Primary Thyroid Lymphoma

Role of Ultrasound-Guided Needle Biopsy

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Objective. The purpose of this study was to describe the sonographic findings of primary thyroid lymphoma and evaluate the role of ultrasound-guided biopsy in diagnosing thyroid lymphoma. ***Methods.*** This study included 6 patients (age range, 56–72 years; mean, 62.5 years). We searched the database of our institution and retrospectively collected data on the thyroid lymphomas that were confirmed pathologically. All of the sonograms and medical records were reviewed retrospectively. ***Results.*** All 6 patients had an enlarged neck mass and underwent ultrasound-guided fine-needle aspiration biopsy. The most notable sonographic feature of primary thyroid lymphoma was a marked hypoechoic mass compared with the residual thyroid tissue. Among the 6 patients with a diagnosis of thyroid lymphoma, 3 (50%) had a diagnosis of lymphoma by ultrasound-guided fine-needle aspiration biopsy. Final pathologic results were obtained by ultrasound-guided core needle biopsy (3/6 patients [50%]) or thyroidectomy (3/6 [50%]). Most patients with thyroid lymphoma (5/6 [83.3%]) were found to have diffuse large B-cell lymphoma and were treated with chemotherapy with or without radiotherapy. In 1 patient with follicular lymphoma, diagnosis and treatment were accomplished by total thyroidectomy. ***Conclusions.*** Our results show that ultrasound-guided core needle biopsy can be a safe and accurate method for diagnosing thyroid lymphoma and may be a suitable replacement for diagnostic thyroid surgery. ***Key words:*** lymphoma; head and neck neoplasms; thyroid biopsy; thyroid neoplasm; ultrasound guidance.

Abbreviations
US-CNB, ultrasound-guided core needle biopsy; US-FNAB, ultrasound-guided fine-needle aspiration biopsy

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Primary thyroid lymphoma is uncommon and accounts for only 2.5% to 5% of all thyroid malignancies.[1,2] Most patients are elderly women and have symptoms of airway obstruction and a rapidly enlarging thyroid mass with a history of longstanding thyroiditis.[2] In patients with primary thyroid lymphoma, the treatment of choice is not surgery but radiation therapy and chemotherapy.[3] However, surgery is often performed to diagnose the primary thyroid lymphoma because of the limitations of ultrasound-guided fine-needle aspiration biopsy (US-FNAB) for diagnosis or subclassification of lymphoma.[1,3] Some reports have described ultrasound-guided core needle biopsy (US-CNB) as an accurate and safe procedure for diagnosing thyroid nodules.[4,5] Recently, for evaluation of cervical lymphadenopathy, several authors suggested that US-CNB could provide sufficient diagnosis and subclassification of lymphoma.[6,7]

The objective of this study was to describe the sonographic findings of primary thyroid lymphoma and evaluate the role of ultrasound-guided biopsy in diagnosing thyroid lymphoma.

Materials and Methods

Between January 2003 and December 2005, 6 patients (4 female and 2 male) had a pathologic diagnosis of thyroid lymphoma. The ages of the 6 patients ranged from 56 to 72 years (mean, 62.5 years). All 6 patients had an enlarged neck mass. Sonography was performed with an HDI 3000 or HDI 5000 system (Philips Medical Systems, Bothell, WA) or an Acuson Sequoia 512 system (Siemens Medical Solutions USA, Inc, Mountain View, CA) for evaluation of the thyroid gland and neck. All 6 sonograms and clinical records were reviewed retrospectively by a radiologist. We searched the patients' medical records for cytologic and pathologic reports as well as follow-up data. The sonograms were analyzed for the location, echogenicity, and disease extent of lymphoma and the underlying thyroid echogenicity.

Ultrasound-guided FNAB was performed in all 6 patients by 1 radiologist with a 23-gauge needle attached to a 20-mL disposable plastic syringe and aspirator. Each lesion was aspirated at least twice. Materials obtained from the aspiration biopsy were expelled onto glass slides and smeared. All smears were placed immediately in 95% alcohol for Papanicolaou staining. The remainder of the material was rinsed in saline for processing as a cell block. Additional immunohistochemical staining was made on a case-by-case basis, according to the cytopathologist's needs. Additional special studies, such as flow cytometry, DNA analysis, and immunophenotyping, were not performed.

