuring serum enzyme activity. Treatment with biotin results in dramatic clinical and biochemical response.Variable neurological presentation has been reported in literature but focal neurological deficit associated with focal lesions in neuroimaging due to acute metabolic decompensation has not been reported with biotinidase deficiency. Herein We repor a case of biotinidase deficiency who presented with stroke

CASE PRESENTATION

Index case was 3 month old, 1st child of healthy unrelated parents, born at term by caesarian delivery after an uncomplicated pregnancy, and had an uneventful perinatal period. He presented with cough & cold for 7 days, abnormal movement of limbs followed by seizure for 3 days, and shallow breathing for 2 days. He was being treated as a case of sepsis and was referred to our institute impending respiratory failure ensues.

On examination, the baby was comatose, hypotonic, with cold extremities and shallow breathing. His pulse rate was 108/min; respiratory rate 30/min with shallow respiration, blood pressure 103/68 mm of Hg, and SpO2 was 90% with FiO2 of 50%. There were erythematous skin rashes with exfoliation over back, groin & thigh, alopecia with easily pluckable hairs with seborrhea. (Figure 1 & 2) Eyes were dried, conjunctiva wrinkled, pupils mildly dilated with sluggish reaction to light. His weight was 4.5Kg and head circumference was 36.5cm. On systemic examination, he was comatose, hypotonic with absent deep tendon reflexes and no cranial nerve palsy and he had firm hepatomegaly of 4 cm without splenomegaly. Fundoscopy could not be done due to exposure keratitis.

His routine blood investigations including complete hemogram, renal and liver function tests, serum electrolytes and blood sugar (120mg/dl) were within the normal range. Urinary sugar and ketone was negative. Septic screening including leukocyte counts, CRP (3.25mg/L), blood culture as well as CSF examination was also negative. Blood gas analysis showed mixed respiratory and metabolic acidosis (PaO2-100, PaCO2-75.3, PH-6.998, HCO3- 17.9, BE- -18). USG of Cranium showed dilated bilateral ventricles without midline shift. MRI Brain revealed bilateral corona radiata & internal capsule acute ischemic insult with supratentorial early brain shrinkage which was suggestive of stroke (Figure-3).

The baby was put on mechanical ventilator and supportive management was done with IV antibiotics, IV fluid, vasopressors and sodium bicarbonate infusion with close monitoring of vitals & urine output. Metabolic acidosis was persisted till day 3 of admission requiring repeated sodium bicarbonate infusion which prompted us to think in line of inborn errors of metabolism (IEM). Biotinidase deficiency was considered as first possibility due to the presence of skin manifestations and biotin (10mg/day) was started. IEM screening was sent from bloodspot. After 2 days of biotin therapy, baby showed dramatic improvement and was extubated on day 8 of admission. His skin rashes gradually started healing with no convulsions, so anticonvulsants were weaned & stopped. He was breastfed on day 10 and discharged from ICU on day 10. Report for IEM showed Biotinidase – 0.03 Absorbance (Normal = >0.36). Biotinidase activity in serum was sent and it was low (0.17 nmol/min/ml) confirming the diagnosis. The patient was discharged with biotin at a dose of 10mg/day orally and advised for regular follow-up. On follow-up at 30 month, the baby was stable with normal anthropological parameters and slight developmental delay and MRI revealing normal findings (figure-4).

DISCUSSION

Biotinidase deficiency is a rare inherited metabolic disorder, only a few cases have been reported in the Indian literature.[3-4]

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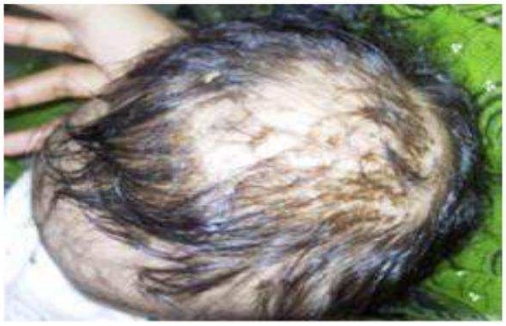

