# Thyroid dyshormonogenesis: a case report of two siblings with a heterozygous variant in the TPO gene.

Vadina T.¹, Konuhova M², Eremyan A.¹, Shreder E.¹, Nagaya E.¹, Zaharova S.¹, Degtyarev M.¹, Bezlepkin O.¹

1. Endocrinology Research Centre, Moscow, Russian Federation. 2. Moscow neonatal screening Centre, Moscow, Russian Federation.

## INTRODUCTION

Congenital hypothyroidism (CH) is an inborn disease with an incidence of 1 case per 3,000 newborns of which 15-20% cases are associated with thyroid dyshormonogenesis. The TPO gene encodes thyroid peroxidase - an enzyme which plays a central role in thyroid gland function. Disease associated with this gene is usually transmitted in an autosomal recessive mode. Hypothyroidism-associated TPO variants are usually biallelic, limited evidence for cases in patients with heterozygous variants exists.

## AIM

to study clinical and genetic characteristics of CH in this family.

## METHOD

- Thyroid imaging was performed using ultrasound (US) and scintigraphy (Te99m).
- Serum thyroglobulin (TG) was detected by ELECSYS immunoassay method, TSH and free T4 were measured by ELECSYS immunoassay method, and TSH and free T4 were measured by ARCHITECT test system.
- Genetic data was obtained with targeted gene panel including 23 genes associated with CH using Illumina MiSeq System in patient 1 and the regions of interest were analyzed with Sanger sequencing.

## RESULTS

### Patient 1 (proband): girl 13 yrs. with CH.

- Neonatal TSH at 200 mU/L.
- US scan and scintigraphy showed in situ thyroid gland with extremely high blood flow and increased radiotracer uptake up to 3.3% (0.8-1.7), pict. 1.
- TG↑ to 445 ng/ml.

*All of these studies were conducted after discontinuation of l-thyroxine therapy for two weeks at the age of 13.*

Patient 2: 10 yrs. The sister with normal thyroid.

Patient 3: 8 yrs. The brother with CH and high level of neonatal TSH up to 180 mU/L. Clinical analysis results are similar to that of the proband in 8 yrs. age - increased ultrasound blood flow, radiotracer uptake to 3.9% and TG up to 273.4 ng/ml.

Patient 4: 3 yrs. The brother with normal thyroid.

### NGS (Panel CH) vs Region of interest (Sanger)

<table>
<thead>
<tr>
<th>NGS (Panel CH)</th>
<th>Region of interest (Sanger)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPO gene c.1188 1193delCGCCAGins10p. (Ala397Profs*76)</td>
<td>TPO gene c.1188 1193delCGCCAGins10p. (Ala397Profs*76)</td>
</tr>
<tr>
<td>TPO gene c.1188 1193delCGCCAGins10p. (Ala397Profs*76)</td>
<td>TPO gene c.1188 1193delCGCCAGins10p. (Ala397Profs*76)</td>
</tr>
<tr>
<td>TPO gene c.1188 1193delCGCCAGins10p. (Ala397Profs*76)</td>
<td>No</td>
</tr>
</tbody>
</table>

### CONTACT INFORMATION

Vadina Tatiana klemenkipediatr@mail.ru
Shreder Ekaterina evshreder@bk.ru