

## FETAL ENDOSCOPIC TRACHEAL OCCLUSION

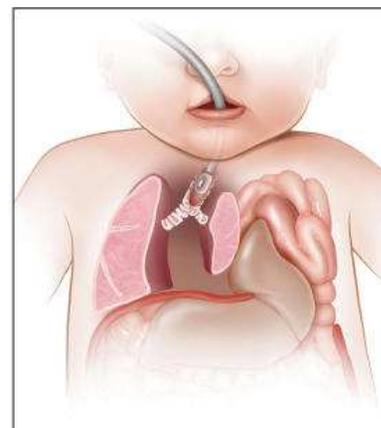
# KNOWING WHAT TO LOOK FOR MAY NOT BE EASY. KNOWING WHERE TO LOOK FOR HELP IS.

**Texas Children's Fetal Center™** is home to one of the nation's largest congenital diaphragmatic hernia (CDH) programs, with outcomes among the best in the country.

Ranging from moderate to severe cases of CDH, we offer fetal endoscopic tracheal occlusion (FETO), a breakthrough research protocol with potential to dramatically improve lung growth prior to birth. Coupled with outstanding multidisciplinary, postnatal surgical care, this treatment gives more babies with CDH a chance at a healthy life. As one of the first in the country to offer FETO, with one of the most experienced staffs in North America, we're proud to be on the leading edge of this revolutionary care.

Send us your toughest cases. We're known for delivering.

Learn more: [women.texaschildrens.org/fetal](https://www.women.texaschildrens.org/fetal) or 1-877-FetalRx



*FETO is a minimally invasive procedure in which a tiny balloon is inserted into the fetus to plug the trachea. The balloon is inflated, left in place for several weeks to allow the fetus' lungs to grow, then removed a few weeks prior to delivery.*



Pavilion  
for Women

# Subacute Thyroiditis—An Often Overlooked Sonographic Diagnosis

## Report of 3 Cases

Margaret Yee Wah Lee, MB, BCh, BAO, Winnie Wing Chuen Lam, MBBS, FRCR, FAMS,  
Wai Yin Wong, MBBS, FRCR

The characteristic sonographic finding of subacute thyroiditis of a heterogeneous poorly defined hypoechoic area in the thyroid gland may mimic that of thyroid malignancy. This finding needs to be interpreted in the correct clinical context to avoid an unnecessary biopsy. We describe 3 patients who underwent thyroid biopsy on the basis of suspicious sonographic findings but who subsequently had a diagnosis of subacute thyroiditis.

**Key Words**—biopsy; sonography; subacute thyroiditis; thyroid function test

Received May 19, 2015, from the Department of Nuclear Medicine and Positron Emission Tomography, Singapore General Hospital, Singapore. Revision requested June 11, 2015. Revised manuscript accepted for publication August 6, 2015.

Address correspondence to Margaret Yee Wah Lee, MB, BCh, BAO, Department of Nuclear Medicine and Positron Emission Tomography, Singapore General Hospital, Outram Road, Singapore 169608, Singapore.

E-mail: margaret.lee@mohh.com.sg

### Abbreviations

Tc, technetium; T<sub>4</sub>, thyroxine; TSH, thyrotropin; T<sub>3</sub>, triiodothyronine

doi:10.7863/ultra.15.05052

The diagnosis of subacute thyroiditis is usually evident on the basis of patients' clinical presentation and biochemical results. Thyroid sonography is rarely required for diagnosis. As such, these patients are seldom encountered in the radiology department. Radiologists who come across a heterogeneous hypoechoic thyroid nodule on sonography may overlook the differential diagnosis of subacute thyroiditis.

We describe 3 patients who presented with nonspecific clinical signs and symptoms that were not typical of subacute thyroiditis. Two of these patients were referred for thyroid sonography to evaluate a palpable thyroid nodule that was considered an incidental finding. In the third patient, sonography was performed to exclude thyroid lymphoma. All 3 patients eventually had a diagnosis of subacute thyroiditis based on cytologic findings or follow-up sonography.

