Subacute Thyroiditis

Christa M. Blose, MPAS, PA-C, Holly Jodon, MPAS, PA-C

Jerry, a 48-year-old white man, is referred to endocrinology for abnormal results of thyroid tests performed four weeks ago (see table for values). Two months ago, Jerry developed an upper respiratory infection (URI) with fever, odynophagia, and anterior neck discomfort. His symptoms resolved after two weeks; however, he has since developed fatigue and nervousness.

The remaining review of systems is unremarkable. Medical history is negative. Jerry denies any factors that can affect thyroid function: He does not take thyroid medication, OTC thyroid supplements, amiodarone, lithium, or interferon-α, does not have high iodine intake, and has not undergone head/neck irradiation. There is no personal or family history of thyroid disease, organ-specific autoimmune disease (ie, vitiligo, myasthenia gravis, or Sjögren syndrome) or systemic autoimmune disease (rheumatoid arthritis, systemic lupus erythematosus, or progressive systemic sclerosis).

Vital signs are stable. On physical examination, his thyroid gland is firm, with slight enlargement of the left lobe and mild tenderness. There are no palpable nodules or cervical adenopathy. The remainder of the exam is unremarkable.

Lab studies (see table) reveal an elevated erythrocyte sedimentation rate (ESR) and suppressed TSH, with normal free thyroxine (T4) and free triiodothyronine (T3) levels. His thyroid peroxidase antibody (Anti-TPO) is negative. Radioactive iodine uptake (RAIU) reveals a low 24-hour uptake of 4% (normal, 5% to 30%).

TABLE
Lab Results for Case Patient

	Time after symptom onset			
	1 mo	2 mo	4 mo	6 mo
TSH (0.40-4.50 μIU/mL)	0.03	0.14	8.23	3.54
Free T4 (0.8-1.8 ng/dL)	2.58	1.74	0.72	1.66
Free T3 (2.3-4.2 pg/mL)		4.12	1.7	3.0
TPO antibody (< 20)		11		
ESR (0-22 mm/h)	55			

Abbreviations: ESR, erythrocyte sedimentation rate; T3, triiodothyronine; T4, thyroxine; TPO, thyroid peroxidase antibody.

Jerry is given the presumptive diagnosis of subacute thyroiditis (SAT). He is advised that the condition will progress through multiple phases—from the initial thyrotoxicosis to euthyroidism to transient hypothyroid—before resolution and is educated on the symptoms and signs to watch for. Since he presented in a euthyroid phase, with only mild anterior neck tenderness, no treatment is indicated. He is instructed to follow up for thyroid function testing in four to six weeks and to call with any symptomatic changes.

Two months later, Jerry returns with complaints of ongoing fatigue, unintentional weight gain, and "mental fog." Physical exam findings are unremarkable except for a small, firm thyroid gland without the tenderness elicited previously. Labwork reveals an elevated TSH with low free T4 and free T3. He is again counseled regarding the natural history of SAT and reassured that his symptoms will abate as his thyroid hormone levels normalize. He is advised to continue the plan of follow-up testing every four to six weeks.

Approximately eight weeks later, Jerry's thyroid function studies indicate normal levels, and he is notified of the results. Jerry comments that his symptoms have completely resolved and he is back to feeling like his usual self. He is discharged to follow-up as needed.

WHAT IS SUBACUTE THYROIDITIS?

Subacute thyroiditis is also known as *de Quervain thyroiditis* or *granulomatous giant cell thyroiditis.*[1,2] The most common cause of thy-

Christa Blose and **Holly Jodon** practice at Metabolic Disease Associates in Erie, Pennsylvania. Jodon is also Associate Director and Associate Professor in the Department of PA Studies at Mercyhurst University in Erie.

roid pain, it is a self-limited inflammatory disorder in which a painful tender goiter is associated with malaise, fever, and transient thyroid dysfunction.[2,3] As with other thyroid disorders, SAT occurs most frequently in women ages 40 to 50.[2,3] Thought to be of viral origin, it usually occurs after a URI and commonly correlates with the peak incidence of viral infections (spring/fall).[2,3]

The disruptive process begins with inflammatory destruction of thyroid follicles.[2] This causes leakage of stored colloid, which is broken down, releasing unregulated T4 and T3 into the circulation and resulting in a thyrotoxicosis that typically lasts six weeks.[1,2,4] Thyroid cells are incapable of producing new thyroid hormone during this time, so as excess circulating hormone is utilized, T4 and T3 levels become normal, then deficient, and the patient transitions through a period of euthyroidism to transient hypothyroidism.[1,2,4] As the disruption of thyroid parenchyma abates, recovery ensues. The follicles regenerate, colloid is repleted, and normal thyroid function is restored.[1-4]

SAT typically lasts four to six months, although painful thyromegaly may persist for one year after resolution of thyroid dysfunction.[2] Throughout the course of SAT, thyroid test results can be confusing, and misdiagnosis of hyperthyroidism or hypothyroidism may occur unless each phase of SAT is recognized.

