Case Presentation
J.K., a 70-year-old woman with type 2 diabetes, is evaluated in an outpatient endocrinology clinic during a routine appointment. She was diagnosed with diabetes 5 years ago and participated in a comprehensive basic diabetes education program approximately 2 years ago.

She regularly checks her blood glucose before breakfast and 2 hours after meals. Fasting blood glucose levels typically range from 105 to 115 mg/dl, whereas postprandial blood glucose levels range from 120 to 160 mg/dl.

J.K. has no known macrovascular or microvascular complications. Her last dilated eye exam was 6 months ago. Additional medical problems include hypertension and asthma.

A review of systems was unremarkable except complaints of mild fatigue and muscle cramps.

J.K.’s current medications include:
- metformin, 500 mg once daily
- lisinopril, 5 mg once daily
- montelukast sodium, 10 mg once daily
- aspirin, 81 mg once daily

A limited physical examination revealed:
- weight: 135 lb
- height: 63 inches
- blood pressure: 110/78 mmHg
- pulse: 64
- skin: dry without rash or jaundice
- neck: thyroid 35 g
- heart: regular sinus rhythm without murmur, lungs clear to auscultation and palpation
- abdomen: soft without tenderness, mass, or bruit
- lower extremities: no edema, Oman’s negative, pedal pulses 3+ bilaterally, Carville normal

J.K.’s laboratory results were as follows:
- hemoglobin A1c: 6.4% (normal: 4.0–6.3%)
- blood glucose: 148 mg/dl (normal: 65–110 mg/dl)
- blood urea nitrogen: 15 mg/dl (normal: 5–29 mg/dl)
- creatinine: 1.1 mg/dl (normal: 0.5–1.4 mg/dl)
- thyroid-stimulating hormone (TSH): 6.0 IU/ml (normal: 0.29–5.11 IU/ml)
- repeat TSH: 7.1 IU/ml
- thyroxine (T4): 9.5 µg/dl (normal: 4.5–12.5 µg/dl)
- free T4: 1.6 µg/dl (normal: 0.9–1.9 µg/dl)
- antimicrosomal antibody: 38.4 IU/ml (normal: 0–35 IU/ml)
- antithyroglobulin antibody: <20 IU/ml (normal: 0–35 IU/ml)
- total cholesterol: 211 mg/dl (normal: 130–200 mg/dl)
- triglyceride: 174 mg/dl (normal: 35–160 mg/dl)
- HDL cholesterol: 51 mg/dl (normal: 30–80 mg/dl)
- LDL cholesterol: 148 mg/dl (normal: <100 mg/dl)

Discussion
J.K. has dyslipidemia, subclinical hypothyroidism, and adequately controlled type 2 diabetes. A mildly elevated TSH level and a normal serum free T4 accompanied by few or no reportable symptoms indicates subclinical hypothyroidism. J.K.’s thyroid is 35 g, whereas a normal-sized thyroid gland in an adult is 20–25 g. In her case, the laboratory results, complaints of mild fatigue and muscle cramps, and small goiter indicate the disease is present. This form of hypothyroidism is found most commonly in elderly women, and it has recently been identified as a strong risk factor for cardiovascular disease (CVD).

Overt hypothyroidism is linked to CVD, but the relationship of subclinical hypothyroidism and CVD has been controversial. Twenty-year follow-up data from the Whickham cohort published in 1996 showed no higher rate of death from CVD in the subclinical hypothyroidism group as compared to the euthyroid group. Therefore, clinicians debated the utility of treating subclinical hypothyroidism. Proposed benefits of treating subclinical hypothyroidism have included preventing the progression to overt hypothyroidism, reducing dyslipidemia, and improving symptoms. Concerns voiced against treatment have included the lack of data supporting treatment efficacy, the cost of treatment, and the potential for over-treatment, which can lead to osteoporosis and atrial fibrillation.

Alternatively, data from the recent Rotterdam cohort indicates that subclinical hypothyroidism is a strong, independent risk factor for CVD, particularly in elderly women. Treatment of subclinical hypothyroidism is necessary in order to reduce cardiovascular risk. The Rotterdam data showed that subclinical hypothyroidism was associated with a greater prevalence of aortic atherosclerosis (odds ratio 1.7) and myocardial infarction (odds ratio 2.3) unaffected by cholesterol level, blood pressure, or smoking status. In addition, women with positive antithyroid antibodies (autoimmune) and subclinical hypothyroidism had a slightly more robust association for aortic atherosclerosis (odds ratio 1.9) and myocardial infarction (3.1). The attributable risk percentage for CVD from subclinical hypothyroidism was...
found to be equivalent to risk factors such as dyslipidemia, hypertension, smoking status, and diabetes. Several postulated mechanisms of action relating subclinical hypothyroidism to atherosclerosis include the effect of thyroid hormone on coagulation and vasodilation, hypofunctioning of the parasympathetic nervous system, and increased homocystine levels.