## Case Descriptions

### Case 1

A 38-year-old woman had pain in the left ear for 6 weeks, which was associated with occasional neck pain. An ear infection was diagnosed by her general practitioner and treated with 2 courses of antibiotics without relief. She was referred to an otolaryngologist, who detected a left thyroid nodule that was nontender to palpation. The patient was afebrile. Her heart rate was 85 beats per minute. There were no overt signs of thyrotoxicosis.

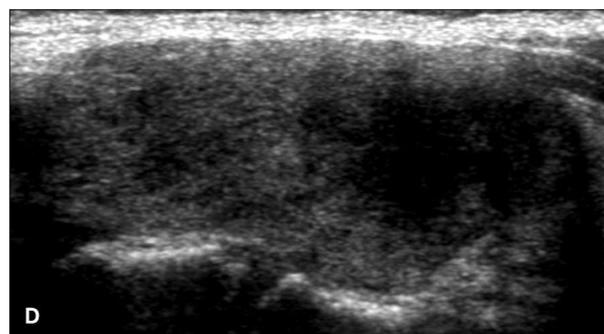
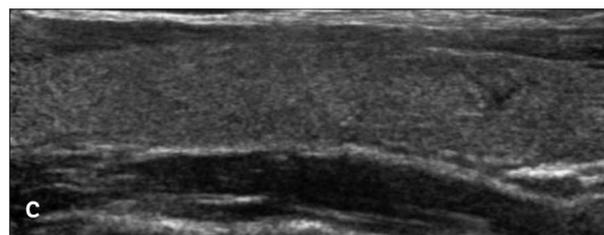
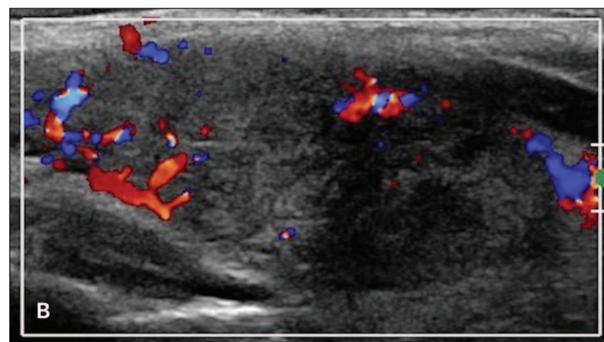
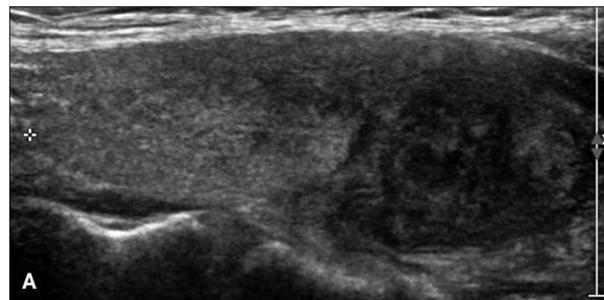
Laboratory investigations showed an elevated erythrocyte sedimentation rate of 58 mm/h (normal range, 0–20 mm/h). The leukocyte count was normal at  $7.3 \times 10^9/L$  (normal range,  $4.0\text{--}10.0 \times 10^9/L$ ). Thyroid function tests revealed biochemical hyperthyroidism: the free thyroxine ( $T_4$ ) level was 21.2 pmol/L (normal range, 8.8–14.4 pmol/L); free triiodothyronine ( $T_3$ ) was 8.0 pmol/L (normal range, 3.2–5.3 pmol/L); and thyrotropin (TSH) was 0.21 mU/L (normal range, 0.65–3.70 mU/L).

The patient was referred for sonography to evaluate the left thyroid nodule. The scan showed poorly defined hypoechoic areas in the left lobe with a heterogeneous nodule measuring  $3.3 \times 1.9 \times 1.7$  cm within the lower pole (Figure 1A), for which biopsy was recommended. The nodule showed peripheral vascularity (Figure 1B). The right lobe was normal (Figure 1C). Fine-needle aspiration cytology revealed heavy infiltration with neutrophils and a granulomatous reaction, with the presence of epithelioid histiocytes and multinucleated giant cells, compatible with subacute thyroiditis.

