Bannayan-Riley-Ruvalcaba Syndrome with PTEN mutation in a patient affected by Congenital Hypothyroidism due to TPO gene alteration

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Born at 31+4 GW, because of PROM. BW 1640 gr (0,4 SDS) – BL 44 cm (1,5 SDS) – CC 29 cm (0,6 SDS) – APGAR 5.9

Neonatal problems: respiratory distress, jaundice, patent ductus arteriosus

Neonatal screening: bTSH 152 ↔ CONGENITAL HYPOTHYROIDISM

<table>
<thead>
<tr>
<th>TSH (mcu/mL)</th>
<th>FT4 (ng/dL)</th>
<th>Antibodies</th>
<th>Therapy</th>
<th>Ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td>1016</td>
<td>&lt;0,4</td>
<td>AbTG, AbTPO, TRAb neg</td>
<td>L-T4 13 mcg/kg/die</td>
<td>Hyperplastic, not homogeneous echotexture</td>
</tr>
</tbody>
</table>

7 months – 6 years 6 months, The follow-up:
- Neuromotor delay: first steps 18 months, first worlds 24 months
- Regular length growth on the 25th percentile
- Regular weight growth on the 25th percentile
- Persistent macrocrania (CC >97th percentile)
- Adequate thyroid function with L-T4 therapy (2.5-3.5 mcg/kg/die)

6 years 6 months, The follow-up:
- Macrocrania (CC >97th percentile)
- Triangular face, frontal bossing, hyperelorism, horizontal eyelids
- Lipoma in left dorso-lombor region + three lipomas in the dorsal and thoracic region surgically removed
- THYREOMEGALY

NGS: Homozigous variation TPO gene (GGCC395, exon 8)

Familial anamnesis:
- GGCC395 TPO, in heterozygous
- Normal thyroid function
- GGCC395 TPO, in heterozygous
- Hypothyroidism, left lobe hypoplasia
- Celiac disease

7 years, Neurological follow-up
- WPPSI-III: QI 70 (85-115): verbal 80, performance 65, processing velocity 78
- Brain MRI and CT: alteration of the orbital roof, hemangioma?

PTEN: heterozygous c.635-1G>C mutation
BANNAYAN-RILEY-RUVALCABA SYNDROME, BRRs (PTEN Hamartoma Tumor Syndrome)

THYROIDECTOMY:
21 adenomatous nodules, 8/8 loss of PTEN expression

• These clinical features (face abnormalities, macrocephaly, subcutaneous lipomas, hemangiomas and multinodular goiter) represent some of the several phenotypic expressions of BRRs.
• The TPO and PTEN mutations may have had a synergic effect on the thyroid involvement in our patient.
• Mutations in the tumor suppressor gene PTEN cause an increased oncologic risk thus prophylactic total thyroidectomy should be considered in selected patients.