Biotinidase Deficiency Presenting as Hyperventilation Syndrome

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Abstract

Biotinidase is responsible for recycling the vitamin, biotin, and making the free biotin available to activate the biotin-dependent carboxylases, including pyruvate carboxylase, which is involved in mitochondrial energy metabolism. Individuals with untreated biotinidase deficiency usually exhibit lethargy, hypotonia, ataxia, cutaneous abnormalities, vision and hearing impairment and developmental delay.

We recently observed a child who presented with hyperventilation syndrome and lactic acidemia who was thought to have a mitochondrial disorder. After six months of multiple hyperventilation episodes in the absence of the usual neurocutaneous features of biotinidase deficiency, the child was determined to be homozygous for a likely pathogenic variant of the biotinidase, BTD, gene. This case prompted us to evaluate retrospectively the presence of respiratory alkalosis and hypocapnia, indicative of hyperventilation syndrome, in other symptomatic individuals with biotinidase deficiency.

The results showed statistically significant hypocapnia at the onset of symptoms which rapidly resolved upon administration of biotin (pCO_2 27.2 ±11.6 vs. 41.5 ± 3.5; normal >35 mmHg).

Selective screening for biotinidase deficiency should be considered in individuals with hypocapnia and respiratory alkalosis. This is particularly important in locations where newborn screening for this disorder is not performed.

Keywords: Biotinidase deficiency; Hyperventilation syndrome; Hypocapnia; Respiratory alkalosis