Silent Thyroiditis

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Silent thyroiditis is an increasingly recognized cause of transient thyrotoxicosis. Inflammatory destruction of thyroid follicles results in release of preformed thyroxine and triiodothyronine. Patients present with symptoms of thyrotoxicosis, but unlike subacute thyroiditis, lack thyroid pain or tenderness. The thyrotoxic state spontaneously resolves in 2 to 12 weeks at which time the patient either returns to a euthyroid state or passes through a transient hypothyroid phase. Diagnostic laboratory findings include elevations of thyroxine and triiodothyronine and a markedly depressed radioactive iodine uptake. It is imperative for the primary care physician to distinguish silent thyroiditis from chronic causes of hyperthyroidism, eg, Graves' disease, since treatment must be palliative rather than definitive. Long-term prognosis is usually excellent.

Over the past decade a newly recognized subacute thyroid disorder has emerged as an important cause of thyrotoxicosis. First described in 1975 by Gluck et al,[1] this disease, like classical subacute thyroiditis, is characterized by inflammation and disruption of normal thyroid architecture resulting in the release of preformed stores of thyroid hormone. Unlike subacute thyroiditis, however, patients lack thyroid pain or tenderness. This subacute form of thyroid disease has been referred to by a variety of terms. Although lymphocytic thyroiditis with spontaneously resolving hyperthyroidism remains the most accurate descriptive term, "silent" and "painless" thyroiditis reflect the absence of thyroid pain and subsequently have gained popularity. Recognition and proper management of this newly described disorder are critical, since its transient nature renders traditional means of treatment ineffective and potentially harmful.

INCIDENCE

Until a decade ago chronic thyroid disease, such as Graves' disease (toxic diffuse goiter), toxic multinodular goiter, and toxic adenoma, accounted for the vast majority of cases of hyperthyroidism. Silent thyroiditis now accounts for upwards of 20 to 30 percent of newly diagnosed cases of thyrotoxicosis.[2-5] While growing physician awareness may account for part of the increased incidence, this silent form of subacute thyroiditis appears to be occurring with increased frequency.[2]

Silent thyroiditis afflicts women more commonly than men in an approximately 2:1 to 3:1 ratio. The majority of patients are between 20 and 40 years of age, although the range is from the first to the ninth decade.[2] The clinician needs to be aware of the frequent occurrence of silent thyroiditis during the postpartum period. Thyroid dysfunction has been found in 5.5 percent of postpartum women.[6] Of those affected, transient thyrotoxicosis alone was found in 50 percent. The remaining patients were equally divided into having transient thyrotoxicosis followed by transient hypothyroidism and transient hypothyroidism alone. Of those patients found to have silent thyroiditis, 10 percent are postpartum women.[7]

PATHOGENESIS

Fundamental to the pathogenesis of the thyrotoxic state in both silent and subacute thyroiditis is destruction of follicular epithelium and loss of integrity of the storage follicle. In this first phase of silent thyroiditis, free triiodothyronine (T_3) and free thyroxine (T_4) are released, producing the clinical manifestations of thyrotoxicosis (Figure 1). Suppressed thyroid-stimulating hormone (TSH) secretion from high levels of circulating T_4 and T_3 and destruction of follicular epithe-

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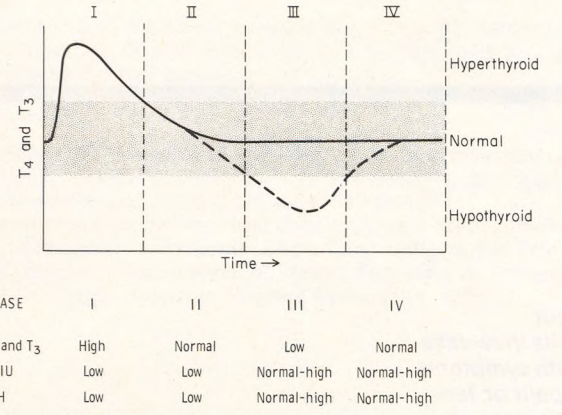

PHASE	I	II	III	IV
T_4 and T_3	High	Normal	Low	Normal
RAIU	Low	Low	Normal-high	Normal-high
TSH	Low	Low	Normal-high	Normal-high

Figure 1. Four phases of silent thyroiditis

TABLE 1. DIFFERENTIAL DIAGNOSIS OF THYROTOXICOSIS ACCORDING TO RADIOACTIVE IODINE UPTAKE (RAIU)

Low RAIU

1. Silent thyroiditis
2. Subacute thyroiditis
3. Graves' disease with iodine excess
4. Iodine-induced hyperthyroidism (Jod-Basedow)
5. Factitious hyperthyroidism
6. Struma ovarii
7. Metastatic thyroid cancer

High RAIU

1. Graves' disease
2. Toxic multinodular goiter
3. Toxic adenoma
4. Pituitary tumor secreting thyroid-stimulating hormone
5. Trophoblastic tumor

lium lead to suppression of iodine uptake, that is, low radioactive iodine uptake. As follicular stores of preformed hormone are depleted, serum levels of T_4 and T_3 normalize (phase 2), although 25 to 40 percent of patients transiently fall into a hypothyroid range (phase 3).[8] During this stage, suppression of TSH secretion is released, with serum TSH rising often to elevated levels. Radioactive iodine uptake returns to normal or supranormal values. Thyroid hormone synthesis is now stimulated by TSH and the increased iodine uptake, returning the patient to a euthyroid state (phase 4).

