Challenging Diagnosis of Postpartum Thyroiditis and Co-Existing Thyroid Nodule

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ABSTRACT

Objective: Postpartum thyroiditis presents as thyrotoxicosis from autoimmune thyroid inflammation that causes release of iodothyronines and diffuse, decreased thyroid uptake of both radioactive iodine and 99mTc-pertechnetate. Thyroiditis with focal “cold” thyroid nodule on thyroid scintigraphy has been previously described and attributed to localized inflammation.

Methods: We report a patient diagnosed with postpartum thyroiditis, in whom an apparently “hot” nodule on initial thyroid pinhole scintigraphy was later noted to be “cold” at follow-up imaging.

Results: Thyroid nodularity co-existing with subacute thyroiditis usually presents as focal “cold” nodules, attributed to localized inflammation in the thyroid. The diagnosis of postpartum thyroiditis in our patient was made more challenging due to the presence of a thyroid nodule with an evolving imaging appearance over time. This led to a potential for misdiagnosis of this “hot” nodule dependent on the timing of having the thyroscintigram performed early in the disease course. We hypothesized that the overactive focus of uptake was due to sparing of a pre-existing colloid nodule by the inflammatory process which later became “cold” in the recovery phase.

Conclusion: The presence of co-existing thyroiditis and thyroid nodules, both common entities, may cause diagnostic difficulty on thyroid scintigraphy due to dynamic, temporal changes in imaging appearance and the variable findings reported in the literature. Clinical surveillance and performing repeat thyroid imaging will allow correct diagnosis and appropriate management of these challenging cases. (AACE Clinical Case Rep. 2018;4:e30–e34)

INTRODUCTION

Thyroid scintigraphy with either 99mTc-pertechnetate or 123I-radiiodine can be used to investigate thyrotoxicosis, distinguishing hyperthyroidism due to Graves disease or an autonomously hyperfunctioning nodule from inflammatory conditions such as subacute, silent, or postpartum thyroiditis. The inflammatory process accompanying thyroiditis produces thyrotoxicosis through cellular disruption of thyroid follicles and release of thyroid hormone and its precursors into the circulation (1-4). The characteristic thyroid scan appearance is of diffuse, decreased thyroid radiotracer uptake with low radioactive iodine uptake (RAIU) obtained with 123I or 131I isotopes and this readily distinguishes thyroiditis from forms of hyperthyroidism due to thyroid hormone overproduction (3,4).
The presence of thyroid nodularity co-existing with subacute thyroiditis has been described, usually presenting as focal “cold” nodules, attributed to localized inflammation in the thyroid (5-7). We report a patient who was diagnosed with postpartum thyroiditis, in whom an apparent “hot” nodule on initial thyroid pinhole scintigraphy was later noted to be actually “cold” at follow-up imaging. The potential for misdiagnosis of this “hot” nodule was dependent on the timing of thyroid scintigraphy and we propose a novel mechanism to explain this early “hot” followed by late “cold” nodule observation. We hypothesized that the overactive focus of uptake was due to sparing of a pre-existing colloid nodule by the inflammatory process which later became “cold” in the recovery phase.

CASE REPORT

A 30-year-old woman presented with fatigue and laboratory abnormalities that included suppressed thyroid-stimulating hormone <0.04 μIU/mL (normal levels are 0.34 to 5.60 μIU/mL), elevated free thyroxine of 5.32 ng/mL (normal levels are 0.58 to 1.64 ng/mL), and elevated total triiodothyronine at 293 ng/dL (normal levels are 70 to 200 ng/dL). She had a 4-month history of heat intolerance and a 20-lb weight gain that had begun soon after an uncomplicated pregnancy and normal vaginal delivery. She denied fevers, sore throat or neck pain. Her only medications were prenatal vitamins and ibuprofen. She denied taking iodine-containing supplements or having a diet with high levels of iodine. She had no history of thyroid dysfunction prior to her pregnancy or neck irradiation and there was no family history of thyroid disease. Her blood pressure was 122/57 mm Hg, pulse rate 84 bpm, respiratory rate 16, temperature 97.4°F, and weight 166 pounds. She had normal extraocular eye movement and no lid-lag or stare, chemosis, or proptosis. Palpation of the neck revealed a non-tender lymphadenopathy, nor tremor.

A 99mTc-pertechnetate thyroid scan demonstrated a large nodule with increased uptake in the right, mid-upper thyroid lobe. There was markedly diminished radiotracer uptake in the remainder of the gland (Fig. 1 A). The scan was interpreted as showing an autonomously hyperfunctioning “hot” thyroid nodule with suppression of the remainder of the normal thyroid gland. However, a 24-h RAIU test with 131I was 1.3% (normal uptakes are 7 to 30%) and the scan showed increased salivary gland and background activity, findings usually associated with subacute thyroiditis, iodine contamination, or factitious thyrotoxicosis. Notably, the patient had not received iodinated intravenous contrast prior to imaging. Thyroid ultrasound showed a complex cystic/solid nodule measuring 1.3 × 1.4 × 1.6 cm with calcifications in the right lobe corresponding to the “hot nodule” on thyroid scan. There was also a heterogeneous nodule measuring 0.5 cm in the left lobe. Repeat thyroid function tests 2 weeks later showed an increase in thyroid-stimulating hormone to 6.54 μIU/L and free thyroxine was slightly low at 0.53 ng/mL. Thyroid function tests one month later demonstrated the patient to be euthyroidal with thyroid-stimulating hormone at 1.72 μIU/mL, free thyroxine at 0.74 ng/dL, and free triiodothyronine at 0.9 pg/mL. She was given a diagnosis of resolving postpartum thyroiditis. The apparent “hot” nodule was of unclear significance and plans were made for a follow-up 99mTc-pertechnetate thyroid scan.

