CME CREDIT

TAKE-HOME POINTS FROM EDUCATIONAL PRESENTATIONS BY CLEVELAND CLINIC FACULTY AND VISITING PROFESSORS

Detecting and managing subclinical hyperthyroidism

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SINCE THE LATE 1980s, when sensitive thyroid-stimulating hormone (TSH) assays were introduced, the serum TSH level has become the single best test of thyroid function. Now that physicians are using TSH assays more widely, they are encountering subclinical thyroid disease more frequently. In most cases, low TSH values either normalize spontaneously or are due to thyroid hormone therapy, but some reflect conditions that require further workup and management.

DEFINITION: LOW TSH, NORMAL T_3 AND T_4

Subclinical hyperthyroidism is generally defined as the combination of all three of the following:

- A TSH level less than 0.1 mU/L (normal 0.4–5.0 mU/L);
- A normal free thyroxine (FT_4) level (0.7–1.8 ng/dL) or a normal free T_4 index (6.4–10.7 µg/dL); and
- A normal triiodothyronine (T_3) level (94–170 ng/dL).

Low serum TSH concentrations may frequently be transient. Among 66 patients with subclinical hyperthyroidism in a British general practice, 40 (61%) had normal concentrations 1 year later.[1] In another study in a primary care center in Sweden, of 53 clinically euthyroid patients who had low serum TSH concentrations, 27 (53%) had normal values 2 to 3 weeks later.[2]

CAUSES OF SUBCLINICAL HYPERTHYROIDISM

Patients may or may not have symptoms. In all cases, causes of low TSH unrelated to hyperthyroidism should be excluded: nonthyroid illnesses, secondary (pituitary) hypothyroidism, central (hypothalamic) hypothyroidism, recovery from hyperthyroidism, drugs (glucocorticoids, dopamine agonists), and spurious test results.

Exogenous thyroid hormone therapy is the most common cause of subclinical hyperthyroidism. Other important causes are:

- Multinodular goiter.
- Solitary (autonomous) thyroid adenoma.
- Subclinical Graves' disease.
- Subacute thyroiditis with transient hyperthyroidism.
- Silent (postpartum) thyroiditis.

CONSEQUENCES OF SUBCLINICAL HYPERTHYROIDISM

Cardiac effects of subclinical hyperthyroidism include atrial fibrillation, frequent atrial premature contractions, sinus tachycardia, and increased left ventricular mass and contractility.[3] Sawin et al[4] followed 2,007 subjects 60 years of age or older for up to 10 years and, after adjusting for other risk factors, found that the risk of developing atrial fibrillation was approximately threefold higher in persons with serum TSH levels ≤ 0.1 mU/L than in those with normal concentrations.

Accelerated bone loss, another potential problem of subclinical hyperthyroidism, is caused by increased bone resorption, especially in postmenopausal women who are not receiving estrogen replacement therapy.[5,6]

Other possible consequences of subclinical hyperthyroidism include increased serum glutathione S-transferase activity, decreased serum creatine kinase activity, and increased sex hormone-binding globulin levels.

The serum TSH level is the single best test of thyroid function

MANAGING SUBCLINICAL HYPERTHYROIDISM

In hypothyroid patients receiving thyroid replacement therapy, the TSH level should be maintained in the normal range. There is probably no need to reduce the dosage in a patient whose serum TSH concentration is only slightly low (ie, 0.25–0.4 mU/L), as there may be some daily fluctuations in TSH levels, and the risks of slightly low values in otherwise-healthy patients is negligible. In addition, frequent manipulations of the dosage may complicate therapy and increase cost.

In patients receiving suppressive treatment for thyroid cancer or benign thyroid disease, the TSH level should be maintained between 0.1 and 0.4 mU/L, unless the patient has aggressive thyroid cancer, in which case the TSH level should be suppressed to undetectable levels (< 0.02 mU/L). In these patients, consideration should be given to the concurrent administration of cardioselective beta blockers, which have been shown to ameliorate most of the cardiac effects of subclinical hyperthyroidism.[7,8]

Thyroid hormone therapy is the most common cause of subclinical hyperthyroidism

In asymptomatic patients with endogenous subclinical hyperthyroidism, one should recheck the TSH level and also check the T_3 level and either the free T_4 level or the free T_4 index. If the T_4 and T_3 levels are normal, then the TSH level should be checked again in 2 to 3 months and then every 6 months. If the TSH level is persistently less than 0.1 mU/L or the patient has conditions to which small degrees of thyroid hormone excess might contribute (eg, atrial fibrillation, other atrial arrhythmias, other cardiac disorders, or accelerated bone loss), further workup and management is necessary.

Twenty-four hour radioactive iodine uptake and scanning may help differentiate between subacute thyroiditis with transient hyperthyroidism (in which the uptake is undetectable, and the natural history is characterized by spontaneous remission) vs conditions that are characterized by high radioactive iodine uptake. These latter conditions include a "hot" nodule (toxic adenoma), toxic diffuse goiter (Graves' disease), or toxic multinodular goiter. Since these latter conditions almost always persist, one should consider treating them with antithyroid medications, radioactive iodine, or surgery.

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Understanding culture clashes in the clinical setting

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IN OUR DIVERSE SOCIETY it is not unusual for physicians to encounter patients and colleagues from a cultural, ethnic, or religious background different from their own. Such differences are often ignored or are only of passing interest when the clinical or collegial encounter is free of problems. For the most part, we assume that other people understand us and that we understand them.

However, occasionally conflict can surface in the form of a "difficult" patient, an "unreasonable" colleague, or a family member who