A week later, the patient noted that the neck pain had worsened and was associated with intermittent fever. She was treated with 400 mg of ibuprofen 3 times per day and 30 mg of prednisolone every morning. Two weeks later, she reported that the pain in the left ear and left side of the neck had subsided. However, she developed pain in the right ear and right side of the neck. Repeated thyroid function tests revealed further suppression of TSH (0.023 mU/L), whereas free  $T_4$  and  $T_3$  remained elevated at 27.3 and 6.6 pmol/L, respectively. On sonography, the heterogeneous echoes in the lower pole of the left lobe had involved the entire lobe. The right lobe, which was previously normal, was now similarly affected (Figure 1D). Bilateral small cervical lymph nodes with benign features were noted. A technetium  $Tc^{99m}$  pertechnetate scan of the thyroid showed a diffuse reduction in radiotracer uptake.

The patient was given a further course of anti-inflammatory medications. By 3 months from the onset of symptoms, her pain had subsided, although the thyroid

**Figure 1.** Images from a 38-year-old woman with subacute thyroiditis of the left lobe and subsequent spread to the right lobe. **A**, Longitudinal sonogram of the left lobe showing poorly defined hypoechoic areas anteriorly and a heterogeneous nodule in the lower pole. **B**, Color Doppler sonogram showing peripheral vascularity anterior to the nodule. **C**, Normal echoes in the right lobe. **D**, Longitudinal section of the right lobe 3 weeks later showing interval enlargement and heterogeneous low echoes.



function tests still showed hyperthyroidism. On follow-up at 4 months, the patient developed biochemical hypothyroidism, with a raised TSH level of 5.62 mU/L and normal free T<sub>4</sub> of 12.1 pmol/L. The thyroid function test results normalized spontaneously on further follow-up at 6 months.

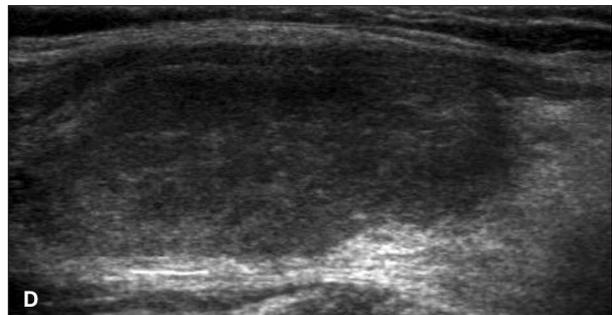
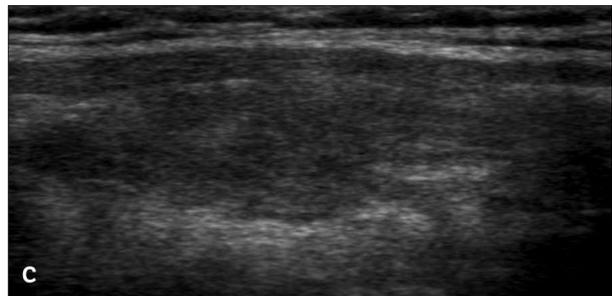
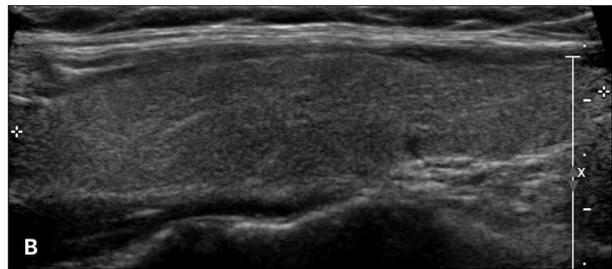
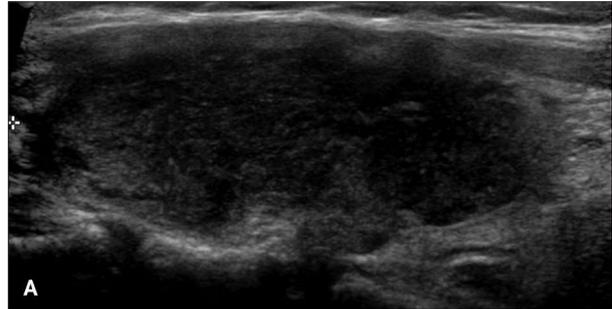
### Case 2

