

Hyperthyroidism

Case 17

HPI: LG is a 35-year-old white woman who presents with a history of anxiety, nervousness, and difficulty sleeping for the past 3 months. She complains of feeling hot and sweaty, even in air-conditioned rooms, and has noticed her heart beating irregularly at times during the day. LG had attributed her anxiety and symptoms to increasing stress at work, but became concerned after friends and family kept commenting on her recent weight loss. She failed to notice it at first, but after stepping on the scale at the gym, LG realized she had lost some 20 lbs over the past 3 months—despite having a voracious appetite. She also complains of having puffy eyes, but thinks it is mostly due to lack of sleep. She would like a prescription for something to help calm her anxiety so she can get some rest and finally get rid of the “bags under her eyes.” LG’s family history is significant for her mother having a history of thyroid disease.

PE: Vitals: Thin, mildly tachypneic female in no acute distress. Skin appears warm and moist. **Head, Eyes, Ears, Nose, and Throat (HEENT):** Prominent eyes with lid lag, stare, and infrequent blinking. Moderate degree of periorbital edema. Patient has difficulty looking up and out but no limitation of downward gaze. **Neck:** Thyroid gland appears diffusely and symmetrically enlarged, soft, and nontender. **Cardiac:** Precordium and carotid pulses hyperdynamic to palpation. No murmurs detected. **Extremities:** Nontender, erythematous nodule on anterior aspect of left lower extremity. Brisk deep tendon reflexes.

Thought Questions

- What is the likely cause of LG’s symptoms and what clues lead you to this conclusion?
- What diagnostic tests would you order to confirm her diagnosis? What would these tests show?
- What is the pathophysiology of this condition?

Basic Science Review and Discussion

LG appears to have many of the classic signs and symptoms of hyperthyroidism. These include heat intolerance, weight loss, tachycardia, arrhythmias, chest pain, palpitations, anxiety, sweating, diarrhea, hyperreflexia, fine hair, and sleep disturbances. Hyperthyroidism can have multiple causes, but the most likely cause in this case is Graves’ disease. The combination of ophthalmopathy (proptosis, extraocular muscle swelling), pretibial myxedema, and diffuse goiter all point to the clinical diagnosis of Graves’ disease as the cause of LG’s hyperthyroidism.

Graves’ Disease Graves’ disease is an **autoimmune hyperthyroidism** caused by **antibodies to the thyroid stimulating hormone (TSH) receptor** in the thyroid gland. It has a female predilection of 5:1 and occurs in about 0.5% of the adult population. Autoantibodies (also known as thyroid-stimulating immunoglobulin) bind to and stimulate the TSH receptor, producing glandular growth and excess secretion of thyroid hormone [preferential tri-iodothyronine (T_3) secretion]. On physical exam, the glandular growth is present as a diffuse

goiter and the preferential secretion of the **active form of thyroid hormone (T_3)** produces moderate to severe thyrotoxicosis. In addition, **infiltrative ophthalmopathy** is present in about 5% of the patients with Graves’ disease. Though LG attributes her puffy eyes to lack of sleep, the swelling and “bags under her eyes” are actually due to antibodies directed against her extraocular eye muscles. These antibodies cause a local immune response and result in inflammation of the muscles and deposition of glycosaminoglycans by orbital fibroblasts. Patients may complain of pain or double vision with reading, burning or tearing of the eyes, and may lose the ability to look up and out. Another rare complication of Graves’ disease is **pretibial myxedema**, which occurs in about 1% of all cases. The nontender erythematous nodule on the anterior aspect of LG’s left leg is an example of pretibial myxedema, which is caused by mucopolysaccharide infiltrate in the skin of the pretibial area.

Laboratory studies can confirm the clinical diagnosis of Graves’ disease. Important thyroid function tests include TSH, free thyroxine (T_4), T_3 , and antithyroid peroxidase antibodies (anti-TPO, also known as antimicrosomal antibodies). TSH from the anterior pituitary is the best thyroid function test, as it will reveal abnormalities well before T_3 or T_4 . In Graves’ disease, TSH levels will be markedly suppressed, while T_4 and T_3 values will be markedly elevated ($T_3/T_4 > 20:1$). Anti-TPO antibody will be positive and serves as a marker for autoimmune thyroid disease. In addition, because the gland is actively taking up iodine for thyroid hormone synthesis, administration of radioactive iodine will show elevated and diffuse uptake, indicating a general increase in thyroid gland activity.