Figure:1: Photograph of the child showing extensive seborrhoea with easily pluckable hair

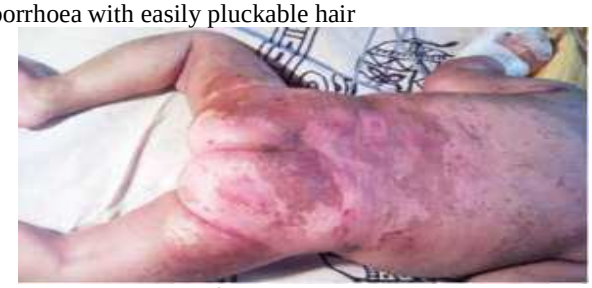

Figure:2 Photograph of the child showing erythematous skin rashes

Clinical manifestations reported are atopic or seborrheic dermatitis, alopecia, ataxia, myoclonic seizure, hypotonia, developmental delay and sensorineural hearing loss.[1-2] However, neurological manifestations in biotinidase deficiency are variable.[5-6] Fits, hypotonia, ataxia and developmental delay have been reported in the case series of 10 cases by Wastell et al while lethargy and seizures were reported by others.[4,7] Hayati AA et al reported bilateral optic neuritis in a 6 year old boy with biotinidase deficiency.[8] Spinal cord involvement presenting as recurrent myelopathy is reported in a 7 year old boy with biotinidase deficiency by Raha et al and spastic tetraparesis was reported in a 3year girl by Komur et al.[3,9] Our patient also presented with hypotonia, lethargy and seizure similar to the cases reported. However, our case showed MRI changes of stroke (i.e. acute ischemia of bilateral corona radiata and internal capsule), which was not reported previously. In a report by Dahiphale et al, similar ischemic changes were described in bilateral parietal lobe and subcortical matter.[4]

Many inherited metabolic disorder may present with stroke during acute metabolic decompensation which remains a diagnostic and treatment challenge and metabolic stroke is described in Fabry disease, MELAS, homocystinuria, organic aciduria and urea cycle defect with no description of biotinidase deficiency as a cause.[10] Early detection and prompt management can prevent complications in biotinidase deficiency which is emphasized by different studies and starting oral biotin therapy empirically on clinical suspicion can dramatically improve the outcome as in our case.

CONCLUSION

In acute focal brain disease, metabolic disorders must be considered as a differential diagnosis. Biotinidase deficiency adds to the list of possible causes of “metabolic stroke" and early supplementation with biotin can be lifesaving and neurological manifestation can be reversed.

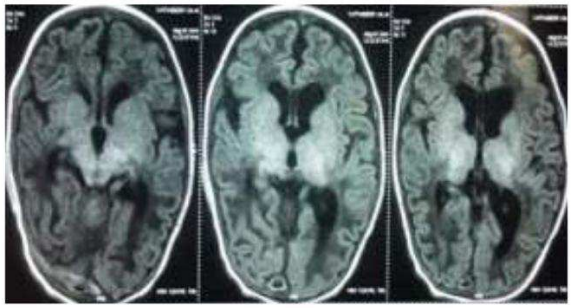

Figure:3 MRI showing acute ischemic lesion in internal capsule & corona radiate

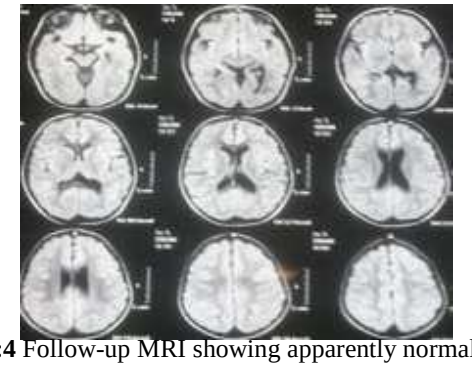

Figure:4 Follow-up MRI showing apparently normal internal capsule & corona radiata

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