"Subacute thyroiditis will progress through multiple phases before resolution."

PRODROME

The precursor URI is followed in days or weeks by the clinical manifestations of SAT. These typically include myalgia, pharyngitis, low-grade fever, and fatigue.[2]

There may be pain of varying degrees in part or all of one or both lobes; the pain often migrates to the entire gland and may radiate to the angle of the jaw or the ear of the affected side(s). Moving the head, swallowing, or coughing aggravates the pain.[2]

The hallmark of SAT is a markedly elevated ESR (often > 100 mm/h).[1-3] Leukocyte count is normal (50% of cases) or only slightly elevated (50%).[2]

THYROTOXIC PHASE

Fifty percent of patients have mild to moderate symptoms of hyperthyroidism, including nervousness, weight loss, heat intolerance, or palpitations; hoarseness or dysphagia may be present.[2] Signs include tremors or tachycardia. The thyroid gland may reveal slight to moderate unilateral enlargement, usually firm in the involved area, and tenderness may be mild, moderate, or severe.[2] Cervical lymphadenopathy is absent.[2] Serum T4 and T3 levels are elevated, and TSH is suppressed.[1-4]

Thyroid antibodies (antithyroid peroxidase antibodies [Anti-TPO or TPOAb] or antithyroglobulin antibodies [Anti-TG or TgAb]) have been found in 42% to 62% of patients with SAT.[2] These transitory immunologic markers develop several weeks after the onset and appear to be a physiologic response to the inflammatory insult to the gland.[2] In most patients, the antibody titer gradually decreases, then disappears as the disease resolves.[2-4]

The 24-hour RAIU is low (< 5%) in the toxic phase of SAT, and thyroid scan will reveal a patchy and irregular distribution of the tracer.[2,3] The thyrotoxicosis during this early phase is caused by the inflammatory release of preformed thyroid hormones (not hyperfunctioning in the gland), resulting in a "low-uptake thyrotoxicosis."[2] This differentiates SAT from the elevated uptake seen in Graves disease (> 30% at 24 hours).[2]

TRANSIENT HYPOTHYROIDISM PHASE

As circulating T4 and T3 are utilized but follicular function remains temporarily impaired, levels decline, resulting in a period of euthyroidism followed by hypothyroidism. TSH levels, previously suppressed in the thyrotoxic phase, now become elevated. This transient hypothyroidism occurs in two-thirds of patients, and the presentation varies from subclinical to pronounced.[2]

RECOVERY PHASE

After several weeks or months, all thyroid function studies return to normal and complete recovery commonly ensues. SAT rarely recurs, most likely due to immunity to the precipitating virus.[1,2,4]

MANAGEMENT

Thyroid function should be monitored by testing every two to four weeks, dependent on the severity of the patient's symptoms and

rate of progression.[1] Often, no treatment is required.[1,2]

Symptomatic relief of mild thyroid pain can be achieved with NSAIDs or aspirin (2 to 3 g/d). Severe symptoms can be treated with short-term prednisone, which should be tapered and discontinued.[1-3] Steroids suppress the inflammatory response, and the dramatic relief of thyroid pain within 24 hours can be diagnostic of SAT.[2]

During the thyrotoxic phase, β-blockers (propranolol) can alleviate adrenergic symptoms, with the dose tapered once the patient is euthyroid.[1-3] Antithyroid medications that directly inhibit thyroid hormone synthesis (eg, methimazole or propylthiouracil) are ineffective due to the lack of T4 and T3 production in the follicular cells after the inflammatory response.[2,3]

During the transient hypothyroid phase, thyroid hormone replacement may be indicated if the TSH level is markedly elevated or the phase refractory. However, levothyroxine therapy should be low dose (< 100 μg) and not be considered lifelong.[2,3]

DIFFERENTIAL DIAGNOSIS

During the prodrome, SAT is often misdiagnosed as pharyngitis. Acute suppurative thyroiditis initially may mimic SAT, but the febrile and leukocytic responses are greater, and localized edema, erythema, and tenderness become more evident as the condition progresses.

Painless or silent thyroiditis is distinguished from SAT by the lack of pain or tenderness and a normal ESR in the presence of a similar pattern of thyroid dysfunction. Graves disease presents with symptoms similar to the thyrotoxic phase of SAT, but T3 is usually disproportionately elevated compared to T4, RAIU is elevated, and thyroid antibodies are prevalent.[2]

CONCLUSION

Primary care providers may encounter SAT at some point, and a level of clinical suspicion must be maintained. Referral to endocrinology may be warranted in some cases; however, textbook cases can often be followed in primary care. Patient education is the foundation of SAT care. Symptomatic treatments may be employed as needed. Fortunately, for most patients, this self-limited disease state rarely leads to complications. **CR**

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