

HOSTED BY



ELSEVIER

Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Medicine

journal homepage: <http://ees.elsevier.com/apjtm>Case report <http://dx.doi.org/10.1016/j.apjtm.2016.06.017>

Coexistence of papillary thyroid microcarcinoma and mucosa-associated lymphoid tissue lymphoma in a context of Hashimoto's thyroiditis

Saul Levy-Blitchtein^{1,2}, Stefany Plasencia-Rebata^{1,2}, Domingo Morales Luna³, Juana del Valle Mendoza^{1,2*}¹School of Medicine, Faculty of Health Sciences, Universidad Peruana de Ciencias Aplicadas (UPC), Av. San Marcos cdra 2 Cedros de Villa, Lima, Peru²Research Center and Innovation of the Health Sciences Faculty, Universidad Peruana de Ciencias Aplicadas (UPC), Av. San Marcos cdra 2 Cedros de Villa, Lima, Peru³Pathologist Service, Hospital Nacional Edgardo Rebagliati Martins (HNERM), Jr. Edgardo Rebagliati 490, Jesús María, Lima, Peru

ARTICLE INFO

Article history:

Received 15 May 2016

Received in revised form 16 Jun 2016

Accepted 21 Jun 2016

Available online 29 Jun 2016

Keywords:

Thyroid cancer-clinical

Hashimoto's thyroiditis

Pathology-thyroid

Thyroid diseases

ABSTRACT

Papillary thyroid cancer (PTC) represents 80–85% of thyroid cancer and its prevalence has been rising in the last decades. Primary thyroid lymphoma (PTL) accounts for 3% of extranodal lymphomas and about 5% of thyroid malignancies, having a prevalence of one or two cases per million people. Mucosa-Associated Lymphoid Tissue lymphoma represents approximately 30% of PTL. Both entities have an indolent course and a very good prognosis. Diagnosis is made by ultrasound and fine needle aspiration (FNA) or surgery specimen pathology. They have also been associated with HT, but pathogenesis and its links remains to be known. Treatment remains controversial and surgery is generally accepted in cases of disease limited to thyroid, as the present. Patients with thyroid nodules should be observed and followed. If there is an enlargement by ultrasound or clinical symptoms, FNA should be performed promptly. Patients with Hashimoto's thyroiditis (HT) deserve additional surveillance, since this condition is associated with both PTC and PTL. In this case, the management with surgery and radioactive iodine ablation therapy was effective for both entities. Patients with thyroid nodules should be properly evaluated with ultrasound and thyroid function tests. If there is an enlargement of the neck, reported by symptoms or ultrasound, it requires further investigation. HT is associated to both PTC and PTL so if the enlargement of the nodules is on this context additional tests such as FNA should be performed. In this case, the patient was managed with surgery and radioactive iodine ablation therapy and it was effective for both entities.

1. Introduction

Thyroid cancer represents 1% of all cancer cases in the United States and it's the most common endocrine malignancy. Papillary thyroid cancer (PTC) represents the most frequent variation at countries with iodine sufficient diet [1] and its prevalence has been rising in the last decades, being about 80–85% [1,2]. More common in women (2.4:1), it has a peak

between third and fifth decades of life [1]. Also, there are exogenous factors: radiation exposure, high-iodine diet, nitrates, western style life and endogenous factors high levels of thyroid stimulating hormone, Hashimoto's thyroiditis (HT) and obesity, associated with PTC [3].

Primary thyroid lymphoma (PTL) accounts for 3% of extranodal lymphomas and about 5% of thyroid malignancies, having a prevalence of one to two cases per million people [4,5]. More common in women (3:1) at seventh decade of life, it develops 5–10 years earlier in men [4]. Its pathogenesis is unknown, but PTL, autoimmune diseases and antigen stimulation have been associated. Patients with HT have 40–80 times more risk, however only 0, 6% develop it [6,7]. It has been proposed that lymphoid tissue develops in the thyroid in a context of a long standing HT into a Mucosa-Associated Lymphoid Tissue (MALT) lymphoma [4].

*Corresponding author: Juana del Valle Mendoza, Peruvian University of Applied Sciences (UPC), Av. San Marcos cdra. 2, Cedros de Villa, Lima, Peru.

Tel: +51 13133333x2704;

Fax: +51 13496025

E-mail: jdellvall@upc.edu.pe

Peer review under the responsibility of Hainan Medical College.

Foundation project: This paper was supported by 4th Incentives for Research of the Universidad Peruana de Ciencias Aplicadas, Lima-Peru (Grant-UPC-401-2014).

2. Case report

A 54-year-old man followed-up due to a goiter enlargement in last nine months, now presents with associated cervical pain, dysphonia and dysphagia to solids. The patient is a former smoker, denies exposition to other toxic agents. He does not have family history of thyroid cancer. His father died of gastric cancer and one son has hypothyroidism. On physical examination, thyroid gland was enlarged asymmetrically. The left lobe was larger than the right and it had a nodule of 4 cm, soft, delimited, not adhered to deep tissue and motile at deglutition. A nodule of 2 cm with the same characteristics was found at right lobe. There was no palpable cervical lymphadenopathy and the rest of the examination and laboratory results were unremarkable. The patient was euthyroid and he didn't take any medication.

Thyroid ultrasonography found a heterogeneous thyroid gland with hypoechoic nodules, one of 36 mm × 22 mm at inferior pole, another nodule of 8 mm at the middle third of left lobe and three nodules of 9 mm, 7 mm and 4 mm at the right lobe. Total thyroidectomy was programmed and performed, without complications. No lymph nodes were removed.

Histopathology found a papillary thyroid microcarcinoma, classic variant, of 5 mm × 3.5 mm (Figure 1A). The main parenchyma showed a low grade lymphoproliferative process, with presence of lymphoid follicles and epithelial complexes at thyroid follicles. It was classified as an extranodal marginal zone B-cell lymphoma of MALT type with compromise of the entire gland (Figure 1B). Immunohistochemistry studies revealed

positivity to CD20 (Figure 1C), CD79a and cytokeratin (Figure 1D) and negativity to CD3, CD10, BCL6 and thyroglobulin. Proliferation rate (Ki67) was 15–20%. The remaining thyroid parenchyma revealed remains of HT.

The patient was discharged home and prescribed levothyroxine 100 mcg. Two months later surveillance tests were performed, consisting of upper endoscopy, computed tomography of neck, thorax, abdomen and pelvis, bone scintigraphy and bone marrow biopsy. They didn't show any evidence of disease. Two months later the patient had ablation therapy with 80mCi of I¹³¹ after withdrawal from thyroid hormone. There was no evidence of disease on his last visit.

3. Discussion

The coexistence of MALT lymphoma and PTC in a context of HT is extremely uncommon, with few cases reported [8–10]. Clinical presentation of these cases is variable. The course can be indolent and only detected by thyroid ultrasound, as the experiences of Cheng *et al* [10] and Vassilatou *et al* [11] or, more typical of PTL, an enlargement of a neck mass [6] that can be with obstructive symptoms as hoarseness [8], dysphonia, neck pain and dysphagia as the present patient or even severe airway obstruction leading to emergency surgery [12], or without them, an isolated enlargement [9].

The diagnosis of these entities can be achieved with thyroid ultrasound and fine needle aspiration (FNA), thyroid biopsy or after thyroidectomy. Thyroid laboratory workup can result in euthyroid without medication [8,9,12] as this patient, subclinical

