Key Summary of Conference Abstract

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,[1] 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.[2]
- 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 heterozygous group (7 patients).

Conclusions

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

Poster presentation at the 41st Annual Meeting of the Society for Inherited Metabolic Disorders

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2. Strovel ET, Cowan TM, Scott AI, et al. Laboratory diagnosis of biotinidase deficiency, 2017 update: a technical standard and guideline of the American College of Medical Genetics and Genomics. *Genet Med.* 2017;19. doi: 10.1038/gim.2017.84