A 3-year-old boy with growth hormone deficiency and clinical features of Ritscher-Schinzel syndrome

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Background

Ritscher-Schinzel (cranio-cerebello-cardiac, 3C, OMIM 220210) syndrome is a very rare recently delineated disorder with:
- Dandy-Walker malformation, cerebellar vermis hypoplasia, enlarged cisterna
- Congenital heart defects other than isolated PAD
- Dysmorphic craniofacial features with cleft palate, ocular coloboma or 4 of the following: prominent occiput or forehead, hypertelorism, micrognathia, down-slanting palpebral fissures, depressed nasal bridge, low-set ears.

Patient presentation

- 3 y 3 m old Caucasian boy with:
  - Short stature
  - Underweight
  - Developmental delay
  - Mild facial dysmorphism
  - Visual problems
  - Episodes of rectal bleeding due to constipation and anal fissures
  - No clinical hypoglycaemia, but registered BGLs < 3 mmol/l

Medical history

- From a 3rd complicated pregnancy via C-section at 37 w. g.
- BW 1750 g (-2.98 SDS), BL 38 cm (-3.89 SDS), HC 32 cm (-1.50 SDS)
- After delivery:
  - Birth asphyxia, RDS
  - PDA and ASD II
  - Pulmonary hypertension, umbilical hernia
  - Asymmetric dilatation of the lateral ventricles with a few periventricular cysts
  - Ventilated for 10 days, anti-failure treatment, no surgical cardiac intervention.
  - At 3 m - bilateral ocular coloboma and strabismus
  - Frequent respiratory and gastrointestinal infections
  - Motor and speech skills delay, estimated IQ 35

Dandy-Walker variant with vermal hypoplasia and moderate non-obstructive communicating hydrocephalus

Auxology

- Height 88.3 cm (-2.84 SDS)
- Weight 9.9 kg (4.41 SDS)
- Weight/height (3.82 SDS)
- BMI 12.86 kg/m² (-3.67 SDS)
- HC 47.9 cm (-1.52 SDS)
- SH/height 0.54 (-0.75 SDS)

- Father’s height 172 cm (-0.87 SDS)
- Mother’s height 166 cm (+0.23 SDS)
- Target height 175.5 cm (-0.36 SDS)

Physical examination

- Unsteady gait
- Craniofacial dysmorphic features with ocular coloboma
- Systolic murmur
- Normal male genitalia
- Reduced fat mass and muscle waste
d- Clinodactyly
- Flat feet with overpronation and cutaneous syndactyly (2nd – 3rd toes)

Laboratory/Imagining investigations

- Normal male karyotype 46,XY

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Result</th>
<th>RR</th>
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<tbody>
<tr>
<td>TSH uIU/mL</td>
<td>5.03</td>
<td>0.4-4.0</td>
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<tr>
<td>FT4 pmol/l</td>
<td>11.4</td>
<td>10.3-24.0</td>
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<tr>
<td>Cortisol nmol/l</td>
<td>376.26</td>
<td>118.0-660.0</td>
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<tr>
<td>IGF-1 ng/ml</td>
<td>50.8</td>
<td>49-289</td>
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- Fasting hypoglycaemia and dyslipidemia
- GHD - two GH stimulation tests with peak GH < 5 ng/ml.
- ECG - mild LVH
- Echo-CG - small restrictive ASD II (3 mm) with mild endocardial hypertrophy and AV regurgitation 0-1 gr.
- Slightly delayed BA (2y 9 m) with mild hypoplasia of 5th distal phalanges
- Normal structure of the spine

Treatment and genetic testing

- rhGH treatment initiated – 0.035 mg/kg/d - no AEs
- mutation analysis of KIAA1996 gene1 (8q24.13; coding for strumpellin) – to reinforce the diagnosis

Ritscher-Schinzel syndrome

- A rare condition with < 50 cases described in the literature.
- Postnatal short stature, noted in most of the patients, could be a result of isolated growth hormone deficiency.


No conflict of interest

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References:
