Hypercholesterolemia in two siblings with THRB mutation

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BACKGROUND

- Resistance to thyroid hormones (RTH) is a rare thyroid disease, characterized by a **reduced sensitivity of target tissues to thyroid hormones**.
- Pathognomonically, thyroid hormones are moderately elevated, whereas TSH levels are inappropriately normal or even mildly elevated.
- Over 100 thyroid hormone receptor beta (THRB) mutations have been reported, which are found in around 85 % of RTH cases.
- Hypercholesterolemia was not previously reported in RTH patients.

OBJECTIVES AND METHODS

- To assess the lipid levels in a Slovenian family (mother, two daughters and a son) with a previously reported THRB **p.Arg243Trp (c.727C>T)** mutation

RESULTS

- Index case was referred to our outpatient clinic due to suspicion of thyroid malfunction at the age of 13.5 years.
- Genetic analysis revealed the THRB mutation, which was later confirmed in her mother, younger sister and brother.
- Familial hypercholesterolemia was excluded.

	Slovenian family with confirmed THRB mutation		
	Index patient	**Younger sister**	**Younger brother**
Clinical signs and symptoms	malaise, subfebrile state, weight loss, marginal tachycardia	asymptomatic, marginal tachycardia	asymptomatic, marginal tachycardia
Peak thyroid hormone levels	TSH 4.65 mE/L (N) fT4 39.9 pmol/L (↑) fT3 10.11 pmol/L (↑)	TSH 10.46 mE/L (↑) fT4 35.81 pmol/L (↑) fT3 14.16 pmol/L (↑)	TSH 4.94 mE/L (↑) fT4 32.68 pmol/L (↑) fT3 12.28 pmol/L (↑)
Thyroid antibodies	absent	absent	absent
Peak cholesterol levels	TC 5.5 mmol/L (↑) LDL 3.1. mmol/L (N) HDL 1.7 mmol/L (N) Tg 1.5 mmol/L (N)	TC 6.6 mmol/L (↑) LDL 4.2 mmol/L (↑) HDL 1.5 mmol/L (N) Tg 1.2 mmol/L (N)	TC 4.5 mmol/L (N) LDL 2.6 mmol/L (N) HDL 1.3 mmol/L (N) Tg 1.4 mmol/L (N)
Thyroid ultrasound examination	enlarged, thickened thyroid gland, isoechogenic, fine granular structure, without nodules, with normal perfusion	normal ultrasound report	slightly enlarged thyroid gland, without nodules
Treatment needed	no	no	no

Table 1: Showing the key clinical features of a Slovenian family with confirmed thyroid hormone resistance β (c727 c> t, p.Arg243Trp) mutation.

Legend: THRB, thyroid hormone resistance β; TSH, thyrotropin; fT_4, free thyroxin; fT_3, free triiodothyronin; TC, total cholesterol levels; LDL, low-density proteins; HDL, high-density proteins; Tg, triglycerides; N, normal.

CONCLUSIONS

- Mild hypercholesterolemia was present in 2 out of 3 family members with confirmed THRB mutation.
- Since the severity of hormonal resistance varies among different tissues, hypercholesterolemia in patients with THRB mutation might indicate the **relatively hypothyroid state in the liver**.

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