

Euthyroid Patient with Elevated Serum Free Thyroxine

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CASE DESCRIPTION

A 32-year-old female patient presented complaining of increased flushing, perspiration and heat intolerance of 3 months' duration. Medical history included idiopathic thrombocytopenic purpura of 4 years' duration, which had been treated by splenectomy after failed immunosuppression with prednisone and azathioprine and was currently in remission. On examination, she was found to be clinically euthyroid without a goiter. She had also developed a diffuse erythematous popular rash on the face and back, with bullous lesions on the chest. Immunofluorescent antibody studies performed on a punch biopsy of skin were positive for several autoantibodies, leading to a diagnosis of subacute cutaneous lupus erythematosus. This diagnosis was further characterized by positive titers of nuclear and doublestranded DNA autoantibodies in the serum. Thyroid function testing on an Advia Centaur[®] Immunoassay System (Siemens Medical Solutions Diagnostics) revealed an increased concentration of serum free thyroxine (FT₄)², 90.1 pmol/L (6.97 ng/dL) (reference range 11.5–22.7 pmol/L), a nonsuppressed thyroidstimulating hormone (TSH) concentration of 1.8 mIU/L (1.8 μIU/mL) (reference range 0.35–5.5 mIU/L), and normal free triiodothyronine (FT₃) concentration of 4.2 pmol/L (0.33 ng/dL) (reference range 3.5–6.5 pmol/L). Repeat investigation 1 and 2 months later revealed a progressive increase in FT₄ to 125.3 pmol/L (9.7 ng/dL) and ≥155 pmol/L (≥12.0 ng/dL), respectively. TSH and FT₃ remained within reference intervals, as did total T₄ by RIA, at 155 nmol/L (12 μg/dL) (reference range 58–161 nmol/L). Furthermore, she tested positive for antithyroperoxidase antibodies at 110 IU/L (reference range <37 IU/L) and antithyroglobulin antibodies at 149 IU/L (reference range <98.1). An investigation of her discordant thyroid function tests was initiated.

Questions to Consider

- What are the possible reasons for discrepancies between thyroid function testing and clinical picture?
- What are the appropriate next steps to resolve the discrepancy between clinical picture and laboratory results?
- What would the clinical picture be if the patient had resistance to thyroid hormone? A pituitary adenoma?

A Girl with Goiter and Inappropriate Thyroid-Stimulating Hormone Secretion

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CASE DESCRIPTION

A 15-year-old white girl presented with neck tenderness. On examination, a nodule was palpated in the right thyroid lobe. The neck was supple without abnormal lymphadenopathy. Eye findings related to Graves' orbitopathy were absent. Weight, height, and blood pressure were unremarkable, but the heart rate was high at 104–114 bpm. The patient had a history of attention deficit hyperactivity disorder (ADHD) and was taking atomoxetine and fluoxetine. There was no history of childhood neck irradiation or family history of thyroid cancer. Several maternal relatives have acquired thyroid dysfunction.

Sonography showed a 2-cm nodule in the right thyroid lobe. Fine-needle aspiration showed benign cytology, but the family requested right thyroid lobectomy for persistent neck tenderness. Preoperative laboratory data revealed a total thyroxine (T₄)³ concentration of 170 nmol/L [reference interval (RI) 67–138 nmol/L] (13.2 µg/dL, RI 5.2–10.7), total triiodothyronine (T₃) concentration of 3.2 nmol/L (RI 1.3–2.4 nmol/L) (206 ng/dL, RI 86–153), a thyroid-stimulating hormone (TSH) concentration of 0.5 mIU/L (RI 0.3–5.0 mIU/L), and a thyroid hormone binding ratio (1/T-uptake) of 1.72 (RI 0.77–1.16) (Table 1). Analyses were conducted by chemiluminescent immunoassay on the Roche Elecsys 2010 platform. Free T₃ and free T₄ indices as calculated by the clinicians were 5.5 nmol/L (RI 1.3–2.4 nmol/L) and 292 nmol/L (RI 67–138 nmol/L), respectively, and, in the context of the patient's normal TSH concentration, suggested the possibility of inappropriate TSH secretion due to resistance to thyroid hormone or a TSH-secreting pituitary adenoma. Analyses for serum free T₄ measured by direct dialysis and RIA were conducted at Mayo Medical Laboratories and revealed a normal free T₄ of 16.8 pmol/L (RI 10.3–25.8 pmol/L) (1.3 ng/dL, RI 1–2 ng/dL). Although certain of the patient's features, including her tachycardia (1, 2), were consistent with the syndrome of inappropriate TSH secretion, this syndrome is extremely rare and the recommended standard of care is to repeat thyroid function tests after ≥1 week (2) to exclude the effects of nonthyroidal illness and to assess the possibility of laboratory artifact (3). Accordingly, the patient's scheduled surgery was postponed to accurately assess her thyroid function status.

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Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the July 2008 issue of *Clinical Chemistry* in approximately 3-4 weeks. To view the case and comments online, go to <http://www.clinchem.org/content/vol54/issue7/> and follow the link to the Clinical Case Study and Commentaries.

Educational Centers

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