PHENOTYPE AND GENOTYPE OF FOUR PATIENTS WITH THYROID HORMONE RESISTANCE SYNDROME DUE TO MUTATIONS IN THE THRB GENE

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BACKGROUND

Resistance to thyroid hormone (RTH) is a dominantly inherited rare disorder (1:400000) mainly due to mutations in the THRB gene that lead to a decreased end-organ responsiveness to thyroid hormone. Clinical and molecular characteristics of four patients with RTH are described.

PATIENTS

Four patients; two boys (8.3 and 9.2 years) and 2 adults (35 year old male and 27 year old female).

METHODS

Direct sequencing analysis of the THRB gene.

RESULTS

TABLE: Four patients from three non-related families.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Clinical signs at presentation</th>
<th>FT4 pmol/L</th>
<th>FT3 pmol/L</th>
<th>TSH mU/L</th>
<th>TSH receptor abs</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.2</td>
<td>Male</td>
<td>Goiter, ADHD, obesity</td>
<td>54.9</td>
<td>15.2</td>
<td>2.55</td>
<td>Negative</td>
<td>p.Pro453Thr</td>
</tr>
<tr>
<td>2</td>
<td>8.3</td>
<td>Male</td>
<td>Goiter, R.tachycardia</td>
<td>26.8</td>
<td>10.25</td>
<td>1.89</td>
<td>Negative</td>
<td>p.Arg438Cys</td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>Female</td>
<td>Goiter, R.tachycardia, tx PTU</td>
<td>24.2</td>
<td>7.42</td>
<td>3.49</td>
<td>Negative</td>
<td>p.Arg438Cys</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Male</td>
<td>Goiter, AF, tx MT</td>
<td>30.2</td>
<td>11.19</td>
<td>2.89</td>
<td>Negative</td>
<td>p.His435Leu</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- Common mutations in the THRB gene are characterized by various phenotypes; clinically asymptomatic, thyroid hormone deprivation suggestive symptoms or thyroid hormone excess symptoms.
- RTH can be suspected in both children and adults with elevated thyroid hormones and not suppressed TSH.
- Prompt molecular diagnosis and genetic counseling could prevent unnecessary tests and inappropriate treatments.

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