

## CLINICAL VIGNETTE

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# A Case of Poorly Controlled Hypothyroidism

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Elaine Parker, MD

A 59-year-old male with a history of type 2 diabetes presented with slow speech and fatigue. The patient's family reported that his symptoms had been worsening over the past year, but the patient had been reluctant to seek medical care. His family reported a generalized functional decline. On physical exam, the patient had dry skin and delayed reflexes. His thyroid gland was not enlarged, without thyroid nodules. He was not taking any medications. He also reported constipation with bowel movements every 3 days and cold intolerance. He denied family history of thyroid disease, history of celiac disease or other autoimmune disorders. Labs included elevated thyroid stimulating hormone (TSH) of 163 milli-international units per liter (mIU/L) and thyroxine (free T4) was .26 ng/dL. He was initially treated with intravenous levothyroxine and transitioned to oral levothyroxine with improving thyroid labs. Adrenal insufficiency was ruled out with ACTH stimulation testing.

At outpatient follow up, the patient is TSH increased to 70 mIU/L with free T4 of 1.18 ng/dL. The patient had been non-compliant with his oral diabetes medication and presented to an outside hospital with sepsis and a diabetic foot ulcer. After this hospitalization, the patient maintained good medical follow-up and became euthyroid. Two years later routine labs showed TSH of 53.36 mIU/L and free T4 of .66 ng/dL. He denied weight gain, constipation, cold intolerance and hair loss. His temperature was normal and had no bradycardia. Physical exam was normal, and the thyroid exam showed no enlargement or nodules. His deep tendon reflexes were normal and had no peripheral edema. His medications included levothyroxine 0.175 mg po daily, insulin aspart 5 units SC tid ac, insulin glargine 8 units SC daily, metformin 1000 mg po bid, pantoprazole 40 mg po daily in the morning, and a multivitamin. His labs showed a sodium of 133 mmol/L, normocytic anemia with a hemoglobin of 12.4 g/dL and MCV of 93, and lipids with total cholesterol of 248 mg/dL and LDL of 131 mg/dL. The patient had declined initiation of a statin. He reported taking his thyroid medication on an empty stomach and separate from his multivitamin and pantoprazole. He reported the pantoprazole was a new medication started after the diagnosis of peptic ulcer disease on endoscopy. Review of his refill pattern demonstrated medication non-adherence.

### Discussion

Hypothyroidism is a common condition in the United States. The prevalence of overt hypothyroidism is 0.3-3.7%.<sup>1</sup> The prevalence of subclinical hypothyroidism is 4-10%. Hypothy-

roidism is 5-8 times more common in women.<sup>2</sup> Thirteen million people in the US who have hypothyroidism are undiagnosed. It is more common in Caucasians, older than 65 years old and women. Other risk factors include type 1 diabetes, celiac disease, Down syndrome and Turner syndrome.<sup>2</sup>

In the US, the most common etiology of primary hypothyroidism is chronic autoimmune thyroiditis or Hashimoto's disease. Hypothyroidism also occurs after thyroid surgery (hemithyroidectomy) and after radioiodine treatment.<sup>3</sup> Eighty percent of patients with Grave's disease treated with radioiodine become hypothyroid and 20% of patients become hypothyroid after hemithyroidectomy.<sup>1</sup> The US Preventive Services Task Force (USPTF) does not recommend routine screening for hypothyroidism in asymptomatic individuals. However, the American Thyroid Association and the American Association of Clinical Endocrinologists recommend intermittent screening.<sup>1</sup> Screening can be considered if the patient has a history of autoimmune disease, head and neck radiation or a family history of thyroid disease.

The diagnosis of hypothyroidism is made with an elevated TSH and a low free T4. An elevated TSH with a normal T4 is consistent with subclinical hypothyroidism. An antithyroid peroxidase antibody (TPO-Ab) can be checked in subclinical hypothyroidism. There is a 2-5% annual risk of progression of subclinical to overt hypothyroidism.<sup>4</sup> Individuals with a positive TPO-Ab have a higher rate of progression to overt hypothyroidism. A low or normal TSH combined with a low free T4 is consistent with secondary or tertiary hypothyroidism indicating a problem with the hypothalamus or pituitary. Primary hypothyroidism is common while secondary hypothyroidism represents only 5% of all cases.<sup>5</sup>

Common symptoms of hypothyroidism include hair loss, cold intolerance, constipation, menstrual irregularities and weight gain. Physical exam findings in more advanced cases can include goiter, delayed relaxation phase of deep tendon reflexes, thin hair, dry skin and peripheral edema. Hypothyroidism can cause elevated total cholesterol and LDL.<sup>1</sup> Other lab findings can include hyponatremia, normocytic anemia, hyperprolactinemia and elevated creatine kinase.

Treatment of hypothyroidism is with thyroid replacement. Levothyroxine is dosed at 1.6 mcg/kg/day in healthy adults. Older adults with ischemic heart disease should be started on levothyroxine 25-50 mcg daily and monitored closely for

angina. Levothyroxine should be taken in the early morning 30 minutes prior to eating. It should not be taken within four hours of calcium or iron containing products. After initiation of treatment, TSH should be re-checked in 4-12 weeks and then every 6-12 months once euthyroid.<sup>1</sup> TSH is at goal in the lower half of the reference range. Desiccated thyroid hormone (Armour thyroid) is not recommended by the American Association of Clinical Endocrinologists. Levothyroxine-liothyronine combination therapy is not recommended to treat hypothyroidism. The American Thyroid Association recommends against the use of this combination drug due to concerns over safety and lack of data regarding efficacy. Randomized controlled trials are needed to clarify these unresolved questions. Treatment of hypothyroidism can improve symptoms and cardiovascular health.<sup>4</sup>

Treatment of hypothyroidism is lifelong. After a change in dose, it takes 4 weeks for the TSH to reflect the new dose. Labs should be repeated in 1-3 months, with dose increases until clinically euthyroid. Overtreatment of hypothyroidism can predispose to osteoporosis and atrial fibrillation.<sup>1</sup> Some patients continue to have persistent symptoms despite optimal treatment and normalized TSH. This occurs in 5-10% of patients who report persistent depression and cognitive complaints.

Common reasons for an elevated TSH in a previously well-controlled patient include non-adherence, switch from brand to generic thyroid hormone replacement and decreased absorption of thyroid medication. Patients should avoid taking levothyroxine with calcium, iron, soy and aluminum-containing antacids as absorption will be impaired. Iodinated contrast agents, amiodarone and kelp all contain high amounts of iodine which can disrupt thyroid function. Amiodarone has a significant iodine load and can cause hypothyroidism in some patients. Lithium treatment can predispose to hypothyroidism by decreasing thyroid hormone production. One study demonstrated prevalence of hypothyroidism 6 times higher in lithium-treated patients.<sup>6</sup> Patients receiving concomitant proton pump inhibitor (PPI) therapy may require a higher dose of levothyroxine. Thyroid hormone requires an acidic environment for optimal uptake in the stomach.

Initially, the etiology of this patient's elevated TSH was unclear. He had not switched from brand to generic thyroid hormone replacement. Upon questioning, he denied taking levothyroxine with calcium or iron containing products that can impair absorption. He denied starting any other new medications other than his PPI which he reported taking 6 hours apart from levothyroxine. A thorough review of medication refill dates did demonstrate medication non-adherence during this interval. The patient was amenable to taking levothyroxine daily and returning for follow up labs. In summary, medication non-adherence is a common cause of an elevated TSH in a previously well-controlled patient with hypothyroidism.

## REFERENCES

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