Difficulties in hypothyroidism and diabetes treatment in patient with GATA6 gene mutation –case report
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Introduction

Patients with GATA6 gene mutations have broad spectrum of clinical presentation, but most of them have pancreatic agenesis or hypotrophy, exocrine pancreatic insufficiency, insulin–treated neonatal diabetes and cardiac malformations. Some of them have significant neurocognitive deficits, hypopituitarism, hypothyroidism, gut abnormalities, biliary atresia, gallbladder agenesis. There are about over 50 cases described worldwide.

Patient’s characteristic

The 5.5 year old female patient with mutation R493X in GATA6 gene is followed up in our Pediatric Diabetology Outpatient Clinic since she was diagnosed with diabetes in second week of life

Clinical phenotype

- Pancreatic hypotrophy,
- insulin dependent diabetes since second week of life,
- exocrine pancreatic insufficiency required enzyme supplementation, meconium ileus, constipations
- tetralogy of Fallot requiring surgery in second year of life, corteion DORV and PS; PI (+++)
- severe hypothyroidism, since she was born
- psychomotor delay
- Left hemiparesis

Anthropometry and development

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>0.5</th>
<th>1</th>
<th>2,16</th>
<th>2,9</th>
<th>4</th>
<th>5,5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length/Height (cm)</td>
<td>50 +0.5SD</td>
<td>62 z–score –3.38</td>
<td>72 z–score –2.58</td>
<td>89 z–score 0.07</td>
<td>96 z–score 0.46</td>
<td>99 z–score –1,48</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>1.5 &lt;–3SD</td>
<td>5,5 z–score –3.5</td>
<td>8,7 z–score –1.77</td>
<td>13,5 z–score –0.17</td>
<td>15,6 z–score 0.64</td>
<td>13,8 z–score –1.6</td>
</tr>
<tr>
<td>Psychomotor development</td>
<td>In range</td>
<td>Left hemiparesis</td>
<td>Left hemiparesis psychomotor delay</td>
<td>Sits without support, left hemiparesis</td>
<td>Sits without support, left hemiparesis</td>
<td>Left hemiparesis walks without support</td>
</tr>
</tbody>
</table>

Diabetes and thyroid treatment

<table>
<thead>
<tr>
<th>Age</th>
<th>0.5</th>
<th>1</th>
<th>2,16</th>
<th>2,9</th>
<th>4</th>
<th>5,5</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDI j/kg</td>
<td>0,75; infusion pump iv</td>
<td>1 CSII</td>
<td>0.7 CSII</td>
<td>0.6 CSII</td>
<td>0.5 CSII</td>
<td>0.44 MDI</td>
</tr>
<tr>
<td>Sample daily glucose profile mmol/l</td>
<td>3,1–17,3</td>
<td>3,1–13,9</td>
<td>11,1–22,2</td>
<td>2,8–19,4</td>
<td>2,7–25</td>
<td>2,7–17,8</td>
</tr>
<tr>
<td>Hba1c %</td>
<td>–</td>
<td>7</td>
<td>11,1</td>
<td>9,3</td>
<td>10</td>
<td>8,7</td>
</tr>
<tr>
<td>L–tyroxine ug/kg</td>
<td>8</td>
<td>7,3</td>
<td>5</td>
<td>3,2</td>
<td>3,2; 2 weeks during hospitalization 4,8</td>
<td>3,4</td>
</tr>
<tr>
<td>TSH uU/ml</td>
<td>4</td>
<td>7,3</td>
<td>0,012</td>
<td>429,4</td>
<td>&gt;1000 3 weeks after hospitalization 1,29</td>
<td>30,86</td>
</tr>
<tr>
<td>FT4 pmol/l</td>
<td>14,2</td>
<td>13,08</td>
<td>7,48</td>
<td>&lt;5,15</td>
<td>&lt;5,15; 3 weeks after hospitalization 22,1</td>
<td>12,75</td>
</tr>
</tbody>
</table>

Other laboratory tests

- antibodies p/TGA negative
- APTT 44 elevated ; INR 1,05 and PT 93– in range
- Serum osmolality 287 mOsm/kg H2O in range
- IGF-1 15,47 ng/ml below limit
- ACTH 34,1 pg/ml in range
- Prolaktyna 1821,76 mU/l (with TSH 1800) –elevated cortisol 371 nmol/l –in range
- C-peptyd 0,1 ng/ml –below limit
- 25OHD 18,8 ng/ml below limit

Diagnostic Imaging

- Abdominal ultrasound examination
  - Hepatomegaly; 117mm;
  - Pancreas was revealed only fragmentarily
  - Gas retention in the intestines; retention of fecal masses in rectum
- Thyroid ultrasound examination
  - Thyroid was not revealed in typical places
- Lung scintigraphy
  - Left pulmonary field – no perfusion
  - Right pulmonary field – weaker perfusion in upper lung lobe
- MRI of hypophysis
  - Mother didn’t agree to the examination

Conclusions

Difficulties in treatment in the patient could result from
- clinical presentation of GATA6 mutation
- problems with cooperation with patient's parents.

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