Case Report

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

CME Credits

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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 extra-nodal 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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Received: 30-01-2020 **Revised:** 27-02-2020 **Accepted:** 13-04-2020 **Available Online:** 25-05-2020

Access this article online

Quick Response Code:

Website: www.jmuonline.org

DOI: 10.4103/JMU.JMU_15_20

How to cite this article: Hu CC, Wang CW, Chen JH. Application of color Doppler ultrasound to evaluate chemotherapeutic effect on primary thyroid lymphoma. J Med Ultrasound 2021;29:60-3.

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/m^2) and bendamustine (Innomustine®, 90 mg/m^2) 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/m^2), cyclophosphamide (750 mg/m^2), and vincristine (2 mg/m^2) by intravenous administration on day 1 and prednisone (100 mg/m^2) 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,

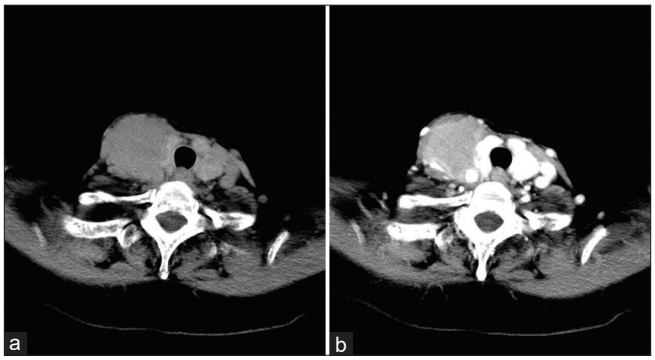

Figure 1: (a) Noncontrast enhanced computed tomography shows a hypodense nodule (size: 4.1 cm × 3.6 cm × 4.5 cm) in the right lobe of thyroid gland. (b) This nodule shows minimal homogeneous enhancement on contrast enhanced computed tomography imaging. The trachea, vessels and soft tissues in the right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

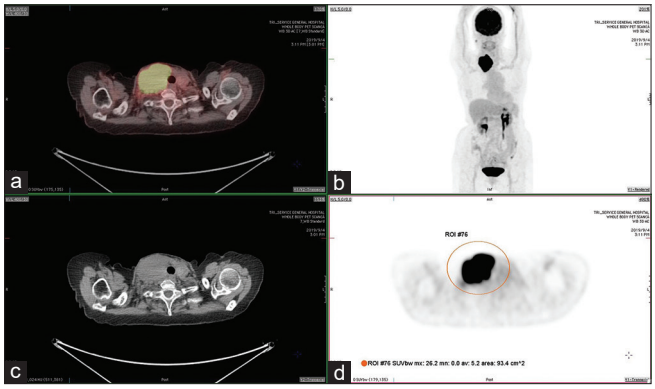

Figure 3: The fluorodeoxyglucose positron emission tomography computed tomography scan (left) reveals a tumor with high-grade hypermetabolic status in the right lobe of thyroid gland. The whole-body positron emission tomography scan (right) shows no other foci with increased fluorodeoxyglucose uptake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

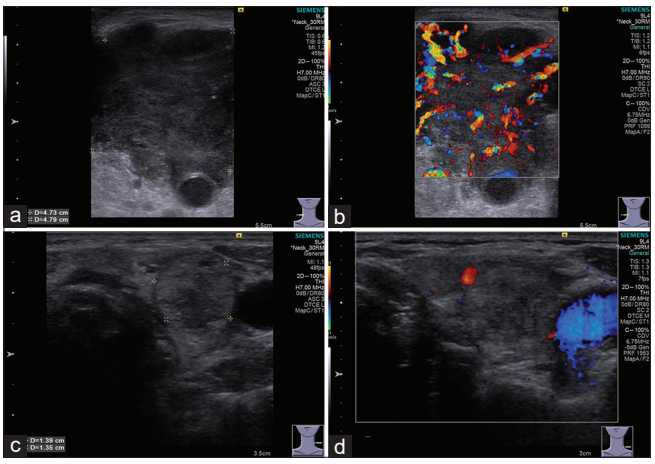

Figure 2: (a) Transverse sonogram of the neck reveals a heterogeneous hypoechoic mass with an irregular border in the right lobe of thyroid gland. Note posterior acoustic enhancement under the nodule. (b) The color Doppler ultrasound shows abundant twisted blood flow signals in the tumor. (c and d) Note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