The prevalence of subclinical hypothyroidism is 4–21% in women and 3–16% in men, with more than 10 million people affected in the United States and approximately 43 million in Europe. Based on the Colorado Thyroid Health Survey conducted in 1995, the incidence of hypothyroidism increases with age. The data showed that the incidence was 21% in women older than 74 years compared to 4% in women aged 18–24 years.

The prevalence of thyroid disease in patients with diabetes is significantly higher than that in the general population. It has been reported as 13.4%, with the highest in patients with type 1 diabetes (31.4%) and lowest in patients with type 2 diabetes (6.8%). In addition to the autoimmune link between type 1 diabetes and thyroid disease, diabetes and thyroid disease are more commonly found in the elderly, further contributing to the high association.

Thyroid function should be evaluated yearly in patients with diabetes. An outpatient diabetes clinic in Scotland randomly screened 1,310 adult patients with diabetes for thyroid disease. The prevalence of thyroid disease was found to be 13.4%, of which 6.8% were diagnosed during the screening. The remainder had previously known disease. The most common thyroid dysfunction was subclinical hypothyroidism (4.8%).

Symptoms of subclinical hypothyroidism are particularly insidious and often overshadowed by coexisting health problems, or the symptoms are attributed to aging. Symptoms include dry skin, poor memory, slow thinking, weak muscles, muscle cramps, feeling cold, puffy eyes, constipation, hoarse voice, and deep voice.

Unfortunately, these symptoms are also found frequently in people without thyroid disease. According to the Colorado Thyroid Health Survey results, people with overt hypothyroidism reported a greater percentage of symptoms than those with subclinical hypothyroidism.

Certain static and changing symptoms have been identified as the highest indicators of hypothyroidism. Static symptoms include constipation, hoarse voice, and deep voice. Changing symptoms include increased constipation, hoarser voice, feeling colder, having puffy eyes, and having weaker muscles. In general, symptoms associated with hypothyroidism are high in specificity but low in sensitivity. Therefore, the absence of a symptom does not rule out thyroid disease.

Dyslipidemia is commonly found in hypothyroidism and subclinical hypothyroidism. Treatment of the thyroid disorder potentially improves dyslipidemia and reduces risk for CVD. In the absence of significant symptoms associated with subclinical hypothyroidism, dyslipidemia may be a key indicator of thyroid failure.

Typically, blood glucose levels are unaffected by hypothyroidism because insulin sensitivity is not altered. In fact, in patients utilizing exogenous insulin, there may be a decrease in insulin requirements from reduced insulin degradation. Therefore, typically, glucose remains stable or improves while a person is hypothyroid. Once thyroid treatment is initiated, patient education and close observation is vital because normalization of the thyroid may potentially lead to higher blood glucose levels and loss of diabetes control.

In contrast, hyperthyroidism causes insulin resistance and may unmask impaired glucose tolerance and diabetes in previously undiagnosed patients. Typically, blood glucose levels are abnormal and trend towards hyperglycemia until treatment is initiated. After the thyroid function stabilizes, the glucose levels usually improve.

Summary

In this case presentation, J.K. has several symptoms and signs indicating the need for thyroid screening and treatment. Her risks for subclinical thyroid disease include her age, sex, underlying diabetes, and symptoms, including small goiter, fatigue, and muscle aches. Her laboratory results indicate dyslipidemia secondary to subclinical hypothyroidism.

Thyroid hormone replacement treatment should be initiated for subclinical hypothyroidism in order to reduce the risk of CVD, improve dyslipidemia, and prevent progression to overt thyroid disease.

Because of her advanced age, levothyroxine, 0.025 mg, was prescribed. The usual full replacement dose of levothyroxine is 75–125 μg a day in women and 125–200 μg a day in men. Elderly patients (age >60 years) require a dose that is 20–30% smaller than usual doses for younger people. Additionally, those with underlying cardiac disease are started on low-dose replacement, and the dose is titrated upward gradually.

Once TSH has normalized in the target lower half of the normal range, the lipid profile should be reevaluated. If dyslipidemia persists, a referral to a dietitian should be made and possibly a lipid-lowering agent should be initiated with the primary goal of reducing cardiovascular risk.

Additional interventions include referral for further diabetes education. J.K.’s postprandial blood glucose levels are mildly elevated. She would benefit from a review of postprandial blood glucose goals and from interventions aimed at reducing postprandial blood glucose levels, especially if they increase after the thyroid is stabilized.

Attentive follow-up is crucial to the success of treatment of subclinical hypothyroidism. Several studies have reported as many as 32–40% of patients on levothyroxine therapy have inadequate replacement, receiving either too much or too little. Therefore, J.K. was asked to return to the outpatient clinic in 2 months.

J.K. was seen at the outpatient clinic 8 weeks after initiation of levothyroxine therapy. Her goiter was smaller, and her fatigue and muscle aches had resolved. Follow-up laboratory results indicated adequate treatment of subclinical hypothyroidism and normalization of dyslipidemia. Her fasting blood glucose levels remained within the target range, and her postprandial blood glucose levels had improved because of increased activity and reduced carbohydrate intake.
References


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