Biotinidase Biochemical and Molecular Analyses: Experience at Quest Diagnostics Nichols Institute Biochemical Genetics Laboratory

Background

- Biotinidase deficiency is an inherited autosomal recessive disorder that can cause low levels of enzyme activity, as well as skin and neurological symptoms, in children. If the condition is identified early (eg, by newborn screening), doses of biotin can prevent symptoms.
- The severity of symptoms depends on the degree of biotinidase deficiency, which can affect treatment decisions. “Deficient” enzyme activity levels indicate the need for treatment, whereas levels between deficient and normal (labeled heterozygous) can make treatment decisions less clear; genetic testing may help in such cases.
- Specific variants in the biotinidase gene (BTD) may affect the degree of biotinidase deficiency. However, the relationship between BTD variants and the degree of deficiency is not well established.
- **Objective:** The investigators examined which BTD variants are most common in patients with different degrees of biotinidase deficiency.

Methods

- This study examined deidentified results from over 10,000 patient specimens submitted for biotinidase enzyme analysis.
- Based on enzyme activity, patients were categorized as having profoundly deficient (0 to 1.3 nmol/mL/min), partially deficient (1.4 to 3.8 nmol/mL/min), or heterozygous (3.9 to 4.7 nmol/mL/min) biotinidase activity.
- For a subset of specimens, clinicians requested BTD gene sequencing, performed using Sanger sequencing.

Results

- Low biotinidase enzyme activity was detected in 1,360 patients, including 132 categorized as profoundly deficient, 720 as partially deficient, and 508 as heterozygous.
- Mutation analysis was performed for 211 patients. Of the 211 15% were profoundly deficient, 73% were partially deficient, and 12% were heterozygous.
- The most common mutations in each category were as follows:
  - Profoundly deficient group: homozygous p.Lys176Asn (5 patients)
  - Partially deficient group: double-mutation allele p.Asp444His/p.Gln456His (30 patients)
  - Heterozygous group: homozygous p.Asp444His (7 patients)
- Five mutations appeared in 2 categories. The most common of these mutations was homozygous p.Asp444His, which was detected in the partially deficient group (17 patients) and the heterogeneous group (7 patients).

Conclusions

- The investigators identified common genetic variants in the BTD gene in patients with different degrees of biotinidase deficiency.
- Such information may be useful in informing treatment decisions.