A 67-year-old woman presented with a 2-week history of fever associated with sore throat, chills, and rigors. She also had left neck swelling for 1 month. On physical examination, there was a 2 × 3-cm nontender swelling in the left side of the neck. Her oropharynx was erythematous with a pustule in the uvula. She was febrile (38.5°C) and tachycardic at 111 beats per minute. Her leukocyte count was raised at  $14.2 \times 10^9$ /L. Her C-reactive protein level was elevated at 111 mg/L (normal range, 0.2–9.1 mg/L). Her medical history was notable for Burkitt lymphoma diagnosed 18 years previously. She had been treated with systemic chemotherapy and radiotherapy to the abdomen with no evidence of disease 3 years after diagnosis. The clinical impression was that of fever secondary to pharyngitis, with further workup of her neck swelling needed to exclude recurrent lymphoma.

Computed tomography of the neck, thorax, abdomen, and pelvis was done, which showed a poorly defined 2-cm infiltrating lesion expanding the left thyroid. There was no evidence of recurrent disease within the thorax, abdomen, and pelvis. Sonography of the thyroid gland was also done, which showed a large hypoechoic solid lesion occupying almost the entire left lobe (Figure 2A). This lesion was deemed to be suspicious for recurrent lymphoma. The right lobe appeared normal (Figure 2B). Several cervical lymph nodes with benign features were noted bilaterally. The patient underwent ultrasound-guided core biopsy of her left thyroid lesion. Histologic analysis showed benign thyroid follicles in dense fibrous stroma. There was no increase in plasma cells to suggest immunoglobulin 4-related disease or multinucleated giant cells to suggest granulomatous thyroiditis. No evidence of malignancy was present.

Her initial thyroid function tests showed that the TSH level was 0.02 mU/L; free T<sub>4</sub> was 32.8 pmol/L; and free T<sub>3</sub> was 6.2 pmol/L. She started taking 20 mg of carbimazole twice per day. Two weeks later, the patient had palpitations, fatigue, and weight loss. Thyroid function tests showed a TSH level of 0.015 mU/L, free T<sub>4</sub> of 41.6 pmol/L, and free T<sub>3</sub> of 6.7 pmol/L. Thyrotropin receptor antibody test results were negative. A Tc<sup>99m</sup> pertechnetate thyroid scan was done, after carbimazole was held off for 3 days, which showed a

**Figure 2.** Images from a 67-year-old woman with subacute thyroiditis of the left lobe and subsequent spread to the right lobe. **A**, Longitudinal sonogram of the left lobe showing an enlarged left lobe with heterogeneous echoes. **B**, Longitudinal sonogram of the normal right lobe. **C**, Longitudinal sonogram after 2 weeks showing a small left lobe with partial normalization of echoes. **D**, Longitudinal section of the right lobe 2 weeks later showing interval enlargement and reduction in echogenicity.



global marked reduction in radiotracer uptake, thus excluding a toxic nodule. Sonographic correlation showed an interval reduction in size of the left lobe, with partial normalization of echogenicity (Figure 2C). Conversely, the right lobe showed interval enlargement and reduction of echogenicity (Figure 2D), with no internal vascularity. Scan findings were interpreted as resolving subacute thyroiditis in the left lobe and interval development of thyroiditis affecting the right lobe. Scintigraphy showed poor thyroidal uptake of  $Tc^{99m}$  pertechnetate. The patient was treated with 400 mg of ibuprofen and 30 mg of propranolol 3 times per day. Thyroid function tests 6 weeks later showed marked improvement: TSH of 0.16 mU/L and free  $T_4$  of 9.6 pmol/L. On follow-up at 3 months, the patient had developed hypothyroidism, with a TSH level of 10.1 mU/L and free  $T_4$  of 8.0 pmol/L. She started taking 25  $\mu$ g of L-thyroxine every morning.

### Case 3

A 43-year-old man with no notable medical history had right-sided headache and intermittent fever for 1 month. The headache was preceded by right-sided neck pain, which subsided after 1 week. He felt mild difficulty in swallowing occasionally. There was no antecedent upper respiratory tract infection. There was no vomiting, nausea, or blurring of vision.

