THE CASE OF CONGENITAL HYPOPITUITARISM DUE TO MUTATION POU1F1 IN 3 AZERBAIJANI NEWBORN BOYS.

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Background:

Growth hormone deficiency in conjunction with the function loss of other anterior pituitary hormones is called combined pituitary hormone deficiency (CPHD).[1] Up to 30% of congenital CPHD cases are associated with mutations of genetic (transcription) factors [2].

POU1F1 mutations are extremely rare among the Indo-European ethnic type (1% of all cases of congenital hypopituitarism) and more common among the Turkic peoples (7.3%, according to Turkish researchers).[3]

Due to the migration and the influx of Azerbaijanis in particular, we can observe such cases more often in St. Petersburg in recent years.

Methods:

3 Azerbaijani boys (one of them born consanguineous marriage) were examined using standard clinical and laboratory methods.

The levels of blood glucose, TSH, free T4, GH, IGF-1, ACTH, cortisol, prolactin and liver function tests were evaluated.

Prop1, POU1F1, HESX1, LHX3, LHX4, OTX2, GL12, SOX3, ARNT2, GHI, GHRH, GHRR, GHSR, IGSF1, PAX6, SHH gene mutations were investigated by a new generation sequencing (NGS) method.

Table 1. The levels of blood hormones.

<table>
<thead>
<tr>
<th>Patient №</th>
<th>Age</th>
<th>Insulin IU/L (2,3-26)</th>
<th>TSH mIU/mL (0,62-8,0)</th>
<th>FT4 pmol/l (10-26)</th>
<th>Cortisol nmol/l (138-635)</th>
<th>GH ng/ml (1,3-9,1)</th>
<th>IGF-1 ng/ml (28 – 156)</th>
<th>PRL mIU/ml (130-627)</th>
</tr>
</thead>
<tbody>
<tr>
<td>№1</td>
<td>2 day of life</td>
<td>0,3</td>
<td>0,012</td>
<td>6,81</td>
<td>533,7</td>
<td>0,002</td>
<td>6,775</td>
<td>4,73</td>
</tr>
<tr>
<td>№2</td>
<td>1,5 month</td>
<td>0,2</td>
<td>0,008</td>
<td>2,27</td>
<td>355,3</td>
<td>0,005</td>
<td>21,32</td>
<td>5,9</td>
</tr>
<tr>
<td>№3</td>
<td>17 day of life</td>
<td>0,2</td>
<td>&lt;0,005</td>
<td>1,88</td>
<td>999,0</td>
<td>&lt;0,05</td>
<td>&lt;15</td>
<td>9,15</td>
</tr>
</tbody>
</table>

Table 2. The levels of blood glucose, biochemical liver function parameters.

<table>
<thead>
<tr>
<th>Patient №</th>
<th>Glucose mmol/l (3,9-6,1)</th>
<th>BiD µmol/L (&lt;20,5)</th>
<th>BiD µmol/L (&lt;10% BiT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0,6</td>
<td>37</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>0,93 - 1,82</td>
<td>358,5</td>
<td>24,9</td>
</tr>
<tr>
<td>3</td>
<td>2,5</td>
<td>355</td>
<td>18</td>
</tr>
</tbody>
</table>

Conclusion

Infant jaundice and/or persistent hypoglycemia require CPHD exclusion, moreover male gender and Turkic ethnic type increase the risk of the POU1F1 mutation.

Thyrotrroph dysfunction degree determines the severity of clinical and laboratory manifestations of the hypothyroidism syndrome and can be associated with the type of genetic defect.

References:

1) Diagnosis and treatment of endocrine diseases in children and adolescents: manual/under the edit of Prof. Shaibalov N. P. – 3 ed, 2017
3) Bas F., Uygurer ZO., Darendeli E. and others. Molecular analysis of PROP1, POU1F1, LHX3, and HESX1 in Turkish patients with combined pituitary hormone deficiency: a multicenter study// Endocrine, 2015 Jun;49(2):479-91. doi: 10.1007/s12020-014-0498-1. Epub 2014 Dec 11.