Rev Clin Esp. 2015;215(7):405–408

Revista Clínica Española

www.elsevier.es/rce

CLINICAL COMMUNICATION

Hodgkin's lymphoma of the thyroid in a woman with autoimmune thyroiditis

Linfoma Hodgkin de tiroides en una mujer con tiroiditis autoinmune

O. Rubio-Puchol[a,b,*], S. Garzón-Pastor[a,b], V. Cortés-Vizcaíno[c], I. Luna-Boquera[a,b], M. Gómez-Balaguer[a,b,d], A. Hernández-Mijares[a,b,d,e]

[a] *Endocrinology Department, University Hospital Dr Peset, Valencia, Spain*
[b] *Medicine Department, University of Valencia, Valencia, Spain*
[c] *Pathological Anatomy Department, University Hospital Dr Peset, Valencia, Spain*
[d] *Foundation for the Promotion of Healthcare and Biomedical Research in the Valencian Community (FISABIO), Valencia, Spain*
[e] *Institute of Health Research INCLIVA, Valencia, Spain*

Received 30 December 2014; accepted 15 February 2015
Available online 24 March 2015

Introduction

Autoimmune thyroiditis is associated with the development of thyroid lymphoma, and in particular mucosa-associated lymphoid tissue (MALT) lymphoma,[1] though this type occurs in only 0.5% of cases.[2] It has been reported that 20–30 years are needed for a lymphoma to develop as a result of autoimmune thyroiditis.[3] The association between thyroiditis and Hodgkin's lymphoma (HL) is more questionable, and is difficult to clarify due to the low number of cases of HL that arise. Nevertheless, in a previous study of 21 HL patients, 7 presented autoimmune thyroiditis.[4] The hypothesis of an association between the two conditions is based on the fact that the thyroid gland does not contain native lymphoid tissue; therefore, intrathyroid lymphoid tissue develops because of the presence of autoimmune thyroiditis. In this context, antigenic stimulation of lymphocytes in autoimmune disorders may trigger a malignant transformation. Primary extranodal HL accounts for less than 2% of extranodal lymphomas[2] and usually occurs due to the spreading of a contiguous lymphatic ganglion or hematogenous dissemination. It is questionable whether this is actually a primary disease, as it usually has an extrathyroid origin. Moreover it is considerably infrequent, with only 37 cases reported until now in the literature.[3] Its diagnosis is confirmed by the presence of Reed–Sternberg cells. We report the case of a patient with autoimmune thyroiditis with a fast-growing thyroid nodule. No evidence was detected of another tumor foci or adjacent lymphadenopathy, which led us to consider a diagnosis of primary thyroid gland HL. The peculiarity of this case lies in that, despite suffering autoimmune thyroiditis, the patient developed HL rather than MALT lymphoma, which is the usual clinical course in such cases.

Patient

A 54-year-old woman was monitored for subclinical autoimmune hypothyroidism with anti-peroxidase antibodies 2933.70 U per mililiter. At the time, she was receiving treatment with 75 μg per day of levothyroxine. Her thyroid function was controlled with TSH 1.90 μIU per mililiter and T4 free 1.3 ng per deciliter. The patient had no family history of thyroid pathology and no personal history of toxic substance abuse. During her initial visit, her cervical

* Corresponding author.
E-mail address: olallarubio@gmail.com (O. Rubio-Puchol).

http://dx.doi.org/10.1016/j.rce.2015.02.013

palpation was found to be normal, and a thyroid ultrasound scan revealed a solid left thyroid nodule with a maximum diameter of 9 mm that was hypoechoic, clearly defined, avascular and without calcification. According to current guidelines of clinical practice,[5] fine needle-aspiration biopsy (FNAB) was not indicated. Ultrasound was scheduled one year later and revealed no significant changes. Three years later, the thyroid lesion began growing rapidly, demonstrating a palpable thyroid nodule with a maximum diameter of 2 cm. Ultrasound revealed an increase in the size of the nodule to 17.8 mm × 22.6 mm, and showed it to be solid, occupying practically all the left thyroid lobe, hypoechoic, unstructured and heterogeneous, with mixed vascularization and without microcalcifications (Fig. 1).