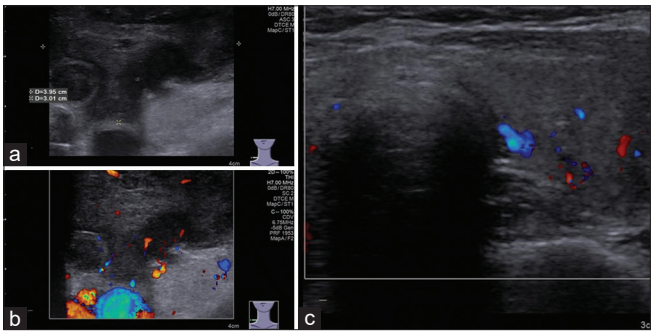

Figure 4: (a) The gray-scale ultrasonography shows no significant decrease of the tumor size (transverse diameters: 4.79 cm × 4.73 cm → 3.95 cm × 3.01 cm; <25% extent). (b) The color Doppler ultrasound shows reduction of twisted blood flow signals in the primary thyroid lymphoma after three cycles of rituximab plus bendamustine. (c) Color Doppler ultrasonographic image of the left thyroid gland is shown

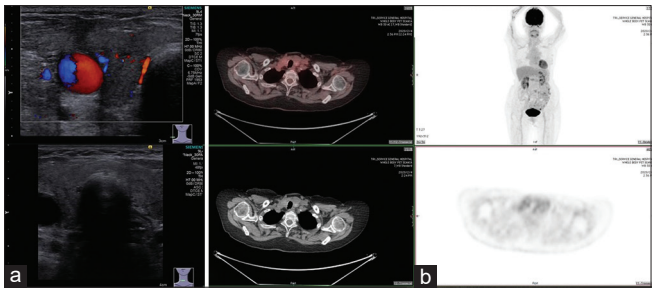

Figure 5: (a) After three cycles of rituximab, cyclophosphamide, vincristine, prednisone, the primary thyroid lymphoma disappears on the color Doppler and gray-scale ultrasonography. (b) Complete remission of the primary thyroid lymphoma is confirmed on the positron emission tomography computed tomography (left) and whole-body positron emission tomography scan (right) after three cycles of rituximab, cyclophosphamide, vincristine, prednisone regimen

confirmed on the following FDG PET-CT and whole-body PET examination [Figure 5b].

Discussion

Color Doppler ultrasound is a useful imaging modality in the evaluation of chemotherapeutic effect on PTL because it can reflect real-time blood flow signals of the tumor. In combination of contrast-enhanced CT, color Doppler ultrasound, like contrast-enhanced ultrasound – administration of intravenous contrast agents consisting of microbubbles/nanobubbles of gas to medical ultrasonography – provides important semi-functional information regarding blood perfusion, during the revision of treatment assessment.[2] Without metabolic information (e.g., blood flow signals) from tumor lesions, contrast-enhanced CT can only provide morphological information, whereas 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 nonuniform distribution.[3] 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 these included nodular, diffuse, and mixed types. Enhanced posterior echoes were typical of thyroid lymphomas of all types.[4] On color Doppler sonography, PTLs exhibit nonspecific vascular pattern, which may either be iso- to hypovascular or have chaotic intranodular vessels.[3,5] The color Doppler imaging of our case was consistent with those in previous literature. Therefore, tissue diagnosis for confirmation is ultimately needed.[6]

The diagnosis of PTL can be difficult, due to cytological similarities between PTL and Hashimoto's thyroiditis, though preparations from FNA are improving in specificity and sensitivity.[7] Therefore, core needle biopsy is suggested in the next step due to its good diagnostic sensitivity and positive predictive value, which helps to reduce diagnostic open surgery.[8] At our hospital, diffuse infiltrative thyroid lesions, which are suspicious of lymphoma on FNA, are examined with core needle biopsy because core needle biopsy successfully subclassifies histological types in 89.7% of neck lymphomas. Besides, core needle biopsy provides an adequate amount of specimen for the detection of prognostic markers, such as Ki-67 and p53, through immunohistochemistry staining, enabling a reliable differentiation between Hashimoto's thyroiditis and anaplastic carcinoma.[7,9]

There are no randomized control trials evaluating treatments for thyroid lymphoma specifically. Historical case series of patients with primary DLBCL of the thyroid have suggested that outcomes are better with a combination of chemotherapy and radiotherapy rather than single modality treatment and this has been recommended in current guidelines.[1] However, chemotherapy alone has yielded a complete response in 77%–100% of patients, and the addition of rituximab improves significantly overall survival of patients with PTL.[10] In our experience, three-dose regimen of rituximab-based chemotherapy alone shows a good disease remission rate of PTL.[9] In our case, the PTL did not subside as expected (<25% extent) after three cycles of rituximab plus bendamustine. We considered that the tumor was refractory or partial responsive to bendamustine, which was self-paid by the patient. Under economic considerations, the chemotherapy regimen was adjusted to R–COP, which was also the standard first-line treatment of PTL for elders.[1]

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.[11] 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

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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