She returned 5 months later and was clinically and chemically euthyroid. A repeat 99mTc-pertechnetate scan showed a dominant, hyperfunctioning nodule in the lateral mid-zone of the right thyroid lobe (Fig. 1 B) against a background of diffuse, increased radiotracer uptake in the remainder of the thyroid gland. The increase in radiotracer uptake was attributed to the recovery phase of thyroiditis. Upon review, the “hot” nodule on the scan 5 months earlier was interpreted as thyroiditis with relative sparing of the nodule by the inflammatory process. As the thyroid nodule now appeared relatively “cold” on scintigraphy compared to the remainder of the thyroid gland, a fine-needle aspiration biopsy was performed. The aspirate contained clusters of benign follicular epithelial cells predominantly in a honeycomb pattern on a background of macrophages with hemosiderin, colloid, and blood, consistent with a colloid nodule.

Thyroid ultrasound 1 year later demonstrated that the right sided complex nodule had increased in size to 2.4 × 1.8 × 1.8 cm. Repeat fine-needle aspiration biopsy was recommended, however the patient elected to have the thyroid nodule surgically removed. Pathologic review of the right thyroid lobe and isthmus demonstrated chronic, lymphocytic thyroiditis on a background of multinodular hyperplasia. There was a right-sided benign colloid nodule with no features of thyroid malignancy. The patient remains well with normal thyroid function.

DISCUSSION

The present case illustrates the difficulty in arriving at the correct diagnosis when there are two co-existing pathophysiologic mechanisms. It also highlights potential problems if image interpretation is solely reliant on pattern recognition. Based on pattern recognition, the initial scan was read as showing a “hot” nodule. This, coupled with the abnormal thyroid function tests, led to the erroneous conclusion that the patient had an autonomously hyperfunctioning thyroid nodule. Cytologic evaluation of the nodule was delayed when the nodule was incorrectly labeled as “hot,” as hyperfunctioning thyroid nodules have low risk for being malignant. However, the interpretation of a Plummer disease was incompatible with the RAIU test results and the decreased radiotracer uptake within the
thyroid relative to the salivary glands. Several weeks after the initial thyroid scan, serum thyroid-stimulating hormone was elevated, suggesting the recovery phase of thyroiditis. A follow-up thyroid scan when the patient was euthyroid demonstrated that this nodule was, in fact, “cold”.

Our patient was diagnosed with postpartum thyroiditis based on the timing of presentation in relationship to recent pregnancy, serial thyroid function tests and the eventual clinical recovery. Postpartum thyroiditis is a variant of silent thyroiditis, estimated to affect 5 to 7% of pregnancies (8). Although the clinical presentation is variable, it most often presents 1 to 2 months postpartum with 2 to 6 weeks of thyrotoxicosis followed by transient hypothyroidism and subsequent recovery (9). An enhanced state of immune tolerance during pregnancy followed by a rebound in immune function after delivery is assumed to be the etiology of the autoimmune syndrome observed in the puerperal period (1,8). The two major diagnostic considerations for thyrotoxicosis after delivery are Graves disease and postpartum thyroiditis which have different treatments. Postpartum thyroiditis may be identified by a milder clinical course (1) and low RAIU (10), although a RAIU test is often not performed because of concomitant breastfeeding (4). Permanent hypothyroidism can occur in 25% of postpartum thyroiditis cases, warranting screening (1,8), and elevated thyroid peroxidase antibodies in postpartum thyroiditis are associated with a higher incidence of permanent hypothyroidism (2).

Nuclear medicine imaging tests in thyroiditis are usually straightforward to interpret, yet the current case...
was challenging due to the presence of two co-existing abnormalities. As noted above, the diagnosis of thyroiditis was missed on the initial imaging. Although not an issue in the present study, thyroid imaging in the recovery phase of thyroiditis can show diffuse increased uptake and RAIU that is above the normal range (3,4). These characteristics may make the nuclear medicine studies obtained during the recovery phase of thyroiditis indistinguishable from that of Graves disease. When this occurs the RAIU may also be increased above the normal range (3,4) and there are examples of patients with silent thyroiditis in the recovery phase being mistakenly treated for Graves (11). To complicate diagnostic matters, Graves disease following episodes of subacute thyroiditis has also been reported (11-13). These 2 diagnoses can often be differentiated based on history and physical examination. Patients with thyroiditis are often less thyrotoxic than those with Graves disease. Moreover, thyroid-stimulating hormone would not be expected to be suppressed in the recovery phase of thyroiditis as is the case in Graves disease. Because of atypical presentations, some authors have cautioned delaying radioactive iodine therapy if there is diagnostic concern for inflammatory thyroiditis and the potential for spontaneous resolution (3).

