Adrenal hypoplasia seemingly first as a primary hypoaldosteronism
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THE CASE

Medical history:
- Male full-term newborn from non-consanguineous parents, caucasian ethnicity
- SGA (small for gestational age) for weight (IUGR during the last month of pregnancy)
- Spontaneous delivery, no complications at birth
- Hospitalization at 11 days of life for ineffective breastfeeding, discharged after registering weigh growth (blood and urine tests were normal)

<table>
<thead>
<tr>
<th>Age</th>
<th>Na+ (n.r. 136-146 mEq/l)</th>
<th>K+ (n.r. 3.5-5.30 mEq/l)</th>
<th>Aldosterone (n.r. 50-300 pg/ml)</th>
<th>Renin (n.r. 4.4-46.1 μU/ml)</th>
<th>ACTH (n.r. 4.3-52 pg/ml)</th>
<th>Cortisol (n.r. 6.7-22.6 μU/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-days-old</td>
<td>110 (natriuria 16 mEq/l)</td>
<td>7.5</td>
<td>38.6</td>
<td>44100</td>
<td>91.4</td>
<td>13.7</td>
</tr>
<tr>
<td>5-months-old</td>
<td>134</td>
<td>4.9</td>
<td>55.9</td>
<td>181.2</td>
<td>124.9</td>
<td>4.4</td>
</tr>
<tr>
<td>7-months-old</td>
<td>139</td>
<td>5.0</td>
<td>45.2</td>
<td>/</td>
<td>/</td>
<td>5.2</td>
</tr>
<tr>
<td>9-months-old</td>
<td>139</td>
<td>4.2</td>
<td>21.5</td>
<td>123.6</td>
<td>300.6</td>
<td>7.4 (urinary cortisol 20ug/24h, n.r. 58-403 μg/24h)</td>
</tr>
<tr>
<td>12-months-old</td>
<td>138</td>
<td>4.4</td>
<td>&lt;10</td>
<td>30.7</td>
<td>89.9</td>
<td>22.8</td>
</tr>
</tbody>
</table>

DIFFERENTIAL DIAGNOSIS
1) Primary Hypoaldosteronism? → genetic analysis of CYP11B2 gene (encoding aldosterone) sequencing did not confirm the hypothesis
2) Congenital adrenal hyperplasia (CAH)? → normal 17-OH-progesterone levels
3) Autoimmune adrenal insufficiency? → Adrenal antibodies negative
4) Adrenoleukodystrophy? → VLCFA negative
5) Congenital adrenal hypoplasia?

DNA analysis performed by Sanger sequencing identified a novel in frame indel mutation in DAX-1 gene 109 (c.848_849delinsCC or p.(Gln283Pro)), confirming the diagnosis of AHC. As expected the mutation was carried by the mother.

EFFECT OF THERAPY
- X-linked Adrenal Hypoplasia Congenita (AHC) is a congenital disorder characterized by adrenal insufficiency sometimes associated with hypogonadotropic hypogonadism (HHG).
- The estimated incidence is 1 in 12500 births.
- Unspecific symptoms and silent family history can hide a life-threatening condition
- Pay attention to presence of dehydration, hyponatremia and hyperkalemia in a vomiting patient without other signs
- Isolated mineralocorticoid deficiency is a rare first manifestation of AHC
- Hyponatremia is always present at the onset, K+ levels can be high or normal
- A tightened endocrinological follow-up allows to discover a glucocorticoid deficiency with subsequent starting of supplementation therapy with hydrocortisone before any adrenal crisis

TAKE HOME MESSAGES

References