On physical examination, his heart rate was 82 beats per minute. He had daily spikes of temperature between 38°C and 39°C. A small right-sided neck swelling was nontender to palpation. He was clinically euthyroid. Laboratory investigations revealed a slightly elevated leukocyte count of  $11.4 \times 10^9/L$  and a raised C-reactive protein level of 81 mg/L. Thyroid function tests showed a mildly elevated free  $T_4$  level of 14.8 pmol/L, normal free  $T_3$  of 4.2 pmol/L, and low TSH of 0.49 mU/L. Results from chest radiography, analysis of cerebrospinal fluid obtained via a lumbar puncture, and a computed tomographic scan of the brain were unremarkable.

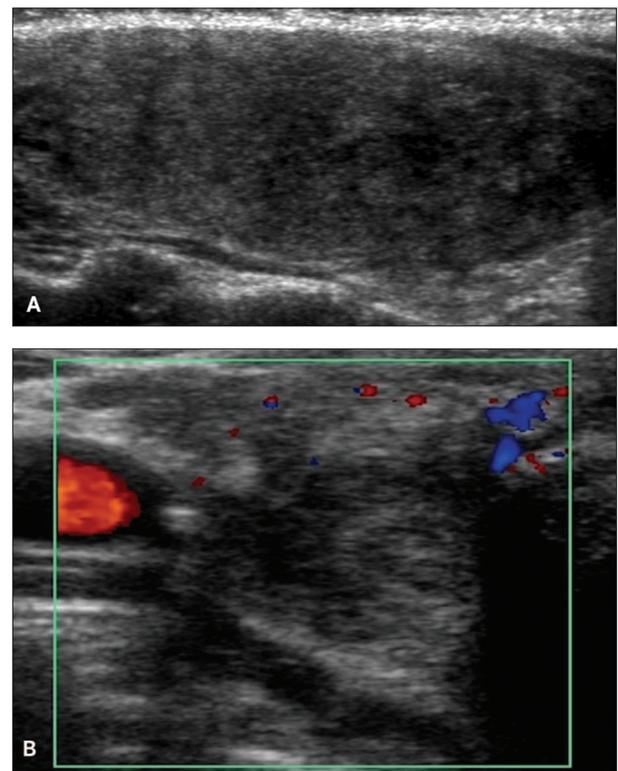
At this stage, the clinical impression was giant cell arteritis, but the patient declined to undergo a diagnostic biopsy of the temporal artery. He was given 1 g of paracetamol 3 times per day for symptomatic relief. In view of the neck swelling, the patient was referred for thyroid scintigraphy, which showed poor radiotracer uptake. Sonography showed an enlarged nodular right lobe comprising heterogeneous echoes with a marked reduction in vascularity (Figure 3). The left lobe was normal in size with a slightly hypoechoic appearance but contained no nodules. No suspicious cervical adenopathy was detected. The scan findings were interpreted as likely subacute thyroiditis, tak-

ing into account the thyroid function tests results; however, thyroid cancer could not be excluded. The referring clinician proceeded to perform a fine-needle aspiration biopsy of the right thyroid. Cytologic analysis revealed follicular cells admixed with lymphocytes and polymorphs. There were prominent granulomas consisting of clustered epithelioid histiocytes and multinucleated giant cells, compatible with subacute thyroiditis. By 2 months after the onset of symptoms, the patient's headache and fever had subsided, with normalization of thyroid function test results on follow-up at 4 months.

### Discussion

Subacute thyroiditis, or de Quervain thyroiditis, is the most common cause of painful thyroiditis.<sup>1</sup> This disease refers to self-limiting thyroiditis of presumed viral etiology. Several possible pathogens have been described, including mumps virus, Epstein-Barr virus, Coxsackie virus, adenovirus, and influenza viruses.<sup>2</sup>

**Figure 3.** Images from a 43-year-old man with subacute thyroiditis. **A**, Longitudinal sonogram showing a swollen right lobe with heterogeneous echoes. **B**, Transverse color Doppler sonogram of the upper pole showing absence of internal vascular flow in the hypoechoic areas.



