Turk J Med Sci
34 (2004) 395-398

SHORT REPORT

Primary Thyroid Lymphoma Arising in the Setting of Hashimoto's Thyroiditis

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Received: April 11, 2004

Key Words: MALT lymphoma, thyroid, Hashimoto's thyroiditis

Primary thyroid lymphomas constitute up to 5% of all thyroid malignancies and can be divided into non-Hodgkin's lymphomas (NHL) of the B and T cell types and Hodgkin's lymphomas. Mucosa-associated lymphoid tissue (MALT) lymphomas are a subset of B cell NHL, and they are listed as marginal zone B cell lymphomas of the MALT type according to the revised European-American lymphoma classification (1) and the more recently proposed World Health Organization classification of hematopoietic and lymphoid tissue neoplasms (2).

MALT lymphomas' most common location is the mucosa of the gastrointestinal tract. However, they may also occur in the lungs, salivary glands, skin, subcutaneous tissue and other sites including the thyroid (3-6). It is thought that lymphomas originating in this wide variety of primary sites represent a malignant transformation of acquired lymphocytic tissue during the course of a chronic inflammatory or an autoimmune process (5).

The thyroid gland contains no native lymphoid tissue. Intrathyroid lymphoid tissue is accrued in various pathological conditions, but more evidently in the course of autoimmune thyroid disease, notably chronic autoimmune thyroiditis (Hashimoto's thyroiditis) (3,7). Histologically, this acquired lymphoid tissue can evolve to lymphoma, including MALT type. Clinically it is characterized by an indolent course and a prognosis better than that of non-MALT lymphomas (5).

We here describe the results of clinical and laboratory tests including histological and immunohistochemical studies of a thyroid lymphoma in association with Hashimoto's thyroiditis, along with a review of the literature.

Case Report

The patient was a 69-year-old woman who presented with a rapidly enlarging neck mass, associated with dysphagia. On clinical examination, the thyroid was diffusely enlarged, most prominent on the right side, firm and painless. The patient was clinically and biochemically hypothyroid. Serum T4 was 4.8 µg/dl (normal, 5-12) and serum TSH was 6.8 mU/l (normal, 0.4-4.6). Antithyroglobulin antibodies were positive (1:100), and antimicrosomal antibodies were not detected. Ultrasound examination revealed hypoechoic areas in both lobes but no cysts. A right thyroid lobectomy was performed revealing a 6 x 5 x 5 cm white fleshy mass.

Microscopic examination revealed a diffuse lymphoid infiltrate effacing the normal thyroid parenchyma in a background of a chronic lymphocytic thyroiditis, with hyperplastic lymphoid follicules and oncocytic change within the follicular epithelium. The thyroid parenchyma was diffusely replaced by a dense atypical lymphoid infiltrate composed of monocytoid lymphocytes with small or slightly irregular nuclear contours, condensed nuclear chromatin, inconspicuous nucleoli, and abundant pale cytoplasm. Centrocyte-like (cleaved) cells, small lymphocytes, plasma cells and occasional centroblast- or immunoblast-like large cells were also evident. These cells gave rise to numerous lymphoepithelial lesions with packed acini (Figure 1). In almost all areas follicular epithelial cells were seen as abundant granular eosinophilic cytoplasm, with some prominent macronucleoli that are characteristic of Hurthle cells (Figure 2).

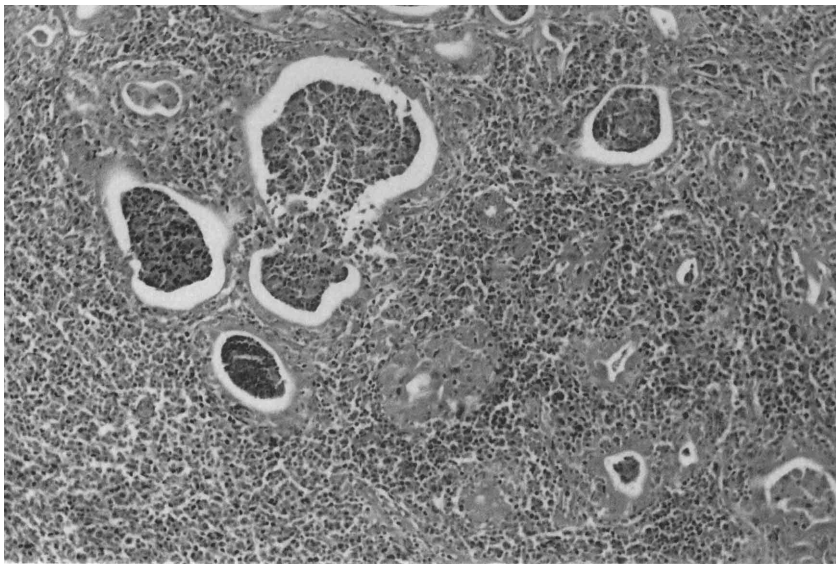

Figure 1. Diffuse effacement of thyroid architecture and residual packed acini or lymphoepithelial lesions (Hematoxylin and eosin x 50).

