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CLINICAL CASE REPORT

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Coexistence of Papillary Thyroid Carcinoma With Thyroid MALT Lymphoma in a Patient With Hashimoto's Thyroiditis

A Clinical Case Report

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Abstract: Papillary thyroid carcinoma (PTC) is the most common type of thyroid neoplasias; however, primary thyroid gland lymphoma (PTL) is uncommon and their simultaneous occurrence is very rare.

Herein, we reported a 25-year-old female patient with Hashimoto's thyroiditis (HT), who developed a small goiter with a palpable 1.2-cm nodule in the right lobe. A fine-needle aspiration (FNA) biopsy revealed atypical follicular epithelial cells and lymphoid cells in a background of lymphocytic thyroiditis. A total thyroidectomy was performed. The pathology showed multicentric papillary thyroid carcinoma, concomitant thyroid mucosa-associated lymphoid tissue (MALT) lymphoma, and Hashimoto's thyroiditis. Postoperatively, he received chemotherapy and radioactive iodine ablation treatment. Nowadays the thyroglobulin of the patient is undetectable, without recurrences at 2 years of follow-up.

It is concluded that the PTC and MALT lymphoma can exist concomitantly, especially in patients with HT. For the diagnostic workup and optional management of this rare coexistence, a multidisciplinary approach and close surveillance are needed.

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Abbreviations: DLBCL = large B-cell lymphoma, FNA = fine-needle aspiration, HT = Hashimoto's thyroiditis, MALT = mucosa-associated lymphoid tissue, NHL = non-Hodgkin's lymphoma, PTC = papillary thyroid carcinoma, PTL = primary thyroid gland lymphoma, TSH = thyroid-stimulating hormone, US = ultrasonography.

INTRODUCTION

Thyroid cancer is the most common endocrine carcinoma, and its incidence rates increased dramatically, by an average of 4.5% per year from 2007 to 2011.[1] As the most prevalent manifestation of thyroid carcinoma, papillary thyroid carcinoma (PTC) accounted for 70% to 80% of all thyroid carcinomas and occurred predominately in women with excellent prognosis.[2] Primary thyroid lymphoma (PTL) is rare, accounting for $< 5\%$ of thyroid malignancies and $< 2\%$ of extranodal lymphomas, with an annual estimated incidence of 2 per 1 million.[3,4] Women are more commonly affected than men, with the ratio of occurrence ranging from 2:1 to 8:1.[4,5] It is strongly associated with Hashimoto's thyroiditis.[6] The concomitance of PTC and PTL in the same patient is rare, and the present case report aims to describe the coexistence of PTC with thyroid mucosa-associated lymphoid tissue (MALT) lymphoma in a background of Hashimoto's thyroiditis. Treatment and follow-up issues are also addressed.

Case Report

A 25-year-old woman underwent a carotid ultrasound examination, which incidentally revealed a small multinodular goiter in August 2012. The results of routine laboratory tests were normal, and serum hormone measurements showed a thyroid-stimulating hormone (TSH) value of 1.99 mU/L (reference range 0.27–4.2), free T_4 value of 17.72 pmol/L (reference range 12.0–22.0), thyroglobulin antibodies of 62.77 IU/mL (reference range 0–115), and peroxidase autoantibody of 48.49 IU/mL (reference range 0–34). Thyroid ultrasonography (US) confirmed the presence of a multinodular goiter; the largest nodule in the right lobe was 1.2 cm in diameter and hypoechoic. The result of US was suspicious of malignancy. Subsequent FNA biopsy showed a co-occurrence of atypical follicular epithelial cells and atypical lymphoid cells, which was also suspicious for malignancy.

Then, in November 2012, a total thyroidectomy was performed without lymph nodes removed. Histopathology examination revealed a papillary thyroid carcinoma (Figure 1B) in the left lobe (Figure 1A: thick arrow), accompanied with B-cell lymphoma of MALT type (Figure 1C) in the extranodal marginal zone (Figure 1A: thin arrow). The nuclei of PTC presented in Figure 1B were enlarged and oval, with nuclear features such as powdery chromatin, nuclear grooves, and small nucleoli, which could help make a diagnosis. As reported previously,[7] the MALT lymphoma had nodular architectures that comprised nearly exclusively of plasmacytoid cells, and at the periphery of the plasmacytic nodules rare lymphoepithelial lesions were presented. Also, several scattered reactive germinal centers were seen in Figure 1C.

