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Toxic Tachycardia

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The Case

A 66-year-old woman with a past medical history of hypertension and breast cancer was admitted with abdominal pain. She complained of 3 weeks of progressive severe right-sided abdominal pain associated with nausea, vomiting, diarrhea, and a few days of constipation. On physical examination, she was in distress secondary to pain and was afebrile but tachycardic. The abdominal exam was notable for diffuse tenderness on palpation without rebound or guarding. The pulmonary, cardiovascular, skin, and neurologic examinations were all unremarkable. All of her laboratory tests were normal. A computed tomography (CT) scan of the abdomen with iodinated contrast was done, which revealed a normal appendix and a colon filled with stool with no obvious explanation for her pain or tachycardia.

Her abdominal pain and tachycardia persisted with no clear etiology. On hospital day 3, a thyroid-stimulating hormone (TSH) level was ordered to determine the cause of the tachycardia. The level was undetectable at Table.)

The patient had no evidence of thyroid storm. The iodinated contrast given for the CT scan could have exacerbated her thyroid disease but fortunately did not. Therapy for her hyperthyroidism was initiated, and she was discharged without complications.

The Commentary

Thyroid disease is common in the general population and in women in particular, with an incidence of hyperthyroidism of one case per thousand per year and a prevalence of almost 0.5%–2%.(1) Hypothyroidism is even more common, present in 2%–3% of the general population, with milder forms of early thyroid failure found in approximately 15% of women in their seventh decade.(2) Failure to diagnose underlying thyroid disease in the acute setting may be associated with a disastrous outcome. Presentation of acute hyper- or hypothyroidism requiring hospitalization is rare. More commonly, an acute nonthyroid systemic illness exacerbates underlying thyroid disease. That is, a patient with underlying uncomplicated thyrotoxicosis may develop thyroid storm in the presence of pneumonia, or gastrointestinal bleeding may push a patient from hypothyroidism into myxedema coma. Both thyroid storm and myxedema coma have

high mortality rates even with therapy.(3) Although atrial arrhythmias are common in hyperthyroidism, thyrotoxic hospital deaths are likely due to ventricular fibrillation and hypothyroid hospital deaths to sick sinus syndrome, hypoventilation, and/or sepsis.

In the above case, the patient presented with primarily abdominal symptoms of unclear etiology after an initial evaluation. The persistently rapid heart rate, probably thought to be a response to her abdominal pain, was a clue to her diagnosis. The possibility of thyrotoxicosis underlying other systemic and/or acute disease in a hospitalized patient should be considered in the presence of unexplained tachycardia, fever out of proportion to the clinical state, unexplained or new tremor, goiter, and certainly when more obvious stigmata of Graves' disease such as ophthalmopathy are present. Clues to the development of thyroid storm (beyond just thyrotoxicosis) could include tachycardia, atrial arrhythmias, nausea, vomiting, and diarrhea (as in this case). Liver function test abnormalities are not uncommon (4), and diffuse abdominal pain and hepatosplenomegaly may occur, although frank abdominal tenderness (as in this case) is unusual.

In the hospital setting, thyrotoxic storm may be precipitated by a number of events. There might be a prior history of Graves' disease with recent withdrawal of antithyroid drugs. Or the precipitant may be severe thermal injury, diabetic ketoacidosis, pulmonary thromboembolism, or stroke. But the most common underlying problem, and often the most vexing to diagnose, is infection. Coexistence of infection and thyroid disease creates challenges in interpreting whether the hyperpyrexia and tachycardia present are due to the thyrotoxicosis or to the infection. In the differential diagnosis, the white blood cell count may be a clue in this regard, with leukocytosis and a left shift in the presence of infection, while leukopenia with relative lymphocytosis may be seen in Graves' disease. When both infection and thyrotoxicosis are present, routine cultures and early initiation of broad-spectrum antibiotic therapy in addition to treatment of thyrotoxic storm are essential.

