

## Case report

# An unusual presentation of biotinidase deficiency in infant: High anion gap metabolic acidosis and *Burkholderia cepacia* sepsis

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## ABSTRACT

Biotinidase deficiency (BD) is an inborn metabolic disorder caused by low enzyme activity giving rise to impaired biotin release from dietary proteins. The first symptoms may be seen at first week following birth until 1 year of age. The goal of the therapy is to increase biotin bioavailability by daily 5-20 mg lifelong biotin replacement. Three-month-old girl born to nonconsanguineous parents, admitted to pediatric intensive care with multiple seizures, breathing difficulty and posturing. Blood investigations showed thrombocytopenia and high anion gap metabolic acidosis (HAGMA). Enzyme assay for biotinidase revealed low activities. Urinary organic acid analysis was normal. Enzyme activity is <10% in severe cases whereas between 10-30% in partial deficiency. BD can cause metabolic ketoacidosis, Hyperammonemia and organic Aciduria. BD behaves like immunodeficiency. Rarely bacterial infection can be seen. Treatment is lifelong biotin replacement.

**Keywords:** Biotin, Biotinidase deficiency, Encephalopathy, High anion gap metabolic acidosis, Sepsis, Seizures

## INTRODUCTION

Biotinidase deficiency (BD) is an inborn metabolic disorder caused by low enzyme activity giving rise to impaired biotin release from dietary proteins. The enzyme activity is within 10-30% in partial type and <10% in severe form.<sup>1,2</sup> The gene encoding biotinidase enzyme has been found in chromosome 3p25. Biotin deficiency can give rise to sensorineural deafness, optic atrophy, seizures, hypotonia, mental retardation, alopecia, dermatitis and ataxia.

The first symptoms may be seen at first week following birth until 1 year of age. The delay in diagnosis and treatment may cause irreversible neurological damage, growth retardation and autistic behaviours. The goal of the therapy is to increase biotin bioavailability by daily 5-20 mg lifelong biotin replacement.<sup>3,4</sup>

## CASE REPORT

Three-month-old girl born to nonconsanguineous parents, admitted to pediatric intensive care with multiple seizures, breathing difficulty and posturing. Outside evaluated for seizures and encephalopathy. EEG showed burst suppression and MRI brain showed periventricular hyperintensities. Treated with multiple antiepileptic (gardenal, levetiracetam, valproate and clobazam). Physical examination revealed tachycardia, signs of poor perfusion, no fever, altered sensorium and deep respiratory efforts with grunting. In view of impending respiratory failure and GCS <8/15, patient was intubated and ventilated. BCG scar and tonsils were present. She had no onychomycosis. Complete blood cell count showed anemia, thrombocytopenia, and normocytic normochromic anemia.

Blood gas showed high anion gap metabolic acidosis, arterial lactates were high, serum ammonia was raised. Blood culture was positive for *Burkholderia cepacia*. Patient treated with fluid resuscitation for shock, sodabarbonate infusion for suspected IEM along with IEM specific medications along with antibiotics based on antibiogram for *Burkholderia cepacia*. IEM was considered due to previous two abortions, history of paternal aunt death at 1 year of age by unexplained encephalopathy and seizures, persistent metabolic acidosis with unprovoked seizures and unexplained encephalopathy.

However, patient being diagnosed early had not developed alopecia and dermatitis. Patient was suspected to have IEM possibly organic academia, congenital lactic acidosis and biotinidase deficiency. TMS sent in view of suspected IEM showed biotinidase deficiency (enzyme activity <20U against normal value <40U). Urinary organic acid analysis was normal. Molecular analysis was not performed for BD. Oral biotin replacement was started in a dose of 5 mg/day along with sodamint which dramatically improved her symptoms i.e encephalopathy, persistent metabolic acidosis and deep rapid breathing. Vision was normal and BERA was normal.

## DISCUSSION

Biotinidase is an enzyme giving source to biotin with releasing it from dietary proteins. The biotin is then utilized by carboxylase enzyme class involved in fatty acid synthesis, amino acid catabolism and gluconeogenesis.<sup>4</sup> Impaired biotin bioavailability causes multiple carboxylase deficiency and thus, secondary ketoacidosis, hyperammonemia and organic aciduria. Various neurocutaneous symptoms like seizures, motor mental retardation, hypotonia, spastic paraparesis, ataxia, sensorineural deafness, optic atrophy, eczematous dermatitis and alopecia are associated with the classical disease.<sup>5,6</sup>

The diagnosis is made with detection of low enzyme activity and genetic mutation analysis besides clinical suspicion.<sup>5</sup> The enzyme activity is <10% in severe forms whereas between 10-30% in partial deficiency. Biotin replacement therapy may improve symptoms except hearing loss.<sup>6-10</sup> BD is a primary immunodeficiency mimic. We report this case to increase awareness about BD in setting of infantile onset seizures, encephalopathy with HAGMA, atypical infections non Candida like *B. cepacia* and to emphasised the importance of early diagnosis and reversal of metabolic acidosis, seizures and infections with biotin replacement and antibiotics.

## CONCLUSION

Though fungal infections are most common organism still bacterial infection (*B. cepacia*) are rarely seen. It may

behave like immunodeficiency. New onset infantile seizure, encephalopathy, high anion gap metabolic acidosis can be totally reversible biotinidase deficiency except sensorineural deafness. Treatment is lifelong biotin replacement.

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