Background Information

Riboflavin transporter deficiency (RTD) is an autosomal recessive heterogeneous metabolic disorder whose symptoms of respiratory problems, sensorineural hearing loss, ataxia, weakness, gross motor delays, and regression overlap the phenotype of many genetic conditions. High doses of riboflavin supplementation has been described previously as improving clinical symptoms in individuals with RTD.

Signs and Symptoms

- Ataxic gait with frequent falls resulting in a preference to sit and scoot
- Proximal muscle weakness resulting in loss of ability to feed herself
- Truncal hypotonia
- Occasional difficulty with swallowing liquids
- Resultant gross motor delay and regression of skills

Methods and Patient

- Patient consent for case presentation was obtained by University of Texas Southwestern Medical Center, Dallas, TX
- Patient was referred for clinical testing with Whole Exome Sequencing provided by GeneDx: WES was performed using standard protocols with exon targets isolated by capture using the Agilent SureSelect Human All Exon V4 kit (Agilent Technologies, Santa Clara, CA).
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Results

- Location of pathogenic and likely pathogenic variants in the SLC52A2 gene. The W45C likely pathogenic variant and the L339P pathogenic variants were identified in the proband (Figure 1).

Table 1. Variants in SLC52A2 detected in the patient

<table>
<thead>
<tr>
<th>Variants in SLC52A2</th>
<th>Publications</th>
<th>Population Data</th>
<th>In-Silico Predictions</th>
<th>Protein Position</th>
<th>Parental Inheritance</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>c.1016 T&gt;C</td>
<td>Functional data support impaired activity, reported in ≥2 unrelated patients who had a path variant in trans</td>
<td>Observed in 7/64708 alleles (0.01%) in Europeans in ExAC</td>
<td>Provean, MutTaster, and CADD predict damaging effect</td>
<td>Conserved, no known functional domain</td>
<td>Paternal</td>
<td>Pathogenic</td>
</tr>
<tr>
<td>c.135 G&gt;T</td>
<td>Not published to our knowledge</td>
<td>Not observed in ExAC</td>
<td>Provean, MutTaster, and CADD predict damaging effect</td>
<td>Conserved, no known functional domain</td>
<td>Maternal</td>
<td>Likely Pathogenic Variant</td>
</tr>
</tbody>
</table>

Summary

- We report a two year old diagnosed with riboflavin transporter deficiency by WES.
- This case highlights that riboflavin transporter deficiency is a treatable metabolic disorder and should be on the differential in patients with gross motor delays, weakness, sensory ataxia, and regression even without evidence of the hallmark features of respiratory problems and sensorineural hearing loss.

References