While both silent and subacute thyroiditis are manifest by similar alterations in thyroid hormone concentration, they differ in a number of important ways. Subacute thyroiditis is thought to have a viral origin and is associated with prodromal symptoms of myalgia, malaise, and fatigue. Histologically, subacute thyroiditis is found to have acute inflammatory changes with polymorphonuclear leukocytes, giant cells, and granulomas. The thyroid gland of patients with silent thyroiditis demonstrates distinctly different histologic features characterized by diffuse or focal lymphocytic infiltration, scant fibrosis, and absence of giant cells and granulomas.[2,7–9] Histologically, this state is reminiscent of chronic lymphocytic (Hashimoto's) thyroiditis, an autoimmune disease of the thyroid. Whether silent thyroiditis is a variant of subacute thyroiditis based on a parallel clinical presentation, a variant of Hashimoto's thyroiditis based on its histologic findings, or a newly recognized disease is still debated.

CLINICAL PRESENTATION

Patients typically present during the initial stage of thyroiditis with overt symptoms of thyrotoxicosis—nervousness, palpitations, tremor, heat intolerance, and weight loss. Contrary to the insidious onset of symptoms typically seen in chronic thyroid diseases such as Graves' disease, onset of symptoms in silent thyroiditis is often sudden and can be pinpointed in time by the patient. The hallmark finding of pain or tenderness of the thyroid seen in subacute thyroiditis is absent in silent thyroiditis. Furthermore, patients with silent thyroiditis lack associated symptoms of malaise, myalgia, fatigue, and fever commonly seen in subacute thyroiditis. Patients may present with the typical eye stare and lid lag indicative of increased sympathetic tone from any cause of hyperthyroidism; however, signs of infiltrative opthalmopathy (limitation of extraocular movements and proptosis) and pretibial myxedema characteristic of Graves' disease are rarely seen in silent thyroiditis. Examination may reveal signs of thyrotoxicosis including a resting tachycardia, warm, moist skin, fine tremor, and a quickened Achilles-tendon relaxation time. In approximately one half the patients, the thyroid is enlarged and often firm, while the remainder lack a goiter.[2,8,10]

There are no historical or physical findings that are diagnostic of silent thyroiditis. In the absence of infiltrative opthalmopathy, it is virtually impossible to distinguish between thyrotoxicosis caused by silent thyroiditis and Graves' disease. Proper diagnosis requires appropriate use of laboratory aids.

LABORATORY EVALUATION

The clinical suspicion of hyperthyroidism can be readily confirmed by measurements of serum concentrations of T_4 and T_3. A T_3/T_4 ratio of less than 20:1 suggests the diagnosis of silent thyroiditis rather than uncomplicated Graves' disease.[11] The critical diagnostic study is measurement of radioactive iodine uptake (RAIU). During the initial thyrotoxic stage of si-

lent thyroiditis, the RAIU is suppressed to values of less than 3 percent. The causes of thyrotoxicosis can be separated into two groups based on either a low or high RAIU reading (Table 1). Other causes of thyrotoxicosis associated with suppressed RAIU can usually be distinguished from silent thyroiditis based on historical or physical findings. Patients with thyrotoxicosis factitia often present a difficult diagnostic challenge. Presence of a low level of serum thyroglobulin is an important diagnostic clue.[12]

Additional laboratory studies are of limited use in silent thyroiditis. Unlike subacute thyroiditis, the erythrocyte sedimentation rate and white blood cell count are usually normal or only mildly elevated in silent thyroiditis. Antithyroid antibodies are frequently present to a modest titer in silent thyroiditis but rarely reach the high titers typical of Hashimoto's thyroiditis.[2,8]

