Normal Thyroid-Stimulating Hormone and Elevated Free Thyroxine in a Patient Presenting with Self-Reported Heart Palpitations

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CASE DESCRIPTION

A 21-year-old male with a history of acute lymphoblastic leukemia in remission presented to endocrinology for consultation regarding abnormal thyroid function tests and self-reported heart palpitations that began 7 months prior. Although the patient reported mild weight loss, he denied other symptoms typically associated with hyperthyroidism including diarrhea, anxiety, and tremor. His family history was notable for Graves disease in his father and unspecified thyroid dysfunction in his maternal aunt.

Physical examination demonstrated a normal-sized thyroid gland, without palpable nodules. At the time of examination, the patient had a normal heart rhythm with no abnormal sounds noted on auscultation. Review of the patient's most recent thyroid function studies demonstrated a thyroid-stimulating hormone (TSH) concentration of 1.360 uIU/mL [0.450–4.500 uIU/mL] and free thyroxine (FT4) concentration of 2.41 ng/dL (31.0 pmol/L) [0.82–1.77 ng/dL (10.5–22.8 pmol/L)] (Table 1). Results from a comprehensive metabolic panel (common electrolytes and tests of liver and kidney function) did not show any significant biochemical abnormalities. Additional laboratory studies showed a normal concentration of total triiodothyronine (TT3) and no presence of thyroid-stimulating immunoglobulins. To rule out the possibility that the elevation in FT4 was due to a laboratory interference, equilibrium dialysis-mass spectrometry was performed which confirmed the presence of an elevated FT4 (3.7 ng/dL (47.6 pmol/L) [0.8–1.7 ng/dL (10.3–21.9 pmol/L)]). Additional studies showed a slightly elevated free triiodothyronine (FT3) of 4.9 pg/mL (7.6 pmol/L) [2.0–4.4 pg/mL (3.1–6.8 pmol/L)], which persisted on subsequent evaluations.

QUESTIONS TO CONSIDER	
1.	What are the pathophysiological causes of a normal TSH in the presence of elevated FT4 and FT3 concentrations?
2.	What are the analytical causes of a normal TSH in the presence of elevated FT4 and FT3 concentrations?
3.	What follow-up testing should be performed to investigate the case?

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Table 1. Pertinent biochemical results.

Analyte	Day 1	Day 82	Day 89	Day 124	Day 139
TSH	1.360 uIU/mL [0.450–4.500]	0.955 uIU/mL [0.450–4.500]	-	1.160 uIU/mL [0.450–4.500]	0.75 uIU/mL [0.45–5.33]
TT4	-	-	-	16.4 ug/dL [4.5–12.0]	17.34 ug/dL [4.50–11.70]
FT4	2.41 ng/dL [0.82–1.77]	3.41 ng/dL [0.82–1.77]	-	-	-
FT4-Dial/MS	-	-	3.7 ng/dL [0.8–1.7]	2.8 ng/dL [0.8–1.7]	4.6 ng/dL [1.1–2.4]
TT3	-	146 ng/dL [71–180]	-	199 ng/dL [71–180]	1.57 ng/mL [0.87–1.78]
FT3	-	-	4.9 pg/mL [2.0–4.4]	5.6 pg/mL [2.0–4.4]	4.08 pg/mL [2.50–3.90]
FTI	-	-	-	5.4 [1.2–4.9]	20.46 ug/mL [4.40–11.40]
TSIG	-	< 0.10 IU/L [0.00–0.55]	-	-	-
TRAB	-	-	<1.10 [0.00–1.75]	-	-
SHBG	-	-	-	-	51 nmol/L [17–56]
Prolactin	-	-	-	-	10.10 ng/mL [4.04–15.20]
Alpha subunit	-	-	0.24 ng/mL [<0.55]	-	-
HAMA	-	-	<56 ng/mL [0–74]	-	-

To convert to SI units: TT4: [ug/dL] × 12.87 = [pmol/L]; FT4: [ng/dL] × 12.87 = [pmol/L]; TT3: [ng/dL] × 0.0154 = [nmol/L]; FT3: [pg/mL] × 1.54 = [pmol/L]; prolactin: [ng/mL] × 1 = [ug/L]; alpha subunit = [ng/mL] × 1.0 = [ug/L]; HAMA = [ng/mL] × 1.0 = [ug/L].
Abbreviations: TT4, total thyroxine; MS, mass spectrometry; TT3, total triiodothyronine; FTI, free thyroxine index; TSIG, thyroid-stimulating immunoglobin; TRAB, thyrotropin receptor antibodies; SHBG, sex hormone-binding globulin.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the April 2025 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/71/4 and follow the link to the Clinical Case Study and Commentaries.

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