The staging procedures revealed no evidence of metastasis and she reported no systemic B symptoms related to lymphoma such as fever, weight loss, or nocturnal sweating. The patient was discharged home on levothyroxine 87.5 μg per day, and then after withdrawal from the thyroid hormone she was referred to the ^{131}I therapy with 100mCi. After ^{131}I treatment, a whole -body scan did not reveal any abnormal iodine uptake. She also received 4 cycles of chemotherapy consisting of

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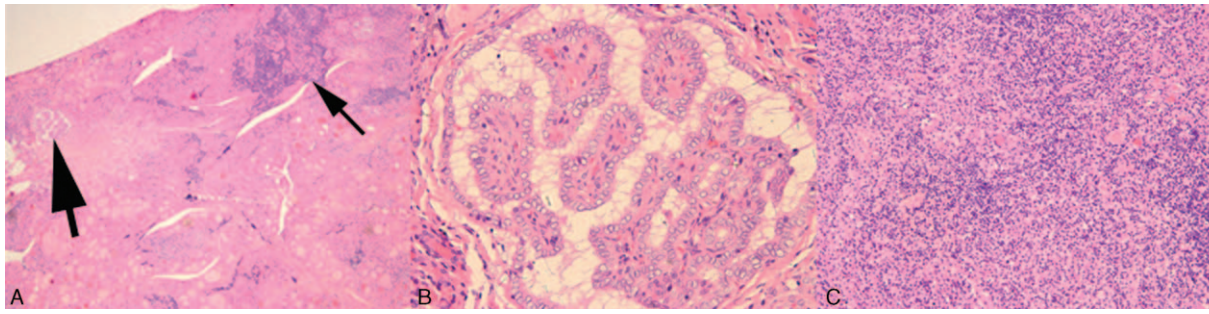

FIGURE 1. (A) Hematoxylin-eosin staining showing papillary thyroid carcinoma (thick arrow) concomitantly with MALT thyroid lymphoma (thin arrow) (10 × magnification). (B) Papillary thyroid carcinoma with a predominant follicular pattern and diagnostic nuclear features (20 × magnification). (C) High magnification highlights sheets of plasmacytoid cells that were the predominant cell population in this MALT lymphoma (20 × magnification). MALT = mucosa associated lymphoid tissue.

cyclophosphamide, vincristine, and prednisone. Nowadays, the patient remains asymptomatic with undetectable serum thyroglobulin and without evidence of recurrences.

This case report was approved by the Ethics Committee of West China Hospital of Sichuan University, Chengdu, China, and the written informed consent was obtained.

DISCUSSION

Thyroid lymphomas are typically B-cell non-Hodgkin's lymphoma (NHL), and the most common subtype of PTL is diffuse large B-cell lymphoma (DLBCL), accounting for >50% of cases, followed by MALT lymphoma, which represents ~10% to 23% of cases.[4,8,9] The most common clinical presentation is a rapidly growing neck mass, which is reported in >70% of cases.[10] Due to mass effect, one-third of cases experience compressive symptoms such as dyspnea, dysphagia, stridor, and hoarseness. In addition, B symptoms including weight loss, fever, and night sweats are reported in 10% of patients.[9,11] The diagnosis of PTL is based on the presence of a combination of morphologic features and immunophenotyping by flow cytometry and immunohistochemistry. However, MALT is often difficult to differentiate from thyroiditis due to the heterogeneous appearance.[12] With regard to the treatment of PTL, there are no randomized, controlled trials evaluating the efficacy of different treatment modalities; thus insight must be obtained from retrospective studies or relevant studies of extranodal NHLs. In general, the treatment may comprise surgery, chemotherapy, or radiotherapy, with the histology and stage considered.[4,10]

The epidemiologic evidence showed that the incidence of PTL is higher in patients with a history of HT.[13,14] It has been established that HT, regarded as a risk factor, played a very important role in the development of thyroid lymphoma.[7,10,15] The prolonged antigenic stimulation of the lymphocytes in the setting of autoimmune thyroiditis predisposes the normal cells to lymphomatous transformation and further to a lymphoid malignancy.[7,16,17] Furthermore, the aberrant somatic hypermutation, which is regarded as a mechanism of lymphomagenesis and represents an early process of B-cell clonal transformation, has been detected in 2 patients with chronic lymphocytic thyroiditis.[16,18]

However, the association between HT and PTC is still debated.[19] A recent review reported that patients undergoing thyroidectomy with coexisting HT had an increased prevalence of PTC, with a favorable disease profile and an improved prognosis.[20] In addition, the thyroid cells with HT have various alterations of some oncogenes like RET/PTC, which might regulate the early stages of tumor development; however many steps of oncogenic transformation are probably unknown.[7,21]

Herein, we presented a case with concomitance of MALT and PTC. In contrast to published cases, our patient was asymptomatic and further evaluated only for the reason of a small nodular goiter. After a staging work-up, there was no evidence of other tissues involvement or metastasis. The patient received the radioactive iodine therapy followed by 4 cycles of chemotherapy consisting of cyclophosphamide, vincristine, and prednisone. Until this date, the patient has no evidence of regional or distant recurrence during the 2 years of follow-up.

Despite the rarity of PTL, it can simultaneously exist with PTC, especially in patients with HT, and the treatment has to prioritize the tumor with worse stage and condition.

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