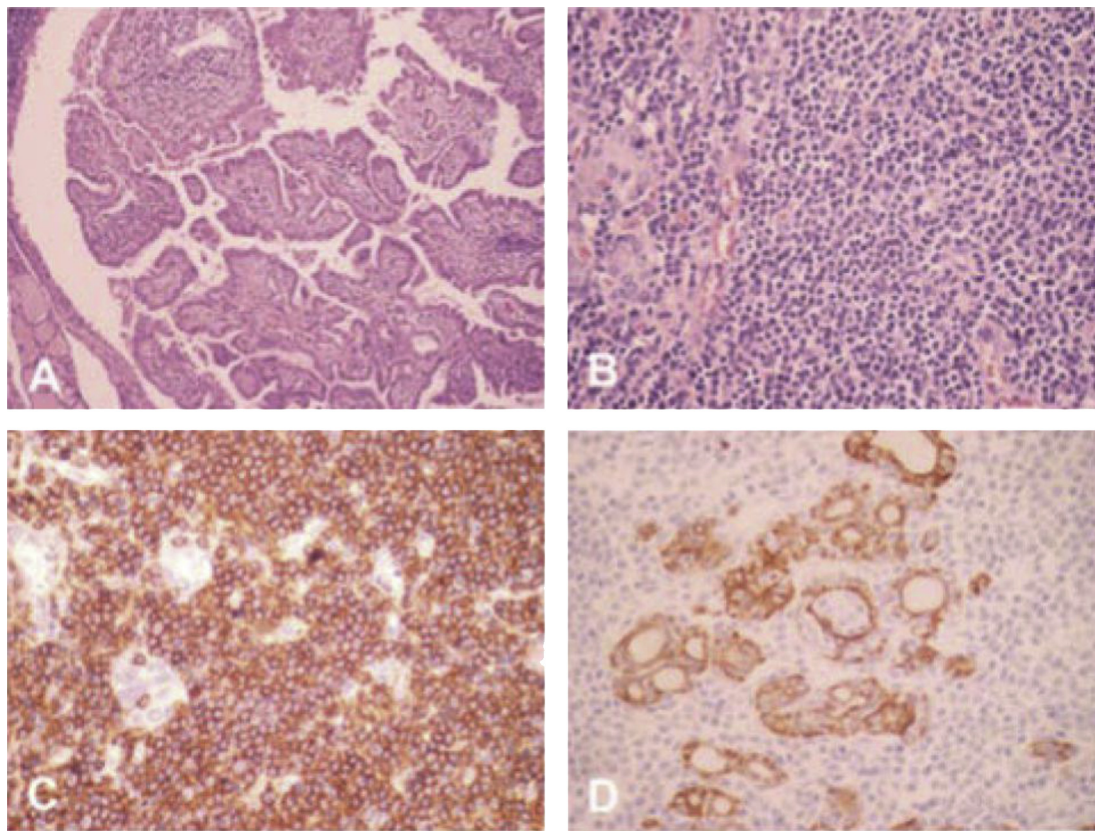


Figure 1. The pathological assessment.

A, Papillary thyroid microcarcinoma (H&E stain, 100× magnification); B, Extranodal marginal zone B-cell lymphoma of MALT type with compromise of the entire gland, tumor cells are strongly positive to CD20 (Immunohistochemistry CD20, 400× magnification); C and D, Tumor lymphocytes invading the epithelium (lymphoepithelial complexes). Remains of thyroid follicles are positive to cytokeratin (Immunohistochemistry Pan CK, 400× magnification).

hyperthyroidism [11] or hypothyroidism (if untreated). Therapeutic approach in cases like this requires prioritizing the most aggressive disease, determined by staging. The other similar cases were managed with surgery alone [8,12] or with adjuvant radioactive iodine treatment [9–11] as this patient.

PTC is the most frequent thyroid cancer and it's managed with surgery and radioactive iodine, therapy is curative often. Generally, it doesn't metastasize out of the neck (5–7%) and is rare as a cause of death. The following workup includes full body scan, neck ultrasound, levels of thyroglobulin and anti-thyroglobulin antibodies [1,2,13].

A fast growing goiter should make suspect of PTL and even more if there are associated cervical lymphadenopathies. FNA sample should be used for cytology, flow cytometry and immunohistochemistry to determine the type because it changes the management and prognosis [6].

Diffuse large B-cell lymphoma represents nearly 70% of PTL and has a more aggressive course. Its treatment consists of combined schemes of rituximab, chemotherapy and radiotherapy; the disease free survival is almost 75% at 5 years, while MALT lymphoma has a better prognosis, with a disease free survival of near 96% at 5 years and its treated with surgery and radiotherapy either alone or in combination. Radiotherapy alone has a success of 70–100%, while thyroidectomy is risky, has not demonstrated to increase overall survival and is reserved for cases with obstructive impairment [4].