MANAGEMENT

A correct diagnosis is essential, since proper management of silent thyroiditis is predicated by the transient nature of the disease. The duration of the initial thyrotoxic phase is usually from two to 16 weeks. Treatment can often be limited to education, reassurance, and observation. If treatment of symptoms is required, then β-adrenergic-blocking drugs, eg, propranolol 20 to 40 mg, four times a day, are effective. Agents that inhibit T_4 and T_3 synthesis, eg, propylthiouracil and methimazole, are not effective in preventing release of preformed hormone and do not affect the course of hyperthyroidism in silent thyroiditis.[13] The transient nature of the thyrotoxic state would contraindicate definitive forms of therapy with iodine 131 or by subtotal thyroidectomy. Recently, it has been found that high doses of prednisone can shorten the thyrotoxic phase but have no effect on the future course of the disease.[13] The risks of prednisone therapy outweigh the benefits of shortening an already transient thyrotoxic phase.[14] Approximately 10 percent of patients may have recurrent episodes of hyperthyroidism within several years of the initial diagnosis.[2,15] Although thyroidectomy is not indicated for the single episode of silent thyroiditis, it has been employed in a few rare patients with recurrent, disabling episodes.[7,13]

Following the depletion of thyroid stores of T_4 and T_3, the patient may develop a hypothyroid phase. Because the hypothyroid state is also transient, lasting an average of three months, reassurance and observation may be all that is required.[8] Severe or prolonged symptoms may require treatment with thyroid hormone. Since permanent hypothyroidism is uncommon, however, thyroid hormone replacement therapy should be discontinued after several months to determine whether normal thyroid function has returned.

PROGNOSIS

As previously stated, recurrent episodes of silent thyroiditis occur in approximately 10 percent of patients. In contrast, recurrent episodes of subacute thyroiditis are rare. Additionally, patients with silent thyroiditis often have a persistent goiter and a positive titer of antithyroid antibodies.[15] Permanent hypothyroidism is a definite although uncommon sequela of silent thyroiditis. Subclinical hypothyroidism, however, may be present in many patients who have recovered from silent thyroiditis.[15] Periodic follow-up evaluation of thyroid function in patients following an episode of silent thyroiditis is prudent.

References

1. Gluck FB, Nusynowitz ML, Plymate S: Chronic lymphocytic thyroiditis, thyrotoxicosis, and low radioactive iodine uptake. N Engl J Med 1975; 293:624-628
2. Nikolai TF, Brosseau J, Kettrick MA, et al: Lymphocytic thyroiditis with spontaneously resolving hyperthyroidism (silent thyroiditis). Arch Intern Med 1980; 140:478-482
3. Dorfman SG, Cooperman MT, Nelson RL, et al: Painless thyroiditis and transient hyperthyroidism with goiter. Ann Intern Med 1977; 86:24-28
4. Morrison J, Caplan RH: Typical and atypical ('silent') subacute thyroiditis in a wife and husband. Arch Intern Med 1978; 138:45-48
5. Klein I, Levey GS: Silent thyroiditis. Ann Intern Med 1982; 96:242-244
6. Amino N, Mori H, Iwatani Y, et al: High prevalence of transient postpartum thyrotoxicosis and hypothyroidism. N Engl J Med 1982; 306:849-852
7. Hamburger JI, Meier DA: Are silent thyroiditis and postpartum silent thyroiditis forms of chronic thyroiditis or different (new) forms of viral thyroiditis? In Hamberger JI, Miller JM (eds): Controversies in Clinical Thyroidology. New York, Springer-Verlag, 1981, pp 21-67
8. Woolf PD: Transient painless thyroiditis with hyperthyroidism: A variant of lymphocytic thyroiditis? Endocr Rev 1980; 1:411-420
9. Inada M, Nishikawa M, Naito K, et al: Reversible changes of the histological abnormalities of the thyroid in patients with painless thyroiditis. J Clin Endocrinol Metab 1981; 52:431-435
10. Levine SN: Current concepts of thyroiditis. Arch Intern Med 1983; 143:1952-1956
11. Amino N, Yabu Y, Miki T, et al: Serum ratio of triiodothyronine to thyroxine, and thyroxine-binding globulin and calcitonin concentrations in Graves' disease and destruction-induced thyrotoxicosis. J Clin Endocrinol Metab 1981; 53:113-116
12. Mariotti S, Martino E, Cupini C, et al: Low serum thyroglobulin as a clue to the diagnosis of thyrotoxicosis factitia. N Engl J Med 1982; 307:410-412
13. Nikolai TF, Coombs GJ, McKenzie AK, et al: Treatment of lymphocytic thyroiditis with spontaneously resolving hyperthyroidism (silent thyroiditis). Arch Intern Med 1982; 142:2281-2283
14. Dorfman S, Sachson R, Feld S: The rationale for treatment of lymphocytic thyroiditis with spontaneously resolving hyperthyroidism. Arch Intern Med 1982; 142:2261-2262
15. Nikolai TF, Coombs GJ, McKenzie AK: Lymphocytic thyroiditis with spontaneously resolving hyperthyroidism and subacute thyroiditis: Long-term follow-up. Arch Intern Med 1981; 141:1455-1458