Two Cousins with the Allan-Herndon-Dudley Syndrome Caused by a Novel MCT8 Mutation

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Background

- MCT8 (monocarboxylate transporter 8) is an active and specific thyroid hormone transporter encoded by a gene located on the X chromosome.
- MCT8 mutations in males cause a rare X-linked disorder known as the Allan-Herndon-Dudley syndrome (AHDS).
- It is characterized by severe psychomotor retardation and abnormal thyroid parameters (high T3, low T4 and normal/high TSH).

Case -1: 4-year and 9-month old boy

- On L-T4 treatment for hypothyroidism
- Congenital hydrocephaly, cerebral palsy and epilepsy.
- Severe neuromotor retardation
- Complete blindness
- The parents were non-consanguineous.
- Family history: similar neuromotor deficits and epilepsy at his uncle and cousin.
- Physical examination revealed severe central hypotonia
- Exaggerated deep tendon reflexes.
- Weight: 18.7 kg (P50),
- Height: 106 cm (P10-25),
- Head circumference: 47 cm (P3-10, -1.29 SDS).
- No goiter
- Unilateral cryptorchidism

Case-2: 2-year and 9-month old boy

- Cousin of first case
- Severe neuromotor retardation
- Complete blindness
- Weight 9,5 kg (-3.1 SDS)
- Head circumference 87.5 cm (10p)
- BMI: 12.4 kg/m2 (-3.4 SDS)
- Blood pressure: 118/75 mmhg
- Strabismus
- No goiter
- Central hypotonia
- External genitourinary system was normal

Laboratory tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Normal level</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4 (ng/dl)</td>
<td>0.82</td>
<td>0.7</td>
<td>0.8-2.2</td>
</tr>
<tr>
<td>T3 (pg/ml)</td>
<td>5.76</td>
<td>5.4</td>
<td>1.7-3.7</td>
</tr>
<tr>
<td>TSH (μU/ml)</td>
<td>0.75</td>
<td>5.5</td>
<td>0.7-6.4</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>248</td>
<td>&gt;250</td>
<td>11.2-78.1</td>
</tr>
</tbody>
</table>

Conclusion

In boys with low FT4 levels in association with severe neurologic findings, serum (FT)3 should be measured. The finding of a low (FT)3 level is highly suggestive for a MCT8 mutation.

• Hemizygous 1-nucleotide deletion in exon 6 of MCT8 (c.1683delC, p.P561fs566X) in both cousins.
• Their mothers (sisters) were heterozygous for the mutation.