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Case Continued LG is diagnosed with Graves' disease and treated successfully with radioactive iodine. She remains euthyroid and symptom free for the next 5 years, but slowly starts to notice increasing fatigue, muscle cramps, and weight gain. She returns to her primary care physician, hoping he may be able to help her once again.

Thought Questions

- What is the most likely cause of LG's symptoms now? What are the associated symptoms of this condition?
- What would LG's lab results show?

Basic Science Review and Discussion

Radioactive iodine (RAI) is the most commonly prescribed treatment for Graves' disease. Iodine 131 (^{131}I) is selectively absorbed by thyroid tissue, where it destroys some or all of the hyperfunctioning thyroid follicles by emitting beta particles. Unfortunately, 50% to 90% of patients with Graves' disease treated this way eventually become hypothyroid. This is the most likely cause of LG's current symptoms. Other signs and symptoms associated with hypothyroidism include

cold intolerance, reduced heart rate, hypoactivity, decreased appetite, decreased reflexes, constipation, cool/dry skin, myxedema (facial/periorbital), and coarse, brittle hair. Hypothyroidism can also be caused by a variety of conditions, the most common of which are RAI therapy for hyperthyroidism and Hashimoto's thyroiditis. **Hashimoto's thyroiditis** is a cell-mediated autoimmune destruction of the thyroid gland. It occurs in 1% to 2% of the population, with a female predilection of 5:1. The condition begins in adolescence, but is usually not evident until after 50 years of age. The result is an atrophic, fibrotic thyroid gland in a patient with the signs and symptoms of hypothyroidism. Laboratory studies for hypothyroidism will reveal an increased TSH and low T_3 , free T_4 levels. Since Hashimoto's thyroiditis is an autoimmune condition, anti-TPO antibody levels will be positive. All permanent forms of hypothyroidism are treated with life-long thyroid hormone replacement.

Case Conclusion LG was started on levothyroxine 100 $\mu\text{g}/\text{day}$ for treatment of her subsequent hypothyroidism. TSH levels were monitored periodically to ensure a euthyroid state.

Thumbnail: Hyper- versus Hypothyroidism

	Hypothyroid	Hyperthyroid
Etiology	Hashimoto's thyroiditis RAI therapy Idiopathic or atrophic thyroiditis Pituitary or hypothalamic disease Thyroid aplasia Inborn defects in hormone synthesis or action	Graves' disease Toxic multinodular goiter Iodide-induced thyrotoxicosis Autonomous hyperfunctioning nodule Subacute thyroiditis Postpartum thyroiditis Factitious thyrotoxicosis
Symptoms	Decreased metabolic rate Cold intolerance Decreased heart rate Weight gain Fatigue, lethargy Myxedema Cool, dry skin Coarse, brittle hair Constipation Hyporeflexia	Increased metabolic rate Heat intolerance Palpitations, irregular heart rate Weight loss Hyperactivity Pretibial myxedema (Graves') Warm, moist skin Fine hair Diarrhea Hyperreflexia
Labs	↑ TSH ↓ total T_4 ↓ free T_4 ↓ T_3 uptake	↓ TSH ↑ total T_4 ↑ free T_4 ↑ T_3 uptake

Key Points

- ▶ The etiology of hyperthyroidism is usually autoimmune, caused by antibodies to the TSH receptor.
- ▶ Signs and symptoms include increased metabolism, heat intolerance, weight loss, arrhythmias, and diarrhea.
- ▶ TSH measurement is the best thyroid function test; TSH levels are markedly decreased in hyperthyroid states.
- ▶ Treatment: radioactive iodine ablation of the overactive thyroid gland.

Questions

1. A 33-year-old woman presents with signs and symptoms of hyperthyroidism. She complains of anxiety, tremor, nervousness, weight loss, and inability to sleep at night. Laboratory evaluation confirms hyperthyroidism with a free T_4 of 25 mg/dL and undetectable levels of TSH. Which of the following is not an appropriate option for treatment of her hyperthyroidism?
 - A. Propylthiouracil (PTU)
 - B. Radioactive iodine
 - C. Levothyroxine (Synthroid)
 - D. Propranolol
 - E. Surgery
2. A 22-year-old woman presents to her obstetrician/gynecologist for follow-up 8 weeks after the delivery of her baby. There were no complications during her pregnancy or during delivery. On this visit, her thyroid gland is diffusely, but minimally enlarged and nontender to palpation. The doctor decides to obtain a thyroid function panel to aid her diagnostic evaluation. In this thyroid function panel, the most sensitive indicator of thyroid function is:
 - A. T_3 uptake
 - B. Free T_4
 - C. Total T_4
 - D. T_3/T_4 ratio
 - E. TSH