In response to these developments, FNAB was carried out and revealed atypically large and multinucleate lymphocytes with features of Reed–Sternberg cells, which raised suspicions of lymphoma (Fig. 2). Given the difficulty in distinguishing between inflammatory and lymphoproliferative processes (especially MALT-type LNH) in a patient with autoimmune thyroiditis, it was decided to repeat FNAB with flow cytometry. Atypical lymphocytes were observed once again, but there was no sign of infiltration due to lymphoma ($CD3^+$ T lymphocytes were observed in 48%, of which 73% were $CD4^+$ and 22% were $CD8^+$; 44% were polyclonal $CD19^+$ B lymphocytes without evidence of immature cells). In light of these results, a biopsy was carried out (left hemithyroidectomy) to confirm a suspected thyroid HL. The intraoperative biopsy suggested autoimmune thyroiditis without any evidence of lymphoma. The definitive pathological anatomy study revealed classic HL of a nodular sclerosis type in the presence of autoimmune thyroiditis, with no apparent affect on the cervical lymph nodes. Immunohistochemistry of Reed–Sternberg cells produced the following results: $CD15^+$ $CD30^+$ $CD20^+$ (weak expression), $CD79a^-$, $MUM1^+$ $PAX5^+$ and $EBER^+$. A gene rearrangement study of T cell receptor (TCR) genes and immunoglobulin heavy chain (IgH) antibodies was carried out by means of quantitative polymerase chain reaction (PCR), whose result was negative. A fluorescence hybridization in situ (FISH) study for MALT-1 produced negative results. A positron emission tomography–computed tomography (PET–CT) scan of the cervicothoracic area, abdomen and pelvis was performed and revealed no hypermetabolic foci suggestive of active tumor disease. Thus, a diagnosis of primary thyroid gland LH (Ann Arbor Stage Ie) secondary to autoimmune thyroiditis was confirmed. As a consequence, ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) chemotherapy was initiated. It is now 8 months since surgery and the patient has completed four ABVD cycles. A recent PET–CT scan revealed no hypermetabolic foci suggestive of active tumor disease, therefore pointing to complete remission.

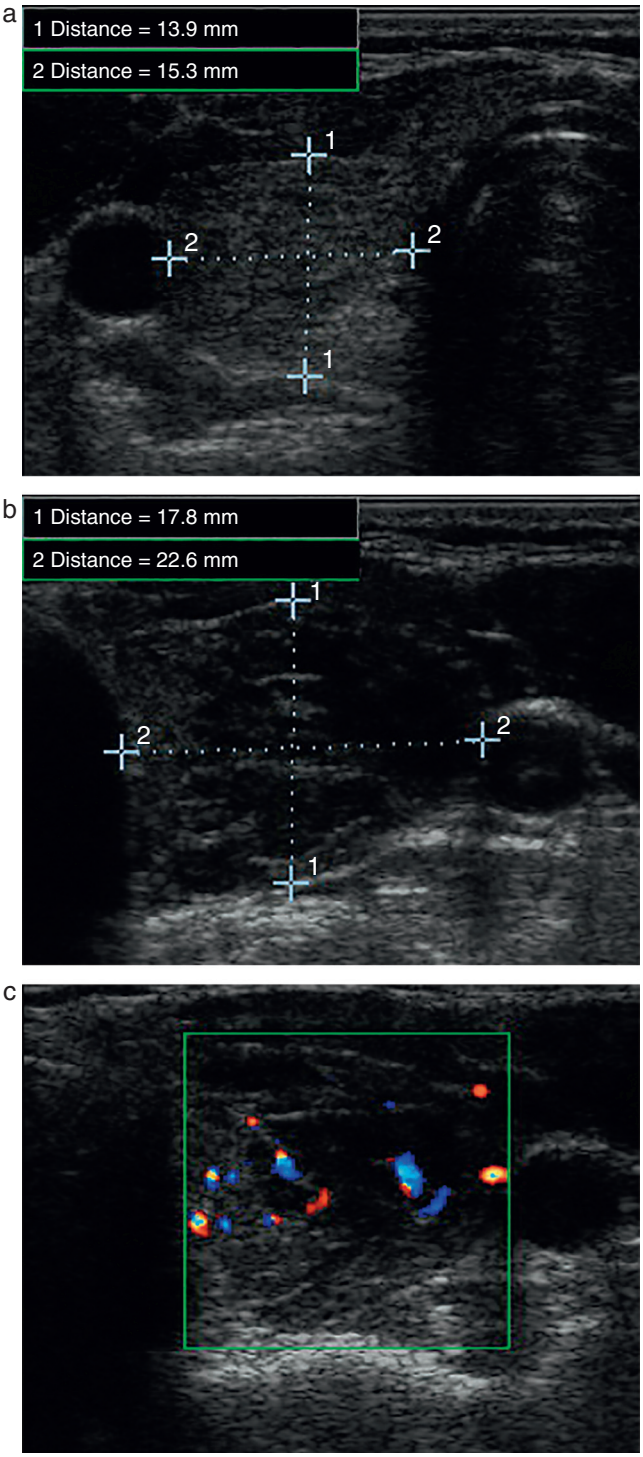

Figure 1 Thyroid ultrasound scan. (a) Right thyroid lobe with typical echogenicity of autoimmune thyroiditis and no nodular formations. (b) Left thyroid lobe occupied by thyroid nodule. (c) Ecodoppler of the left thyroid nodule showing mixed vascularization.

Discussion

Approximately 75–80% of thyroid HL patients are women, in contrast to extrathyroid HL patients, among which the incident rate is similar in both sexes.[3] The average age of patients is 40 years,[4] which is lower than that of thyroid NHL patients, who tend to be in their sixth decade of life. In 80% of thyroid HL cases, there is a rapid increase of a uni- or bilateral cervical mass. Other symptoms are shortness of breath (65%) and dysphagia (53%). Most patients have concomitant lymphadenopathy at the time of diagnosis. What are known as B symptoms (fever, sweating, loss of weight) are frequent (33%) and are considered a sign