CLINICAL VIGNETTE

Coexisting Hashimoto's Hypothyroidism and Graves' Hyperthyroidism

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Background

Hashimoto's thyroiditis and Graves' disease are autoimmune thyroid conditions with opposing clinical manifestations. Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis, is the most common cause of hypothyroidism, while Graves' disease causes autoimmune hyperthyroidism. The large majority of autoimmune thyroid disease presents with either hypothyroidism or hyperthyroidism and maintains this pattern of thyroid dysfunction. However, a small percentage of patients may have coexisting Hashimoto's and Graves' disease and present with alternating hypothyroidism and thyrotoxicosis which presents diagnostic challenges.

Case 1

A 35-year-old female with longstanding Hashimoto's hypothyroidism presents for evaluation of a low thyroid stimulating hormone (TSH). She had been on thyroid hormone since age 18. Until three months prior to presentation she had been on a stable dose of levothyroxine 150 mcg daily with a consistently normal TSH. Three months prior to presentation labs showed hyperthyroidism with a TSH <0.02 mcIU/mL (0.3 - 4.7 mcIU/mL) and her outside physician lowered her dose of levothyroxine to 137 mcg due to presumed iatrogenic hyperthyroidism. On presentation her TSH was still <0.02 mcIU/mL with free t4 2.7 ng/dL (0.8 - 1.7 ng/dL) and free t3 557 pg/dL (222 - 383 pg/dL). Notably, her weight was 93.4 kg which correlates to a calculated weight-based dose of roughly 150 mcg of levothyroxine. Given that the degree of hyperthyroidism seemed unusual for her current dose of thyroid hormone a thyroid stimulating immunoglobulin (TSI) was checked. TSI was elevated at 2.26 IU/L (<0.54 IU/L) consistent with Graves' disease. Thyroid peroxidase antibody (TPO) was also positive at 115 IU/mL (<20 IU/mL). Levothyroxine was stopped and 6 weeks later thyroid function improved but subclinical hyperthyroidism remained with TSH <0.02 mcIU/mL, free t3 329 pg/dL and free t4 1.3 ng/dL. Labs continued to show subclinical hyperthyroidism 10 weeks after cessation of thyroid hormone. The patient desired pregnancy in the next year. Options for active surveillance, antithyroid drugs, radioactive iodine, and surgery were discussed. She opted to start propylthiouracil (PTU) 50 mg BID with the goal to optimize thyroid function prior to a planned pregnancy. Within 1 month of starting PTU, she became pregnant and subsequently was able to stop PTU given normal thyroid function testing.

Case 2

A 50-year-old female with no past medical history presented with weight loss, fatigue and hair loss and was found to have a TSH of 0.03 mcIU/mL with free t4 1.7 ng/dL and TSI of 3.64 IU/L consistent with Graves' hyperthyroidism. She was referred to endocrinology clinic for treatment of Graves' disease. One month after initial presentation and prior to any treatment repeat labs revealed a TSH of 38.9 mcIU/mL, free t4 0.5 ng/dL and a positive TPO antibody of 506 IU/mL consistent with Hashimoto's hypothyroidism. The diagnosis of hashitoxicosis was considered but thought to be unlikely given the high TSI level. Repeat labs one week later showed TSH 93.7 mcIU/mL with free t4 0.5 ng/dL. She was started on levothyroxine 100 mcg daily. Repeat TSH four weeks later was normal at 2.2 mcIU/mL. Patient was maintained on this dose for an additional four months. At this time, she presented to endocrinology clinic with worsening fatigue and occasional tremors and was found to have an undetectable TSH with free t4 3.0 ng/dL consistent with recurrence of her Graves' disease. Thyroid hormone was stopped with normalization of thyroid function 2 month later. She is currently off of all thyroid medication with normal thyroid function and pending follow up.

Discussion

These cases demonstrate that select patients with autoimmune thyroid disease can experience periods of alternating hyperthyroidism and hypothyroidism due to the coexistence of Hashimoto's and Graves' disease. Hashimoto's hypothyroidism is characterized by development of autoantibodies that cause an immune response and lead to destruction of the thyroid gland. Graves' disease results from thyroid-stimulating antibodies that activate the thyrotropin receptor.[1] In certain cases, patients can have coexisting antagonistic and agonistic autoantibodies directed at the thyrotropin receptor.[1] This is an important clinical concept to keep in mind when patients have labs that are not otherwise well explained by the clinical situation.

Studies reporting the incidence of Hashimoto's hypothyroidism following Graves' disease are extremely limited. Some have reported that over a mean follow up period of 10 years 2.1% of patients with Graves' disease develop hypothyroidism off antithyroid medications.[2] Another very small study found that 6 of 15 patients developed an abnormal TSH 20-27 years after antithyroid drug treatment.[3] Data supporting the prevalence of

Graves' disease following Hashimoto's hypothyroidism is even more sparse and limited to case reports and series. One case series of 8 patients demonstrated three groups of changes in thyroid function and clinical course: 1) transient hyperthyroidism due to Graves' disease following hypothyroidism; 2) persistent hyperthyroidism due to Graves' disease following hypothyroidism; and 3) persistent hypothyroidism in the presence of an atrophic thyroid gland with positive thyroid stimulating antibodies.[4] Changes in thyroid function and clinical course for patients with coexisting Hashimoto's and Graves' disease seems to be decided by the activity level in the blood of the different antagonistic and agonistic antibodies and responsiveness of the thyrotropin receptor in the thyroid gland to the different antibodies.[1,4]

Despite the lack of clinical data to understand the exact prevalence of experiencing both autoimmune hypothyroidism and hyperthyroidism, there are important clinical considerations to keep in mind to provide optimal care to patients. When patients with Hashimoto's hypothyroidism present with an unexpectedly low TSH various possible etiologies need to be considered. Aside from iatrogenic hyperthyroidism which is by far the most common cause, we need to consider new onset Graves' disease as a possible etiology. Additionally, it is important to make sure the patient is not taking high doses of biotin which can result in spurious thyroid function testing. Biotin use can result in falsely high levels of free T4 and free T3 and falsely low levels of TSH, leading to an inaccurate diagnosis of hyperthyroidism.[5] If a patient has a persistently low TSH despite dose reductions in levothyroxine to below weight based dosing of 1.6 mcg/kg and has been off of biotin for at least 2 days, providers should have a low threshold to rule out Graves' disease. Conversely, when patients with Graves' disease who are treated with anti-thyroid medications develop an elevated TSH despite reductions in anti-thyroid medication, practitioners must consider the presence of thyroid blocking antibodies. A predominance of thyroid blocking antibodies could necessitate cessation of anti-thyroid medication and possible initiation of thyroid hormone.

In conclusion, when a patient with autoimmune thyroid disease presents with unexplained, abnormal thyroid function testing it is important to consider whether they could have coexisting Hashimoto's and Graves' disease.

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