The mechanism that may associate HT with these two entities is yet to be determined. Nevertheless, the autoimmune process and antigen exposure seem to have an important role in the pathogenesis [4]. Total thyroidectomy represented an effective measure at experience of Cheng *et al* [10] and Melo *et al* [9], with six years and two years without recurrence respectively [12]. There is not information about long term effects so appropriate surveillance must be done. This report adds information about the coexistence of these entities and the experience we had with its management. Also, we remark that thyroid nodules must be observed and followed, granting a FNA if there are clinical symptoms or enlargement at the neck. Patients with HT in the context of the enlargement of the goiter by symptoms or ultrasound, deserve additional surveillance because that condition is associated with both PTL and PTC.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Acknowledgments

The authors would like to thank Dora Blitchtein for helpful comments on the manuscript. JDVM support was provided by 4th Incentives for Research of the Universidad Peruana de Ciencias Aplicadas, Lima-Peru (Grant-UPC-401-2014).

References

- [1] LiVolsi VA. Papillary thyroid carcinoma: an update. *Mod Pathol* 2011; **24**(2): S1-S9.
- [2] Kim WB. A closer look at papillary thyroid carcinoma. *Endocrinol Metab (Seoul)* 2015; **30**(1): 1-6.
- [3] Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. *J Cancer Epidemiol* 2013; **2013**: 965212; <http://dx.doi.org/10.1155/2013/965212>.
- [4] Walsh S, Lowery AJ, Evoy D, McDermott EW, Prichard RS. Thyroid lymphoma: recent advances in diagnosis and optimal management strategies. *Oncologist* 2013; **18**(9): 994-1003.
- [5] Stein SA, Wartofsky L. Primary thyroid lymphoma: a clinical review. *J Clin Endocrinol Metab* 2013; **98**(8): 3131-3138.
- [6] Pedersen RK, Pedersen NT. Primary non-Hodgkin's lymphoma of the thyroid gland: a population based study. *Histopathology* 1996; **28**(1): 25-32.
- [7] Holm LE, Blomgren H, Lowhagen T. Cancer risks in patients with chronic lymphocytic thyroiditis. *N Engl J Med* 1985; **312**(10): 601-604.
- [8] Nam YJ, Kim BH, Lee SK, Jeon YK, Kim SS, Jung WJ, et al. Co-occurrence of papillary thyroid carcinoma and mucosa-associated lymphoid tissue lymphoma in a patient with long-standing hashimoto thyroiditis. *Endocrinol Metab (Seoul)* 2013; **28**(4): 341-345.
- [9] Melo GM, Sguilar DA, Petiti CM, Eichstaedt AG, Caiado RR, Souza RA. Concomitant thyroid Malt lymphoma and papillary thyroid carcinoma. *Arq Bras Endocrinol Metabol* 2010; **54**(4): 425-428.
- [10] Cheng V, Brainard J, Nasr C. Co-occurrence of papillary thyroid carcinoma and primary lymphoma of the thyroid in a patient with long-standing Hashimoto's thyroiditis. *Thyroid* 2012; **22**(6): 647-650.
- [11] Vassilatou E, Economopoulos T, Tzanela M, Rontogianni D, Karakitsos P, Magou C, et al. Coexistence of differentiated thyroid carcinoma with primary thyroid lymphoma in a background of Hashimoto's thyroiditis. *J Clin Oncol* 2011; **29**(25): e709-e712.
- [12] Tarui T, Ishikawa N, Kadoya S, Watanabe G. Co-occurrence of papillary thyroid cancer and MALT lymphoma of the thyroid with severe airway obstruction: a case report and review of the literature. *Int J Surg Case Rep* 2014; **5**(9): 594-597.
- [13] Kim TY, Kim WG, Kim WB, Shong YK. Current status and future perspectives in differentiated thyroid cancer. *Endocrinol Metab (Seoul)* 2014; **29**(3): 217-225.