Co-existence of subacute thyroiditis and focal abnormalities on thyroid scans has been previously reported. Most reports are cases of a localized “cold” nodule on a thyroid scan due to a focal area of inflammation (5-7, 14-16), although one rare case of a “hot” nodule was attributed to focal inflammation (17). Both thyroid nodules and thyroiditis are common entities, and different forms of thyroiditis may occur within a nodular thyroid gland. A euthyroid patient with a solitary, painless “cold” nodule on scintigraphy had a biopsy suggesting localized inflammation, which was attributed to a localized form of thyroiditis (14). This patient later developed thyrotoxicosis, diffuse thyroiditis on thyroid scan, and a low-normal RAU. In the recovery phase the patient became euthyroid, RAU was 36% and the nodule completely resolved. It was concluded that the patient had a focal area of thyroiditis early on and this became more generalized. A similar case was reported in a 9-year-old boy with a painful thyroid nodule that was “cold” on scintigraphy (15). Thyroiditis was suspected due to symptoms of cervical pain and fever, with elevation of erythrocyte sedimentation rate and white cell count. Antithyroglobulin and antimicrosomal antibodies were negative. The presumptive diagnosis was a localized form of subacute thyroiditis and treatment with corticosteroids led to full recovery and normalization of the thyroid scan (15). Eight patients with thyroid nodules secondary to a circumscribed form of subacute thyroiditis was previously reported (5). These nodules were firm and painful and associated with cervical discomfort. Thyroid scintigraphy showed the nodules to be “cold” in 6 cases, iso-intense in one and “hot” in one case. These patients had a rapidly favorable clinical course: 4 nodules disappeared complete-ly, 3 regressed in less than 6 months, and 1 persisted, requiring excision (5). In another series, 11 patients with subacute thyroiditis had elevated erythrocyte sedimentation rate and a painful, solitary nodule that was cold on thyroid scintigraphy (6). In all patients, the cold nodules resolved by follow-up imaging. The authors note that localized thyroiditis may present in a painful nodule even in euthyroid patients (6). A case of postpartum thyroiditis with a “cold” nodule and subsequent development of Graves disease has also been reported (7).

There have been even fewer cases of a “hot” thyroid nodule occurring concomitantly with thyroiditis. A 57-year-old woman with a painful, tender nodule that was “hot” on scintigraphy was reported (17). Fine-needle aspiration demonstrated multinuclear giant cells consistent with inflammation. Following 2 months of prednisone treatment, the nodule disappeared and the thyroid scan normalized (17). This “hot” nodule was believed to have been caused by a “localized” inflammatory process although the mechanism of increased 123I-radioiodine uptake was unknown (17). Another patient was reported to have co-existing autonomously functioning “hot” nodule and subacute thyroiditis (18). Fine-needle aspiration showed a benign nodule without inflammatory features (18). This nodule persisted on follow-up thyroid scan and apparently was spared the inflammation that resulted in reduced radiotracer uptake in the remainder of the thyroid.

To the best of our knowledge, this is the first reported case of co-existing thyroiditis and thyroid nodule in which sequential imaging and the evolving clinical course were key to arriving at the correct diagnosis. We postulate a novel mechanism for the observed changing focal imaging findings. We postulate that focal sparing of a pre-existing colloid nodule by the inflammatory process causes the nodule to appear relatively “hot” in relationship to the remainder of the affected thyroid. In the recovery phase, when there is “rebound” increased radiotracer uptake in the thyroid, the nodule appears either “cold” or normal in comparison to surrounding thyroid tissues. Of note, our protocol for thyroid scans uses 99mTc-pertechnetate as the radiotracer, which represents trapping function. In contrast, 123I-radioiodine represents both trapping and organification thyroid function. This difference in function can occasionally lead to discordance between scans when evaluating thyroid nodules, such as the so-called “hot” nodule on 99mTc-pertechnetate and “cold” nodule on 123I-radioiodine. We believe, but cannot verify, that our observations would have been the same if 123I-radioiodine had been used as the radiotracer instead.

The present case illustrates the potential for erroneous interpretations of nuclear medicine thyroid studies when multiple pathophysiological processes co-exist. For most patients having thyroid imaging for thyrotoxicosis, repeat imaging is rarely performed. However, for patients with co-existing thyroiditis and thyroid nodule, this is not the
case. Care should be taken when assigning a nodule to be “hot” if RAIU is low or there is clinical suspicion for thyroiditis. Assignment of a nodule as “hot” or “cold” may require waiting until recovery from thyroiditis.

CONCLUSION

The presence of co-existing thyroiditis and thyroid nodules, both common entities, may cause diagnostic difficulty. This is due to dynamic changes in thyroid scintigraphy that occur as thyroid function changes during the different phases of thyroiditis. Clinical surveillance and repeat thyroid imaging will lead to the correct diagnosis and appropriate management in these challenging cases.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

REFERENCES

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