For final pathologic confirmation, 3 patients underwent US-CNB, and the remaining 3 underwent surgery. All US-CNBs were performed by the same radiologist who performed the US-FNABs. Biopsies were performed on the patients, who received local anesthesia, after a small skin incision was made. Thyroid tissues were obtained by a freehand CNB technique, repeated 3 or 4 times, using a 7.5- to 12-MHz ultrasound transducer and a short-excursion (12-mm) spring-loaded automated gun (Pro-Mag 1.2; Manan Medical Products, Inc, Northbrook, IL) with a 16-gauge cutting needle. Additional histochemical and immunohistochemical stains were used when needed. Patients were monitored for 1 hour after the procedure to ensure that there was no bleeding. There were no complications, such as bleeding or severe neck pain. For evaluating the quality of US-CNB, sample adequacy was assessed as a subjective judgment by the cytopathologist.

Results

All 6 patients had an enlarged neck mass. Two patients also had hoarseness or throat discomfort. All patients had a history of chronic hypothyroidism or Hashimoto thyroiditis. The most notable sonographic feature in all 6 patients was a marked hypoechoic mass compared with the residual thyroid tissue (Figure 1). On sonography, 2 of these 6 cases showed contiguous spread from 1 lobe into the contralateral lobe through the isthmus of the thyroid gland (Figure 2).

Cytopathologic results of FNAB, CNB, and surgery are summarized in Table 1. Lymphoma was correctly diagnosed in 3 (50%) of the 6 cases by FNAB. In the remaining 3 patients, the cytologic findings were nondiagnostic, lymphocytic thyroiditis, and suspicious low-grade lymphoma, respectively. For pathologic confirmation, CNB and surgery were conducted in 3 patients each. All CNB specimens were considered adequate for histologic diagnosis. Three patients underwent surgery by their clinicians' request. Most of the thyroid lymphomas (5/6 patients [83.3%]) were revealed to be diffuse large B-cell lymphoma; the remaining diagnosis was made pathologically and was revealed to be follicular lymphoma.

Three patients with diffuse large B-cell lymphoma diagnosed by CNB were treated with chemotherapy (cyclophosphamide, mitoxantrone, vincristine, and prednisone) with (n = 1) or without (n = 2) radiation therapy. Two patients with diffuse large B-cell lymphoma diagnosed by surgery were treated with adjuvant chemotherapy. One patient with follicular lymphoma diagnosed by surgery did not receive any other adjuvant treatment. Five of the 6 patients with lymphoma were followed for 12 to 39 months without evidence of lymphoma recurrence. The remaining patient died of septic shock during chemotherapy.

Discussion

Most patients with thyroid lymphoma have symptoms of a rapidly enlarging thyroid mass or airway obstruction.[8,9] The sonographic findings of thyroid lymphoma were reported to be extremely hypoechoic masses intermingled with echogenic structures, although the echogenicity of the unaffected thyroid tissue was also low because of coexisting thyroiditis.[8,10] Although clinical and sonographic features of thyroid lymphoma have been reported,[8,9] pathologic confirmation is obligatory because of its rare incidence and the difficulty of differentiating it from other thyroid tumors. In some cases, lymphocytic thyroiditis and anaplastic carcinoma should be differentiated from thyroid lymphoma. Lymphocytic thyroiditis is usually seen as diffusely heterogeneous with hypoechogenicity on sonography, although focal lymphocytic thyroiditis has a wide variety of appearances.[11] Although an etiologic association of Hashimoto thyroiditis with development of thyroid lymphoma has been confirmed by epidemiologic studies,[12] there is no satisfactory screening imaging that can help identify the early transformation of Hashimoto thyroiditis into lymphoma.[13] Therefore, when a patient with Hashimoto thyroiditis has a rapidly enlarging thyroid gland, extremely hypoechoic masses intermingled with echogenic structures on sonography can be helpful. If a patient has a rapidly enlarging neck mass, anaplastic carcinoma of the thyroid gland can be suspected. Takashima et al[14] reported the computed tomographic features of anaplastic carcinoma of the thyroid gland, which more commonly has calcifications and necrosis than does primary thyroid lymphoma. In addition, anaplastic thyroid carcinoma more frequently