Thyroid storm may also occur in postoperative patients ("surgical storm") or may be precipitated by exposure to moderately high doses of iodine ("Jod-Basedow" thyrotoxicosis) such as that received as a radiologic contrast agent with CT scanning. In the present case, there was not sufficient time during this brief hospitalization for the iodine-containing contrast dye to aggravate the woman's thyrotoxic state as this would typically require weeks to occur, but she would need to be followed more carefully in the future as a result of the exposure. Another common clinical setting for iodine-induced thyrotoxicosis is the patient with arrhythmia being treated with amiodarone.(5) Amiodarone contains 37% iodine; the 74,000 mcg of iodine present in one 200-mg tablet can overwhelm a thyroid gland that usually requires only 150 mcg/day for hormone synthesis. Amiodarone-induced thyrotoxicosis typically presents months after starting therapy. The thyroid function tests in amiodarone-treated patients can be difficult to interpret, and endocrinologic consultation is advisable.

Although the clinical presentation in this case is not suggestive of myxedema, hypothyroidism is so common in older women that the diagnosis should be considered in the acute care setting in this subset of patients. Clinical clues to the presence of underlying hypothyroidism may include alterations in mental status, somnolence, slow speech, peripheral edema, pleural effusions, low voltage on electrocardiogram (EKG), hyponatremia, and elevated creatine phosphokinase. Of particular danger to patients with myxedema is the administration of agents that can suppress respiration and lead to carbon dioxide

retention; hypoventilation and hypercarbia in this setting may result in progressive deterioration into coma. Candidate pharmaceuticals in this category include opiates, hypnotics, sedatives, and anesthetics. Indeed, a patient with underlying hypothyroidism may be admitted for a surgical procedure and simply fail to recover normally postoperatively.(6)

Although hyperthyroidism is the likely diagnosis in this case, one should consider the possibility that this patient did not have thyrotoxicosis at all, in spite of the low TSH and a high free T4. The standard laboratory tests of thyroid function are often altered in the setting of acute illness, even with normal thyroid activity. The TSH is often suppressed in sick hospitalized patients as part of the so-called "euthyroid sick" syndrome (7), and elevations in both total and free T4 may be seen as well. The strongest proof of thyroid hyperfunction in the acute setting is the *free* T3 measurement (elevated in this patient), but this is an assay that is not ubiquitously available. *Total* T3 measurement is both readily available and more accurate in hospital laboratories. In patients with systemic illness, the T3 is uniformly low due to inhibition of conversion of T4. In this case, a low value would have indicated that this patient was not thyrotoxic but rather was manifesting the euthyroid sick syndrome (which is benign and requires no intervention). Even hypothyroid patients with classically elevated serum TSH levels while ambulatory will have suppression of their TSH levels when sick. Administration of steroids or dopamine is another reason for spuriously low TSH in the acute care setting. Because of these changes in TSH in the hospital setting, only ambulatory measurements should be relied upon for screening, case-finding, or more routine diagnosis.(8) However, TSH measurement for the diagnosis of thyroid disease, even in the hospital setting, can be relied upon when the level is quite elevated, generally indicating hypothyroidism.

Take-Home Points

- Exacerbation of underlying thyroid disease in the setting of acute illness may lead to thyroid storm or myxedema coma, both of which can be life-threatening.
- Thyrotoxicosis or thyroid storm may present with persistent tachycardia, new tremor, or fever out of proportion to the clinical state in the setting of acute hospitalization.
- Thyrotoxicosis or thyroid storm may be precipitated by a number of clinical stressors including surgery, iodine contrast load, infection, trauma, or amiodarone for arrhythmia.
- Acute illness may alter laboratory tests of thyroid status even in the setting of normal thyroid function.

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Table

Table. Useful Definitions in Thyroid Disease*

Thyrotoxicosis—The state produced by excessive quantities of endogenous or exogenous thyroid hormone.

Thyroid storm—The exacerbation of symptoms of hyperthyroidism; severe thyrotoxicosis; [may be] marked by rapid pulse (140–170/minute), nausea, diarrhea, fever, loss of weight, extreme nervousness, and a sudden rise in the metabolic rate.

Myxedema coma—A severe and often fatal syndrome of extreme hypothyroidism; patients typically are comatose with hypothermia, depression of respiration, bradycardia, and hypotension.

Euthyroid sick syndrome—Abnormalities of circulating thyroid hormone levels that develop in the course of an acute, severe illness in the absence of underlying thyroid disease.

*From Stedman's Medical Dictionary.

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