Clinically, patients present with constant anterior neck pain that typically radiates to the jaw or ear, which may be aggravated by swallowing.<sup>2,3</sup> Patients often have a preceding history of an upper respiratory tract infection with a prodromal phase of low-grade fever and malaise.<sup>1-3</sup> The thyroid gland is tender to palpation, and a small diffuse goiter may be present.<sup>4</sup> Occasionally, subacute thyroiditis can present with a nontender nodule.<sup>3,5</sup> The clinical course includes 3 characteristic phases. There is an early hyperthyroid phase caused by leakage of follicular contents and preformed thyroid hormone lasting 3 to 6 weeks.<sup>2</sup> This phase is followed by a hypothyroid phase in 30% of patients, which is caused by depletion of preformed thyroid hormone and may last several months. There is then typically eventual recovery, with patients resuming their euthyroid state.<sup>2</sup> In addition, there is elevation of the erythrocyte sedimentation rate and C-reactive protein level. The leukocyte count may be normal or slightly elevated.<sup>1</sup>

Subacute thyroiditis is usually diagnosed clinically, supported by biochemical investigations. Imaging and cytologic analysis are rarely required.<sup>2</sup> Subacute thyroiditis produces a characteristic sonographic finding of poorly defined hypoechoic areas with a heterogeneous echo pattern,<sup>6-8</sup> which is difficult to differentiate from malignancy. Several investigators have scrutinized the characteristics of the hypoechoic areas as potential discriminators between subacute thyroiditis and malignancy. Park et al<sup>6</sup> reported that poorly defined hypoechoic avascular areas without round or ovoid mass formation on multiple imaging planes were features of benignity. In such cases, follow-up sonography is recommended rather than biopsy. However, biopsy is needed to exclude malignancy in those lesions that appear as focal masses.<sup>6</sup> In a recent study, Pan et al<sup>9</sup> reported that sonographic features that would more likely predict atypical subacute thyroiditis rather than malignancy included poorly defined margins and a centripetal reduction in echogenicity. Whereas the diagnostic sensitivity and specificity of poorly defined margins for atypical subacute thyroiditis were 87% and 81% respectively, a centripetal reduction in echogenicity yielded 100% specificity for atypical subacute thyroiditis. Thus, routine biopsy of lesions with the latter characteristic may not be needed.<sup>9</sup>

Other sonographic features of subacute thyroiditis have been described. There is absent vascular flow on color Doppler sonography in the acute stage and slightly increased vascularity in the recovery stage.<sup>7</sup> In particular, internal vascularity in contrast to peripheral or mixed vascularity is a useful discriminator for ruling out subacute thyroiditis.<sup>9</sup> In our series of 3 patients, the hypoechoic regions showed absent internal vascularity. Subacute thyroiditis involving

only one lobe of the thyroid may give the appearance of a nodule on sonography. In the recovery phase, both the echogenicity and thyroid size will normalize.<sup>8</sup> Fifty percent of patients with subacute thyroiditis who have unilateral neck pain have spread of the hypoechoic areas to the contralateral gland within 7 days of onset.<sup>10</sup> The latter characteristic is exemplified in cases 1 and 2, in which the patients underwent follow-up sonography. In particular, the characteristic recovery of the affected lobe and development of new hypoechoic areas in the contralateral lobe in case 2 helped reinforce the diagnosis of subacute thyroiditis, despite the absence of typical features on cytologic analysis. It has been reported that fine-needle aspiration performed during the acute phase of subacute thyroiditis may also pose challenges to the cytopathologist because of the lack of certain characteristic features such as follicular cells with intravacuolar granules, epithelioid granulomas, and multinucleated giant cells.<sup>11,12</sup>

