CLINICAL VIGNETTE

Iodine Excess and Thyroid Dysfunction

Lillian Chen, M.D.; Arti D. Shah, M.D.; and Rumi Cader, M.D., M.P.H.

Case Presentation

A 71-year-old Japanese male with a history of type 2 diabetes mellitus and hypertension presented for his annual exam. He was asymptomatic. Routine labs revealed abnormal thyroid function tests (TFTs) including a thyroid stimulating hormone (TSH) of 6.4 mcIU/mL (normal 0.3-4.7), free T3 (fT3) of 293 pg/dL (normal 222-383), and free T4 (fT4) of 1.0 ng/dL (normal 0.8-1.6). Anti-thyroid peroxidase antibody was elevated at 77.7 IU/mL (normal ≤ 20). Repeat labs 6 months later showed normal TFTs with a TSH of 2.7 mcIU/mL, fT3 of 349 pg/dL, and fT4 of 1.1 ng/dL. However, three months later, fT3 was elevated at 404 pg/dL and fT4 remained stable. TSH remained in the normal range; however, it had further decreased to 1.7mcIU/mL. Additional tests including a thyroid stimulating immunoglobulin (TSI) and thyrotropin-binding inhibitoryimmunoglobulin (TBII) were negative. At UCLA, the electrochemiluminescence Immunoassay (ECLIA) (Cobas, Roche Diagnostics, Mannheim, Germany) is used to measure the TSH. As the presence of heterophile antibodies can interfere with the TSH assay,[1] this was also evaluated and found to be negative. Thyroid ultrasound showed a homogenous thyroid gland with minimal vascularity and scattered subcentimeter nodules.

A detailed history revealed that he had recently traveled to Japan and had significantly increased his intake of iodine-rich foods including dried shrimp and seaweed. A 24-hour urine iodine was elevated at 728 mcg (normal 75-500), confirming elevated total body stores of iodine. This was thought to be the cause of his abnormal thyroid tests.

The patient was advised to decrease his intake of iodine-rich foods. Repeat TFTs three months later showed a TSH of 2.0 mcIU/mL, fT4 of 1.2 ng/dL, and fT3 of 376 pg/dL. Six months later, labs showed a TSH of 2.6 mcIU/mL, fT4 of 1.2 ng/dL, and fT3 of 283 pg/dL. Thyroid tests had returned to normal. The patient continues to monitor his iodine intake.

Discussion

Iodine is necessary for thyroid hormone synthesis. The recommended daily intake of iodine in non-pregnant adults is 150 µg.[2] Sources of iodine include dietary iodine (such as iodized salt and seafood), dietary supplements, amiodarone, and iodinated contrast. Iodine content in food can be variable. Intake of seaweed (kelp) is a common cause of iodine excess as it can contain as much as 8 mg of iodine per 1 g of kelp.[3]

Excess iodine exposure is associated with thyroid dysfunction. Those with underlying thyroid conditions such as autoimmune thyroiditis including Hashimoto's thyroiditis, painless thyroiditis, subacute thyroiditis, and postpartum thyroiditis are more likely to become hypothyroid following exposure to large amounts of iodine, especially in iodine-sufficient countries.[4] This occurs due to an inability to escape from a phenomenon known as the Wolff-Chaikoff effect, which occurs as a result of excess iodine causing inhibition of intrathyroidal deiodinase, and this leads to decreased thyroid hormone synthesis.[5] People with normal thyroid function are able to escape the Wolff-Chaikoff effect and resume normal thyroid hormone synthesis within a few days.[6] However, those with underlying thyroid disease can become hypothyroid and may require thyroid hormone therapy.[6] Usually, adaptive mechanisms allow thyroid hormone synthesis to return to normal levels in these patients after two to four weeks of continued iodine exposure.[7] However, some will require long-term thyroid hormone therapy.[6]

Iodine excess can also lead to hyperthyroidism. This commonly occurs in areas of iodine deficiency and is seen in patients with a nodular goiter or in euthyroid Graves' disease after treatment with anti-thyroid medication.[8] This occurs due to the availability of increased substrate in the presence of autonomous thyroid tissue and is referred to as the Jod-Basedow phenomenon.[9]

Thyroid function tests are usually straightforward to interpret, but discordance between the thyroid hormone levels and TSH can occur. This can be seen due to assay interference by heterophile antibodies or human anti-mouse antibodies,[10] poor compliance with thyroid replacement therapy, excess iodine exposure (including iodine-rich foods and amiodarone), non-thyroidal illness, and pregnancy. Less common causes include TSH-secreting pituitary adenoma, resistance to thyroid hormone, and disorders of thyroid hormone transport or metabolism (including familial dysalbuminemic hyperthyroxinemia).[11]

In this case, aside from being very rare, a TSH-secreting tumor was unlikely given the decreasing TSH with the rise in fT3. Prior normal thyroid function and lack of family history make resistance to thyroid hormone or disorders of thyroid hormone transport unlikely. With thyroid hormone resistance, other clinical features are often seen including developmental delay, delayed bone age, and short stature.[12] Other etiologies were easily excluded based on the patient's history and the negative

heterophile antibody. An elevated 24-hour urinary iodine cinches the diagnosis of iodine excess causing thyroid dysfunction, in this case causing an elevated free T3 and normalization of his subclinical hypothyroidism with improvement after the patient decreased his iodine intake.

This case highlights the importance of obtaining a thorough history of iodine intake and exposure when abnormal thyroid test results are obtained. In addition, it is important to be aware that such exposures can lead to either hypothyroidism or hyperthyroidism, and it can be subclinical or overt.

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