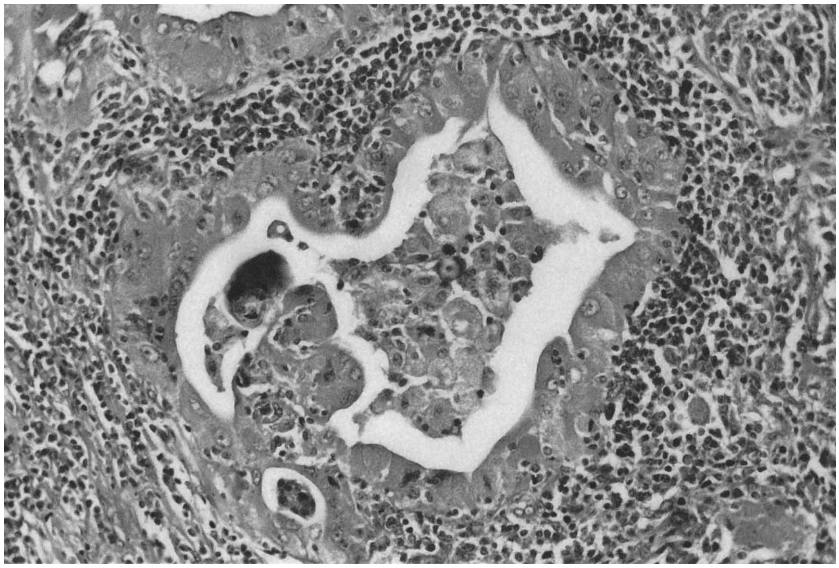

Figure 2. Residual thyroid follicules with Hurthle's cell change (Hematoxylin and eosin x 100).

Immunohistochemistry confirmed the B cell nature of the atypical cells; most lymphocytes in diffuse areas as well as packed LEL were positive for CD20, CD22 and CD79a, and negative for CD3, CD5 and CD10. Small clusters of monoclonal κ light chain restriction were also identified.

At the time of this report (2 years after surgery), the patient continues to have an uneventful clinical course. No radiotherapy or chemotheraphy was used. The patient will be followed up at 6-month intervals.

Thyroid MALT lymphomas are characterized by the presence of atypical lymphoid cells, which originate within the marginal zone of the lymphoid follicules and can extend to the interfollicular space (4,8,9). As seen in our patient the typical histologic features of Hashimoto's thyroiditis, such as oncocytic change in follicular cells, small lymphocytes and reactive follicules, may also be present. The abundance of reactive components in the presence of a low-grade neoplastic process may obscure the diagnosis when evaluation is limited.

Lymphoepithelial lesions arise from invasion marginal zone cells into the thyroid follicular epithelium and are a characteristic, but not a pathogonomic feature of MALT lymphomas. Lymphoepithelial lesions in chronic lymphocytic thyroiditis and other benign lymphocytic infiltrates of the thyroid are infrequent and tend to be small (3,8). In contrast lymphoepithelial lesions in MALT lymphomas of the thyroid gland tend to be more frequent and larger with distended or stuffed acini, as were common in our case.

Immunohistochemical studies were done to determine the nature of the atypical lymphoid cells. MALT lymphomas express B cell associated antigens (CD20, CD22 and CD79a) and are negative for CD5, CD10 and CD3. Immunohistochemical studies are a useful adjunct to diagnosis in excluding B cell chronic lymphocytic leukemia (B-CLL), mantle cell lymphoma and follicle center lymphoma (1,7,8).

Molecular studies of the Ig gene, such as the Southern blot technique, have emerged as a reliable and specific method for the identification of lymphocytic clone(s) and diagnosis of lymphoma in thyroid specimens (3). In recent years PCR-based assays have offered some advantages over the Southern blot technique, including higher sensivity and a smaller amount of tissue being required (10).

The optimal treatment and follow-up of patients with thyroid maltomas remain controversial at present. Retrospective reports suggest indolent behavior and an excellent clinical prognosis for this subset of thyroid lymphomas. In general the choice of treatment modality depends on the stage of the disease: surgery and/or radiotherapy are used in localized disease, supplemented with chemotherapy in disseminated cases (9,11).

MALT lymphomas limited to the thyroid have a good prognosis with an overall 5-year survival rate of 70% to nearly 100% with combined radiation therapy and chemotherapy regardless of the histologic grade. Advanced stage, tumor bulk and extracapsular extension are the factors that have the most adverse effect on prognosis and are associated with increased risk of relapse (6,8).

In conclusion, this case illustrates that low-grade NHL of the MALT type may arise in the setting of chronic autoimmune thyroiditis and this situation makes it distinctive from other extranodal presentations of non-Hodgkin's lymphoma. Follow-up care and long term results of treatment of patients with thyroid lymphoma are not fully established, as maltoma presenting in the thyroid gland is an uncommon malignancy.

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