Primary mucosa-associated lymphoid tissue thyroid lymphoma: a rare thyroid neoplasm of extrathroid origin

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Abstract

Primary thyroid lymphoma is a rare malignancy, representing 2-8% of all thyroid malignancies and 1-2% of all extranodal lymphomas. The majority of cases concern non-Hodgkin’s lymphoma of B cell origin, following by Hodgkin’s disease, T cell lymphomas and rarely marginal zone B-cell mucosa-associated lymphoid tissue (MALT) lymphomas. MALT lymphomas have been associated with long-standing autoimmune Hashimoto’s thyroiditis. We present the case of a 44-years-old woman with thyroid MALT lymphoma in the background of multinodular goiter of autoimmune origin.

Introduction

Primary thyroid lymphoma represents 2-8% of all thyroid malignancies and 1-2% of all extranodal lymphomas. Most thyroid lymphomas are non-Hodgkin’s lymphomas of B cell origin, following by Hodgkin’s disease, T cell lymphomas and rarely marginal zone B-cell mucosa-associated lymphoid tissue (MALT) lymphomas. MALT lymphomas, which account for 25% of primary lymphomas, arise mainly in the stomach (60-70%), but they also can be found in organs such as the orbit, salivary gland, lung, intestine, liver and thyroid gland. Normally, thyroid gland is devoid of lymphoid tissue while this is reversed during the course of autoimmune diseases such as Hashimoto’s thyroiditis. It has been evident that thyroid MALT lymphomas occur in 0.5% of the cases with Hashimoto’s thyroiditis, even after a long period of lymphocytic infiltration which reaches as long as 30 years. A concurrence with papillary thyroid carcinoma has been also reported. The clinical presentation include an enlarging neck mass, dysphagia, hoarseness, dyspnea and usually the patients are euthyroid. Most often the diagnosis is difficult, based either on the morphological or clinical characteristics and flow cytometry, Southern blotting or PCR need to be performed. Herein, we describe the case of a 44-years-old female who was diagnosed with thyroid MALT lymphoma in the background of autoimmune thyroiditis.

Case Report

A 44-years-old, obese, woman, with autoimmune thyroiditis on L-thyroxine treatment (100 µg/d), was referred to our department for further evaluation of a rapidly growing mass of the right lobe of the thyroid gland, associated with gradually increased pain and dyspnea. The laboratory evaluation of the patient revealed normal TSH levels and positive thyroid antibodies, indicating a properly treated autoimmune thyroiditis. A Doppler ultrasound of the thyroid gland revealed multiple hypoechoic nodules (max. diam 2 cm) with microcalcifications and increased peripheral and central vascularity. A fine needle aspiration was performed, which showed suspicious for malignancy findings of the nodule while a lymphoproliferative infiltration of the thyroid parenchyma and histocytes, mainly with epithelioid morphology, were also observed. Her sister and her mother had the diagnosis of occult papillary thyroid cancer on the background of autoimmune thyroiditis, which had been diagnosed at the age of 35 years.

Due to the suspicious ultrasound and cytologic findings, the positive for thyroid cancer family history and the difficulty of having a systematic follow up, total thyroidectomy was performed. The pathology showed thyroid MALT lymphoma on the background of autoimmune Hashimoto’s thyroiditis. More specifically, the HE staining, in addition to chronic lymphocytic thyroiditis, showed a characteristic infiltration of the thyroid tissue with monoclonal plasma cells and big epithelial histocytes. The immunohistochemical study revealed monoclonal cytoplasmic immunoglobulin expression of clg-λ in the plasma cell population (Figure 1).

The patient underwent further evaluation with gastroscopy and scanning tomography of the neck, thorax and pelvis which were all negative. Bone marrow biopsy reported a reactive marrow and the immunohistochemical study (anti-CD3/CD20/CD138, Glycoporin A, κ and λ light chain immunoglobulin) was negative for the presence of MALT lymphoma.

The potential benefits of being further treated by radiotherapy and/or chemotherapy, were discussed with the oncologists and the final decision was the annual follow up. Two years after she is well, with no evidence of local or systematic disease, adequately replaced with L-thyroxine.

Discussion

The present report, refers to a patient with thyroid MALT lymphoma on the background of autoimmune thyroiditis.

Primary thyroid MALT lymphoma is a quite rare neoplasm accounting for 2-8% of all thyroid malignancies and 1-2% of all extranodal lymphomas. It tends to present in women during their seventh decade of life, while our case refers to a middle-aged woman. Men with thyroid MALT lymphoma, exhibit a worse prognosis, compared to the well differentiated thyroid cancer.