Figure 1. Images from a 56-year-old man with hypothyroidism for 3 years and a recently enlarging neck mass. **A**, Transverse sonogram of the left thyroid gland shows an enlarged and markedly hypoechoic mass compared with the hypoechogenicity of the right thyroid gland. **B**, Ultrasound-guided core needle biopsy was performed (left, before firing; right, after firing; arrows indicate the needle). **C**, Core needle biopsy specimen shows diffuse proliferation of large lymphoid cells with vesicular nuclei mixed with a small number of reactive small lymphocytes (hematoxylin-eosin, original magnification ×200).

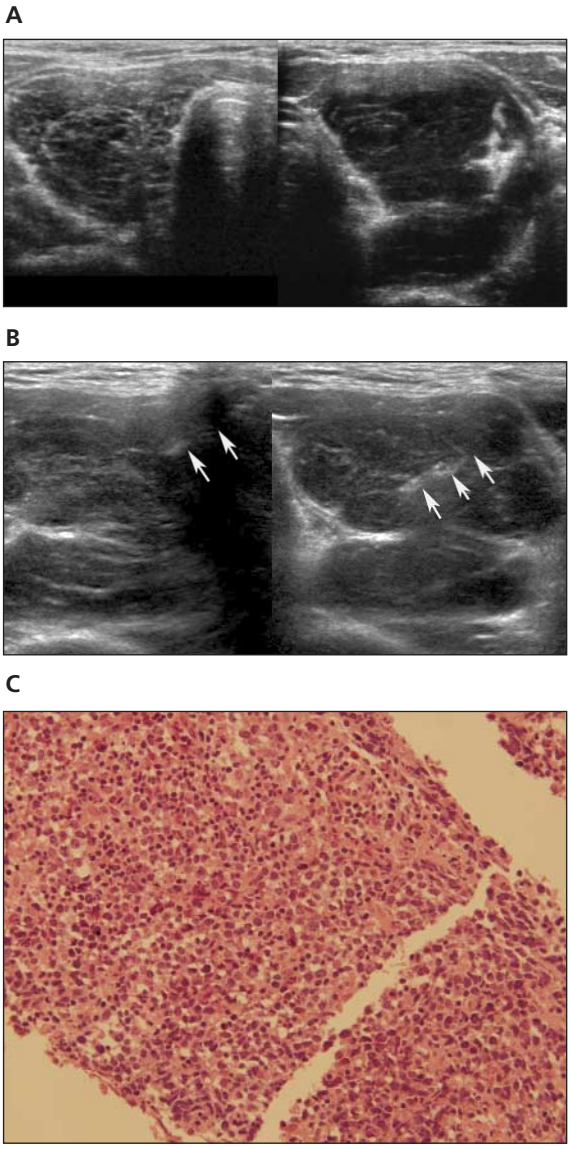

Figure 2. Transverse sonogram from a 63-year-old woman with known Hashimoto thyroiditis and a recently enlarging neck mass shows marked hypoechogenicity of the left thyroid gland and right isthmus.

