Application of Color Doppler Ultrasound to Evaluate Chemotherapeutic Effect on Primary Thyroid Lymphoma

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Abstract

Primary thyroid lymphoma (PTL) is a rare disease which responds well to rituximab-based chemotherapy. Here, we describe a case who was diagnosed through core needle biopsy as having diffuse large B-cell lymphoma in the right lobe of thyroid gland. Positron emission tomography computed tomography (PET-CT) revealed no other foci of hot spots, so PTL was considered. She was treated with rituximab plus bendamustine for three cycles, and color Doppler ultrasound revealed significant reduction of blood flow signals in the tumor but no significant decrease of its size (<25% extent). Then, the chemotherapy regimen was adjusted to rituximab, cyclophosphamide, vincristine, prednisone (R–COP), and complete remission was noted on ultrasound and PET-CT after three cycles of R–COP treatment. This case is reported to tell that color Doppler ultrasound, in addition to PET-CT, is useful to evaluate chemotherapeutic effect on PTLs.

Keywords: Doppler, lymphoma, thyroid neoplasms, ultrasonography

INTRODUCTION

The head-and-neck is a common site of extranodal non-Hodgkin’s lymphoma. The most common sites for extranodal lymphoma of the head and neck are Waldeyer’s ring, most frequently the tonsil, and the salivary glands, usually the parotid. Primary thyroid lymphoma (PTL) accounts for 1%–2% of all extranodal lymphomas and 1%–5% of all thyroid malignancies. It is more common in women and the median age of presentation is in the seventh decade.[1] In previous literature, sonographic features of PTL at initial diagnosis have been reported, but sonographic images of PTL being treated with chemotherapy were rarely described. In this article, we presented serial sonographic imaging of PTL being treated with chemotherapy alone. We aim to evaluate whether color Doppler ultrasound can be applied to evaluate chemotherapeutic effect on PTL.

CASE REPORT

A 79-year-old Taiwanese woman came to the otolaryngologic clinic of our hospital due to an enlarging painless mass over the right neck region in the past 3 months. She denied fever, night sweats, dyspnea, hoarseness, dysphagia, dysphasia, or stridor. On physical examination, the right thyroid lobe was noted to be enlarged and firm. There was a palpable mass in the front of her neck, which moved during swallowing. She had no history of Hashimoto’s thyroiditis or cervical irradiation, and her thyroid function test was within the normal range (thyroid-stimulating hormone: 2.01 nIU/mL; free T4: 1.24 ng/dL; thyroglobulin: 1.62 ng/mL; anti-thyroperoxidase: 1.03 IU/mL; and thyroglobulin antibody: 1.81 IU/mL).

The patient had received computed tomography (CT) at hospital outside, which revealed a hypodense nodule with minimal enhancement on the right lobe of thyroid gland [Figure 1]. Its size was approximately 4.1 cm × 3.6 cm, with a longitudinal dimension of 4.5 cm. The trachea, vessels, and soft tissues in the right neck were under pressure and displaced toward the left side. She underwent fine-needle aspiration (FNA) at that hospital, and the cytologic results were suspicious of lymphoma.

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In order to obtain more definite results, this woman was referred to the radiological department of our hospital for core needle biopsy. During core needle biopsy, the neck color Doppler ultrasound showed a large heterogeneous hypoechoic mass with an irregular border in the right lobe of thyroid gland. There were twisted and chaotic intranodular vessels, but no defined calcification, hemorrhage, or necrotic portion was observed within the mass, which exhibited indistinct margins and posterior acoustic enhancement [Figure 2a and b]. The pathology revealed diffuse large B-cell lymphoma (DLBCL). For staging the disease, a fluorodeoxyglucose (FDG) positron emission tomography (PET) scan was performed, revealing high-grade hypermetabolic lymphomatous disease, confined in the right thyroid gland, suggesting PTL Ann Arbor stage I [Figure 3].