Most commonly, it presents as a painless rapidly growing thyroid mass, as in our case, while general symptoms like fever, nocturnal sweating and weight loss mostly suggest sec-

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Key words: thyroid MALT lymphoma, thyroiditis Hashimoto.

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secondary thyroid infiltration by lymphoma of
another organ.1-3,8,9

Although *H. pylori* infection has been asso-
ciated with gastric MALT lymphoma in addition
to coronary artery disease and type 1 and 2 dia-
betes mellitus10-13 this relationship has not
been adequately addressed for thyroid MALT
lymphoma. The existing data support that
autoimmune thyroiditis seems to be a risk fac-
tor for the development of thyroid MALT
lymphoma due to an acquired pathological trans-
formation of the intrathyroidal lymphoid tis-
sue.14 Most often the concurrence of thyroid
MALT lymphoma with autoimmune thyroiditis
creates a lot of problems in its diagnosis. In
autoimmune thyroiditis the two main micro-
scopical findings are lymphocytic infiltration
of the stroma and oxyphilic change of the fol-
licular epithelium. On the other side, the char-
acteristics of thyroid MALT lymphoma include
the atypical lymphoid cells originated within
the marginal zone of the lymphoid follicles and
extended into the interfollicular space, the thy-
roid follicular epithelium and the germinal
centers. In certain cases, immunocytochem-
istry (CD 20, CD 43, $\lambda$- and $\kappa$- light chains),
but also flow cytometry and PCR, are needed to
confirm the diagnosis of thyroid MALT lym-
phoma.2,9,15

A lot of questions have been raised regard-
ing the follow up of patients with thyroid MALT
lymphomas. The first step consists of a careful
systematic evaluation of the patient in order
to characterize the thyroid MALT lymphoma as
primary. This includes a thorough physical
examination, a full biochemical investigation,
evaluation of the gastrointestinal tract (gast-
roscopy, colonoscopy), a bone marrow biopsy
and scanning of the neck, chest and abdomen.
The second step is the staging of the tumor
according to the system proposed by Ann Arbor
and modified by Myssoff.7,10,17

Many dilemmas have been raised regarding
the proper management of patients with thy-
roid MALT lymphoma. Retrospective reports
suggest an indolent behavior and excellent
clinical prognosis for this subset of thyroid
lymphomas, leading to the conclusion that sin-
gle modality therapy with either surgery or
radiation may have a treatment role. However,
in the absence of randomized clinical trials to
compare different treatment options (thy-
roidectomy, radiotherapy, chemotherapy) in
patients with thyroid MALT lymphoma, there
are not widely accepted guidelines and thus
therapeutical protocols should be planned in
an individual base. Total thyroidectomy is the
treatment of choice in patients with compres-
sive goiter and localized thyroid MALT
lymphoma. Radiotherapy is used as primary thera-
pri in patients with stage IE and IIE and as
adjuvant therapy for those with suspected
residual disease after thyroidectomy. Chemotherapy is usually indicated for patients
with disease stages IIIE and IV but prognostic
data are unavailable because of the rarity of
this condition. In patients with localized dis-
ease, as in our patient, the preferred treatment
is total thyroidectomy while the benefit from
applying radiotherapy in a total dose of 40 Gy,
or chemotherapy, is questionable and with its
toxicity being a major issue.1,2,6,8,17-20

In conclusion, our case of a concurrence of
primary thyroid MALT lymphoma and autoim-
mune thyroiditis, is trying to emphasize the
need of a careful evaluation of any palpable
thyroid mass. This could be a benign lesion but
also a malignant lesion, including not only
neoplasms of thyroid tissue but also metastat-
ic from other sites or primary neoplasms of
extrathyroidal origin, as the case of lym-

![Figure 1. A) Hematoxylin and eosin (H&E) staining showing mucosa-associated lymphoid tissue (MALT) thyroid lymphoma; B) immunohistochemical evaluation reported MALT-balls; C) D) E) F) G) serial sections immunostained for CD79+, CD20+, clg-$\lambda$, clg-$\kappa$, L26, respectively.](image-url)
phomas and rarely MALT lymphomas. Moreover, this case in addition to the existing published cases, illustrates that the nature of follow-up care and long-term results of treatment of patients with primary thyroid MALT lymphomas are not fully established.

References

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