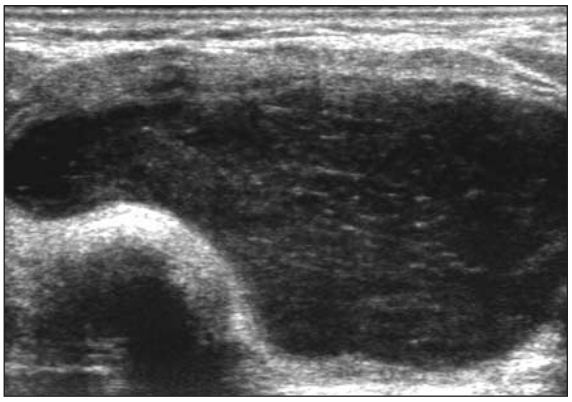

Table 1. Pathologic Results of FNAB, CNB, and Surgical Biopsy

Age, y/sex	FNAB Cytologic Findings	CNB Pathologic Findings	Surgical Biopsy Pathologic Findings
56/Male	Diffuse large B-cell lymphoma	Diffuse large B-cell lymphoma	Not done
57/Male	Diffuse large B-cell lymphoma	Diffuse large B-cell lymphoma	Not done
63/Female	Diffuse large B-cell lymphoma	Diffuse large B-cell lymphoma	Not done
64/Female	Possibility of lymphocytic thyroiditis	Not done	Diffuse large B-cell lymphoma
63/Female	Nondiagnostic	Not done	Diffuse large B-cell lymphoma
72/Female	Low-grade mucosa-associated lymphoid tissue-type lymphoma	Not done	Follicular lymphoma

invades the surrounding structures and more often invades the regional lymph nodes than does primary thyroid lymphoma.[14] In our series, all 6 cases showed the characteristic clinical and sonographic features of thyroid lymphoma: a rapidly enlarging neck mass and an enlarged and marked area of hypoechogenicity compared with the decreased echogenicity of the opposite side.[8,10] For the diagnosis of thyroid nodules, US-FNAB is a widely accepted technique. However, a limitation of US-FNAB is nondiagnostic sampling, which occurs in 10% to 20% of cases.[15] Although US-CNB cannot be used as a routine diagnostic tool for thyroid nodules, it is a good alternative because of its high diagnostic yield and accuracy in repeated nondiagnostic FNAB cases.[4,5] In this series, the nondiagnostic sampling rate for US-FNAB was 16.7% (1/6), and sensitivity was 50%.

In making a diagnosis of thyroid lymphoma, the role of surgery is limited because patients with thyroid lymphoma are usually treated with radiation therapy and chemotherapy.[3] With the adoption of the Revised European American Lymphoma/World Health Organization classification for non-Hodgkin lymphoma, several reports have stated that FNAB has become accepted as a means of primary diagnosis of lymphoma because of the development of many cytopathologic techniques, including immunocytochemistry, flow cytometry, DNA analysis, and immunophenotyping.[16–18] However, Ota et al[19] showed that US-FNAB for diagnosing thyroid lymphoma had a relatively high false-negative rate (12.5%); nevertheless, it had a high positive predictive value (97.1%). In our institution, pathologic confirmation procedures such as surgery and needle biopsy have been performed before determination of therapeutic strategies to decrease the misdiagnosis of thyroid lymphoma and to better classify its histologic subtypes. Some researchers reported that US-CNB allowed for diagnosis of lymphoma in cervical lymphadenopathy,[6,7] and US-CNB for diagnosis of lymphoma involving neck nodes had a high diagnostic yield, with sensitivity of 94.3%, specificity of 100%, and accuracy of 95.2%.[7] Furthermore, the histologic subclassification of lymphoma was sufficient for therapeutic purposes, and treatment was performed on the basis of the results of the CNB.[7] We found that US-FNAB was able to confirm the final diagnosis and histologic subclassification in 3 patients, bypassing the need for surgery. These results support the previous suggestions that needle biopsy can avoid unnecessary surgical intervention to diagnose thyroid lymphoma.[3,10] The 3 patients who underwent US-CNB had neither acute nor delayed complications. The relatively large size of thyroid lymphoma can facilitate CNB without damage to adjacent structures in the area. From the 3 or 4 US-CNB procedures in the patients of this series, we obtained sufficient specimens to make a definitive diagnosis of thyroid lymphoma and to determine the histologic type.

In conclusion, our results show that US-CNB can be a safe and accurate method for diagnosing thyroid lymphoma and may be a suitable replacement for diagnostic thyroid surgery.

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