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The authors have nothing to disclose

A 10- year-old girl with thyroid hormone resistance (βTHR)- case report

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Objectives

Thyroid hormone resistance (THR) is a rare syndrome that is characterized by a reduced response to thyroid hormones at the tissue level. The disorder is caused by a genetic mutation in the thyroid hormone receptor. The most common are mutations in the heterozygous gene encoding the thyroid hormone receptor (THRβ) isoform. Laboratory tests usually show elevated levels of thyroid hormones at which TSH levels are not inhibited - within or above normal levels. The clinical symptoms of the syndrome are the resultant of euthyroid state in tissues where the mutated receptor predominates, and hyperthyroidism where excess T3 affects on normal receptor forms.

Case report with laboratory tests

We present a case of a 10-year-old girl with signs of hyperthyroidism and abnormal thyroid function tests who was hospitalized in Department of Pediatrics, Endocrinology, Diabetology with a Cardiology Division, Medical University of Bialystok, Poland. Her physical examination had revealed café au lait spot on abdomen skin, goiter, vascular murmur louder above right lobe of thyroid, tachycardia and heart murmur. In laboratory tests we found elevated serum levels of thyroid hormones: **fT3- 14,55 pg/ml** (norm: 2,7- 5,2) and **fT4- 4,95 ng/dl** (norm: 1,1-1,7 ng/dl) coexisted with normal concentration of **TSH -3,64 uIU/l**. The thyroid autoantibodies (anti-TPO, anti-Tg, TRAb) were negative. In TRH stimulating test TSH concentration increased after TRH administration.

	0	20min	30min	60min
TSH	3,66	34,61	33,51	23,16
fT4	5,81	6,0	5,83	7,1
fT3	12,19	11,97	12,85	18,59
PRL	3,8	23,9	49.0	52

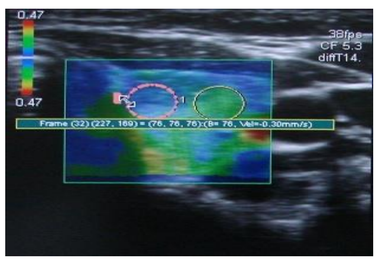
Sonography revealed normoechogenic, asymetric (right lobe bigger than left) thyroid gland with hypoechogenic 5 x 4 mm area in left lobe, vascular flow was slightly increased in down parts of both lobes. Finale needle aspiration biopsy was performed. Result was benign in Bethesda II.
Magnetic resonance imaging (MRI) showed normal pituitary gland and excluded pituitary adenoma.

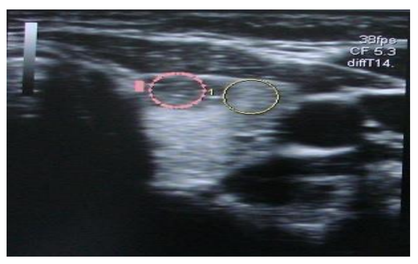
The diagnosis has been confirmed by next- generation sequencing, which exposed a pathogenic variant c.1034G>A in one copy of THR gene. The mutation is known and associated with THR.

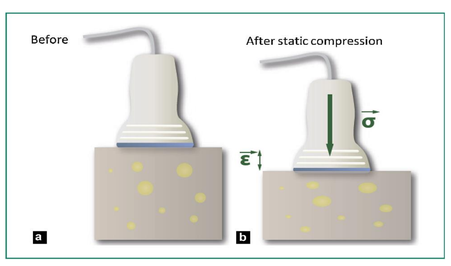
For therapy we used Magnesium, Vitamin D, Vitamin B complex and Propranolole at a dose 10 mg three times a day, then was changed into 20 mg three times a day. She is currently stable on this medication.

References:
1.Refetoff S., Basset D., Beck-Peccoz P. et al.: Classification and Proposed Nomenclature for Inherited Defects of Thyroid Hormone Action, Cell Transport, and Metabolism. Thyroid 2014:24(3) 407-409
2.Dumitrescu A. M. Refetoff S. The syndromes od reduced sensivity to thyroid hormones. Biochim Biophys Acta 2013:2(2) 76.82
3. Brent G.A: Mechanisms of thyroid hormone action. J. Clin. Invest. 2012; 122:9: 3035-3043

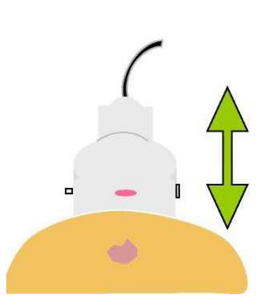
radiology and genetic tests

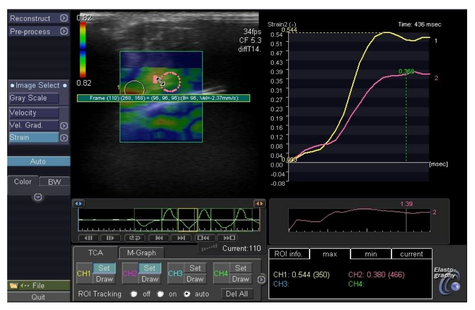






- **Elastograms showing the deformation of tissue in real time- slight deformation of tissue may indicate malignant change**
Blue - hard tissue-low deformation
Green - normal tissue - the average deformation
Red - soft tissue - large deformation

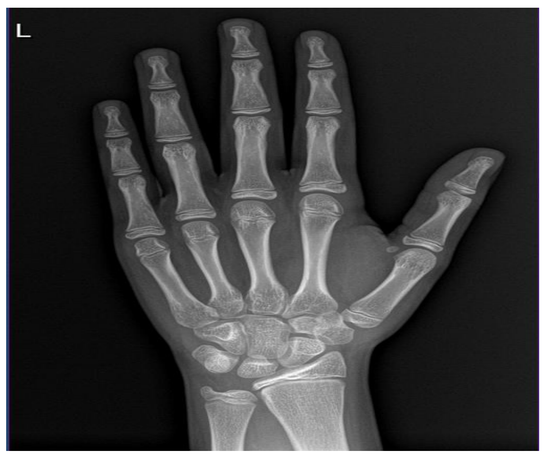




CH1-yellow curve
CH2-pink curve

Elastography showing soft thyroid nodule; strain ratio 1.39

CH1-covers an area of normal tissue ROI 1 for normal tissue
CH2-covers an area of ROI 2 for pathological tissue
TLR-ratio between ROI 1 and ROI 2, if ratio is >3 suspicion of malignancy



bone age- 11 years old

Gene	Variant	Location of variant	Amino acid change	Variability of the variant	Reference	Pathogenicity
THRB	NM 001128176 c.1034G>A	Exon 10/11	P Gly345Asp	heterozygote	rs28999970	pathogenic variant

genetic results

Conclusions

Although thyroid hormone resistance is rare, this disorder should be considered in patients with clinical manifestation and thyroid laboratory tests suggested its presence. Mutations of *TRβ* gene can be seen in various clinical presentations, from isolated bichemical thyroid function abnormalities to thyrotoxicosis or hypothyroidism symptoms. The patients need individualized management.