Low Free T4 in a 13-Year-Old Girl with Short Stature and Blurry Vision

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CASE DESCRIPTION

A 13-year-old female with no significant past medical history presented to a pediatric endocrinology clinic for evaluation of short stature. The patient was referred by her primary care provider who was concerned that, although growing well initially, she had dropped across growth percentiles in the last few years. She was accompanied by her mother and father, who were 4'11" and 5' 5", respectively. According to her parents, the patient was born full term, following an uncomplicated pregnancy and delivery, with a normal birth weight and normal genitalia. The patient denied prior head trauma; however, she gave a history of fatigue as well as headaches after school. Additionally, the patient reported visual problems and recently had been told she needed glasses, although she was still waiting to be seen by an ophthalmologist.

Given the lack of dysmorphic features and the short statures of the patient's parents, constitutional delay of growth and puberty or familial short stature were favored as the differential diagnosis of the patient's short stature. However, due to the patient's decreased height velocity, the clinician decided to order a spectrum of laboratory tests to rule out endocrine deficiency as a potential etiology. This panel included: free thyroxine (T4), thyroid stimulating hormone (TSH), insulinlike growth factor-1 (IGF-1), and IGFBP-3. Insulinlike growth factor binding protein-3 (IGFBP-3) was normal, but IGF-1 was decreased (Table 1). Additionally, free T4 was low and TSH elevated (Table 1). Additional laboratory studies were ordered to further investigate the patient's hypothyroidism. Anti-thyroperoxidase antibodies and anti-thyroglobulin antibodies were both negative.

QUESTIONS TO CONSIDER
• What are the major differential diagnoses to consider in a child presenting with the chief complaint of short stature?
• What are the expected laboratory results that distinguish primary from secondary and tertiary hypothyroidism?
• What are the causes of secondary (central) endocrine deficiencies (e.g., hypothyroidism)?

https://doi.org/10.1093/clinchem/hvad122

Table 1. Pertinent laboratory findings[a].

Laboratory assay	Result	Reference interval
Tissue Transglutaminase Antibody, U/mL	<2	0-3
Free T4, ng/dL	<0.6	0.6-1.1
TSH, micrIU/mL	4.81	0.7-3.35
Anti-thyroperoxidase antibody, U/mL	1	<9
Anti-thyroglobulin antibody, U/mL	<1	<4
IGF-1, ng/mL	99	131-545
IGFBP-3, mg/L	3.52	2.52-6.29
Cortisol 8 AM, mcg/dL	<0.9	3.0-17.1
Cortisol 30 min, mcg/dL (cosyntropin stimulation test, 1 mcgr, i.v.)	5.1	7-10
Cortisol 60 min (mcg/dL) (cosyntropin stimulation test, 1 mcgr, i.v.)	3.7	18-20
FSH, mIU/mL	2.1	Tanner stage 1 (age < 9.2 years): 1.0-4.2 Tanner stage 2 (age 9.2 to 13.7 years): 1.0-10.8 Tanner stage 3 (age 10.0 to 14.4 years): 1.5-12.8 Tanner stage 4 (age 10.7 to 15.6 years): 1.5-11.7 Tanner stage 5 (age 11.8 to 18.6 years): 1.0-9.2
LH, mIU/mL	0.306	Tanner stage 1 (age < 9.2 years): 0.02-0.18 Tanner stage 2 (age 9.2 to 13.7 years): 0.02-4.7 Tanner stage 3 (age 10.0 to 14.4 years): 0.10-12.0 Tanner stage 4-5 (age 10.7 to 18.6 years): 0.4-11.7
Estradiol, pg/mL	< 1.0	Tanner stage 1 (age < 9.2 years): 5.0-20 Tanner stage 2 (age 9.2 to 13.7 years): 10-24 Tanner stage 3 (age 10.0 to 14.4 years): 7.0-60 Tanner stage 4 (age 10.7 to 15.6 years): 21-85 Tanner stage 5 (age 11.8 to 18.6 years): 34-170
Prolactin, ng/mL	30.2	1 to 19 years: 3.2-18.5

[a]Use the following conversion factors to convert to SI units: Free T4 ×12.9 pmol/L; TSH ×1 mIU/L; IGF-1 × 1 mcgr/L; cortisol ×27.6 nmol/L; follicle-stimulating hormone (FSH) ×1 IU/L; luteinizing hormone (LH) ×1 IU/L; estradiol ×3.69 pmol/L; prolactin ×21 mIU/L.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the October 2023 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/69/10 and follow the link to the Clinical Case Study and Commentaries.

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