After consulting oncology specialists, she started rituximab-based chemotherapy and received serial sonographic follow-up. After three cycles of rituximab plus bendamustine – rituximab (375 mg/m²) and bendamustine (Innomustine®, 90 mg/m²) by intravenous administration on day 1 were administered every 3 weeks for each cycle – neck color Doppler ultrasound showed a significant reduction of twisted blood flow signals in the PTL but no significant decrease (<25% extent) of the tumor size [Figure 4]. Therefore, chemotherapy regimen was adjusted to rituximab, cyclophosphamide, vincristine, prednisone (R–COP). After three cycles of R–COP, i.e., rituximab (375 mg/m²), cyclophosphamide (750 mg/m²), and vincristine (2 mg/m²) by intravenous administration on day 1 and prednisone (100 mg/m²) by oral administration on day 1–5 were administered every 3 weeks for each cycle, the PTL disappeared on the color Doppler and gray-scale ultrasonography [Figure 5a]. The patient was treated with R–COP regimen until complete remission of the disease.

**Figure 1:** (a) Noncontrast enhanced computed tomography shows a hypodense nodule (size: 4.1 cm × 3.6 cm × 4.5 cm) in the right lobe of thyroid gland. (b) This nodule shows minimal homogeneous enhancement on contrast enhanced computed tomography imaging. The trachea, vessels and soft tissues in the right neck are under pressure and displaced toward the left side.

**Figure 2:** (a) Transverse sonogram of the neck reveals a heterogeneous hypoechoic mass with an irregular border in the right lobe of thyroid gland. Note posterior acoustic enhancement under the nodule. (b) The color Doppler ultrasound shows abundant twisted blood flow signals in the tumor. (c and d) Note a nodular goiter in the left lobe of thyroid gland with minimal blood flow signals.

**Figure 3:** The fluorodeoxyglucose positron emission tomography computed tomography scan (left) reveals a tumor with high-grade hypermetabolic status in the right lobe of thyroid gland. The whole-body positron emission tomography scan (right) shows no other foci with increased fluorodeoxyglucose uptake out of the thyroid gland. Therefore, the primary thyroid lymphoma is diagnosed based on the pathological result from core needle biopsy.

**Figure 4:** (a) The gray-scale ultrasonography shows no significant decrease of the tumor size (transverse diameters: 4.79 cm × 4.73 cm → 3.95 cm × 3.01 cm; <25% extent). (b) The color Doppler ultrasound shows reduction of twisted blood flow signals in the primary thyroid lymphoma after three cycles of rituximab plus bendamustine. (c) Color Doppler ultrasonographic image of the left thyroid gland is shown.
In our experience, three-dose chemotherapy alone has yielded good results in our case. The therapeutic strategy should be adjusted based on the patient’s condition and preferences. For instance, when a patient, such as our case, responds well to chemotherapy, there are changes in the tumor metabolism that start before a visible decrease in size can be detected, which leads to a false-negative result in the treatment response assessment with contrast-enhanced CT imaging.

In general, DLBCL is a highly vascularized neoplasm, as it usually enhances avidly on contrast-enhanced imaging studies. In one study, comparing sonographic features of PTL and nodular goiters [Figure 2], the blood flow signals in benign tumors are generally travelling naturally and present a uniform distribution, while malignant tumors are normally characterized by twisted blood flow signals and a non-uniform distribution. The characteristics of the blood flow signals in our case are coincident with those of malignant tumors. In previous literature, sonographic appearances of PTL were reported as three types based on internal echoes, borders, and posterior echoes, which are suspicious of lymphoma on FNA, are examined with core needle biopsy because a false-negative result in the treatment response assessment with contrast-enhanced CT imaging.

In the current consensus, FDG PET-CT has been routinely used to monitor therapy response in patients with lymphoma and can identify individuals with treatment resistance to certain forms of chemotherapy, early in the course which provides the clinician a sufficient time window to change the therapeutic strategy. We describe this case to inform that color Doppler ultrasound is an alternative imaging modality in evaluation of chemotherapeutic effect on PTL. Twisted blood flow signals reduced sooner than shrinkage of the tumor when it was treated with chemotherapy. Because only one case was reported in this study, the value of color Doppler ultrasonography in the evaluation of chemotherapeutic effect on PTL needs more case series to be demonstrated.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be used for educational and research purposes, informed of all risks, potential benefits, and alternatives to the study. The patient consent forms. In the form the patient has given her consent for her images and other clinical information to be used for educational and research purposes, informed of all risks, potential benefits, and alternatives to the study.
reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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