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

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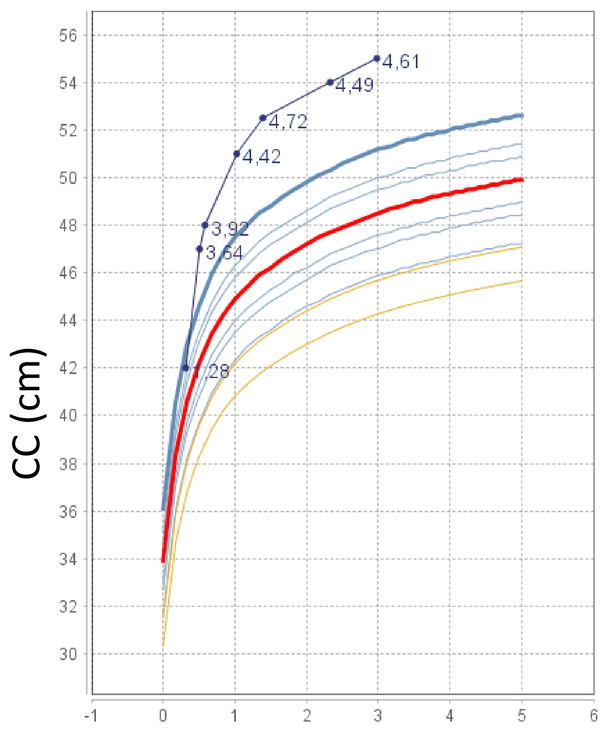
There are no conflicts of interest

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				
TSH (mcu/mL)	***FT4 (ng/dL)***	***Antibodies***	***Therapy***	***Ultrasound***
1016	<0,4	AbTG, AbTPO, TRAb neg	→ L-T4 13 mcg/kg/die	Hyperplastic, not omogeneous echotexture

Head circumference >97° ple



***Brain MRI (7 months)*:** minimal amplification of the subarachnoid space and light reduction of the mielinization signal.

***7 months – 6 years 6 months*, The follow-up:**

- Neuromotor dalay: first steps 18 months, first worlds 24 months
- Regular lenght growth on the 25° ple
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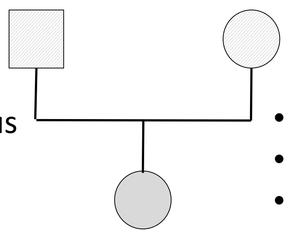
- Persistent macrocrania (CC > 97° ple)
- Adequate thyroid function with L-T4 therapy (2,5-3,5 mcg/kg/die)

***6 years 6 months,* The follow-up:**

- Macrocrania (CC >97° ple)
- Triangular face, frontal bossing, hyperthelorism, horizontal eyelids
- Lipoma in left dorso-lombar 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 heterozigous
- Normal thyroid function

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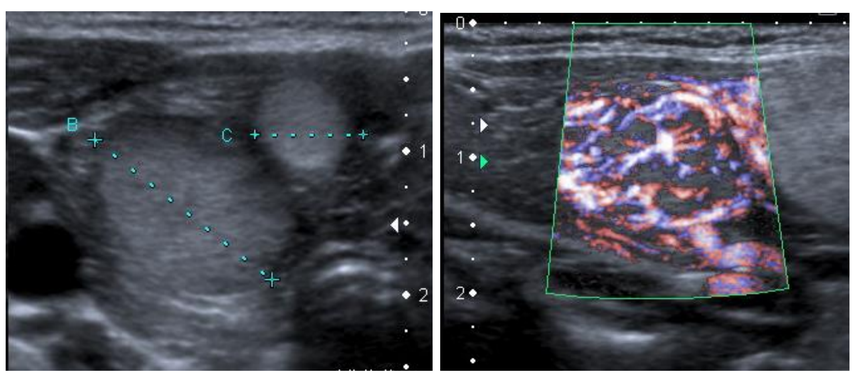
- Hypothyroidism, left lobe hypoplasia
- Caeliac disease

6 years 6 months, Thyroid ultrasound

- Right lobe: at least 5 nodules (7-16 mm)
- Left lobe: at least 4 nodules (6-15 mm)

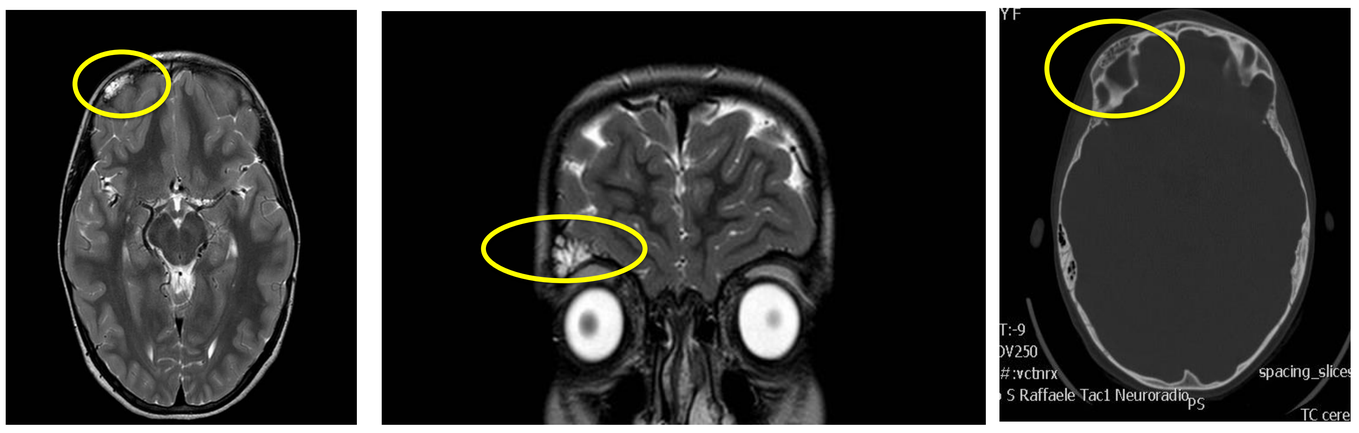
7 years, Thyroid ultrasound

- Right lobe: at least 6-7 nodules (4-19 mm)
- Left lobe: 6 nodules (6-17 mm)



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 horbital roof, hemangioma?



PTEN: heterozigous 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.