In our 3 patients, the diagnosis was initially elusive because of their atypical clinical presentations. The indications for thyroid sonography in these patients were to evaluate thyroid nodules that were seemingly unrelated to the primary diagnosis. In all 3 patients, sonography showed poorly defined hypoechoic areas with absent internal vascularity. As malignancy could not be excluded on the basis of these findings alone, the patients underwent fine-needle aspiration biopsy. However, the patient records revealed newly diagnosed hyperthyroidism, which could have prompted the sonologists to alert the clinicians to the diagnosis of subacute thyroiditis with greater confidence. Moreover, our patients had scintigrams showing poor thyroidal Tc<sup>99m</sup> pertechnetate uptake. A Tc<sup>99m</sup> pertechnetate thyroid scan is useful in the setting of hyperthyroidism to differentiate between the differential diagnoses of Graves disease, an autonomous toxic nodule, and subacute thyroiditis.<sup>13</sup> Graves disease will show diffuse increased isotope uptake in the gland, whereas subacute thyroiditis will show diffuse reduced isotope uptake. On the other hand, an autonomous toxic nodule will show focal increased uptake in the nodule with suppression of isotope uptake in the rest of the gland. This differentiation is important, as treatment differs greatly. Graves disease and autonomous nodules can be treated with antithyroid drugs or radioiodine therapy, whereas subacute thyroiditis is typically self-limiting.

In conclusion, the sonographic appearance of the thyroid during the acute phase of subacute thyroiditis may mimic thyroid carcinoma or lymphoma. Sonologists who encounter a heterogeneous hypoechoic nodule, notably in the absence of adenopathy that would be suspicious for

malignancy, may find it useful to refer to the patients' clinical presentations, biochemical results, and thyroid scintigraphy. In particular, if the thyroid function test shows a low TSH result in a patient without a history of hyperthyroidism, together with poor thyroid radiotracer uptake, subacute thyroiditis is very likely. Instead of recommending a biopsy of the hypoechoic areas, it would be prudent to schedule follow-up sonography to document normalization of echogenicity and to uncover any suspicious thyroid nodules that may have been obscured by the inflammatory changes.

## References

1. Pearce EN, Farwell AP, Braverman LE. Thyroiditis. *N Engl J Med* 2003; 348:2646–2655.
2. Samuels MH. Subacute, silent, and postpartum thyroiditis. *Med Clin North Am* 2012; 96:223–233.
3. Fatourechi V, Aniszewski JP, Fatourechi GZE, Atkinson EJ, Jacobsen SJ. Clinical features and outcome of subacute thyroiditis in an incidence cohort: Olmsted County, Minnesota, study. *J Clin Endocrinol Metab* 2003; 88:2100–2105.
4. Alfadda AA, Sallam RM, Elawad GE, Al Dhukair H, Alyahya MM. Subacute thyroiditis: clinical presentation and long term outcome. *Int J Endocrinol* 2014; 794943.
5. Daniels GH. Atypical subacute thyroiditis: preliminary observations. *Thyroid* 2001; 11:691–695.
6. Park SY, Kim EK, Kim MJ, et al. Ultrasonographic characteristics of subacute granulomatous thyroiditis. *Korean J Radiol* 2006; 7:229–234.
7. Frates MC, Marqusee E, Benson CB, Alexander EK. Subacute granulomatous (de Quervain) thyroiditis: grayscale and color Doppler sonographic characteristics. *J Ultrasound Med* 2013; 32:505–511.
8. Ruchala M, Szczepanek-Parulska E, Zybek A, et al. The role of sonoelastography in acute, subacute and chronic thyroiditis: a novel application of the method. *Eur J Endocrinol* 2012; 166:425–432.
9. Pan FS, Wang W, Wang Y, et al. Sonographic features of thyroid nodules that may help distinguish clinically atypical subacute thyroiditis from thyroid malignancy. *J Ultrasound Med* 2015; 34:689–696.
10. Nishihara E, Ohye H, Amino N, et al. Clinical characteristics of 852 patients with subacute thyroiditis before treatment. *Intern Med* 2008; 47:725–729.
11. García Solano J, Giménez Bascañana A, Sola Pérez J, et al. Fine-needle aspiration of subacute granulomatous thyroiditis (De Quervain's thyroiditis): a clinico-cytologic review of 36 cases. *Diagn Cytopathol* 1997; 16:214–220.
12. Ofner C, Hittmair A, Krll I, et al. Fine needle aspiration cytodiagnosis of subacute (de Quervain's) thyroiditis in an endemic goitre area. *Cytopathology* 1994; 5:33–40.
13. Sarkar SD. Benign thyroid disease: what is the role of nuclear medicine? *Semin Nucl Med* 2006; 36:185–193.