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BRIEF REPORT

Classical Hodgkin's lymphoma of the thyroid

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KEYWORDS
Hodgkin's disease;
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Abstract Hodgkin's lymphoma is characterized by the presence of Reed–Sternberg cells. The majority of cases originate at nodal sites and only rarely does it occur in extranodal locations. Here we report a case of a woman with a classical Hodgkin's lymphoma of the thyroid developed from a Hashimoto thyroiditis. She presented with a mass in her thyroid which was surgically removed. Biopsy showed a nodular sclerosis classical Hodgkin's lymphoma. Our results were similar to previously reported cases. It would appear that the lesions grew over a MALT tissue created by the lymphoid proliferation of the thyroiditis. Differential diagnosis was made between the different types of lymphomas considering those most commonly occurring in extranodal lymphoid tissues. A final diagnosis was reached after consideration of the histopathology, immunophenotyping and molecular biology.

PALABRAS CLAVE
Enfermedad de Hodgkin, Células de Reed–Sternberg, Glándula tiroides, Enfermedad de Hashimoto

Linfoma de Hodgkin clásico del tiroides

Resumen El linfoma de Hodgkin se caracteriza por la presencia de células de Reed–Sternberg. La mayor parte de los casos se originan en ganglios linfáticos y raramente en localizaciones extranodales. Comunicamos un caso de una paciente con un linfoma de Hodgkin clásico desarrollado sobre una tiroiditis de Hashimoto. Se presentó como una masa tiroidea que fue extirpada. Histológicamente mostró un linfoma de Hodgkin clásico de tipo esclerosis nodular. Nuestros resultados concuerdan con casos publicados anteriormente. La lesión posiblemente se originó sobre un tejido MALT creado por la proliferación linfoide relacionada con la tiroiditis. Realizamos

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diagnósticos diferenciales entre diferentes tipos de linfoma que tienen lugar en tejido linfoide extranodal. El diagnóstico final fue realizado tras considerar su histopatología, inmunofenotipo y genética molecular.

Introduction

Hodgkin's lymphoma (HL) is a pathological entity characterized by the presence of Reed–Sternberg cells (RSC) and their inflammatory infiltrate. It is now considered as a lymphoid neoplasm of B-cell origin.[1] The annual incidence of HL is about 3 new cases per 100,000 habitants; 95% of HL are classical (CHL) and the rest 5% are considered nodular lymphocyte predominant HL (NLPHL). Within the CHL, the nodular sclerosis subtype (NSCHL) is considered the most frequent in western countries, followed by the mixed-cellularity subtype (MCCHL) that is more common in developing countries.[2] Nowadays, with the combination of field radiation therapies and chemotherapy, control ratios and long term survival for HL exceed 80%.[3]

The majority of HL develops at nodal sites. In some extremely rare cases the first manifestation of HL appears in extranodal sites such as the gastrointestinal tract, nasopharynx (ex: Waldeyer's ring),[4] central nervous system or the kidneys.[5] Extranodal involvement is usually associated with the non-Hodgkin's lymphoma (NHL). The most frequent primary thyroid lymphomas (PTL) are of B cell origin; in which the most common subtype is diffuse B cell lymphoma (comprising up to 70% of PTL cases) followed by extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT).[6]

Hashimoto thyroiditis (HT) is an autoimmune disease that induces a lymphocytic proliferation in the thyroid, i.e. it induces the presence of lymphocytes in a lymphoid free tissue. HT is a risk factor for the development of PTL.[7] Here we present a case of a patient with Hashimoto's thyroiditis who developed a primary CHL of the thyroid.

Case report

A 53-year-old European woman presented for the first time in 2009 with a palpable nodule on her left thyroid lobe. On ultrasound a nodular hypoechoic mass was found measuring 1.2 cm at its largest dimension. Her past medical history was unremarkable and her blood analysis showed primary hypothyroidism (TSH: 11 mcIU/ml (reference range [rr] = 0.4–4), T4: 0.8 ng/dl (rr = 4.5–11.2)) with increased anti-thyroid peroxidase antibodies (2.933 IU/ml (rr = 0–60)). A diagnosis of Hashimoto thyroiditis was made and treatment was prescribed (Levothyroxine 75 mcg). On subsequent annual controls she remained stable until 2013 when she returned to the clinic with a new neck mass without palpable lymph nodes.

Ultrasound revealed a nodule [1.8 cm × 2.1 cm] in the left thyroid that replaced the whole parenchyma. The remaining tissue was well vascularized and showed no calcifications. A fine needle aspiration biopsy (FNAB) was performed and cytology revealed atypical Sternberg cells surrounded by a background of small lymphocytes, suspicious of Hodgkin's lymphoma (Fig. 1). A 2nd FNAB was obtained for flow cytometry, which showed a mixed population of mature T cells and non-neoplastic B cells (CD3–CD4 73%, CD3–CD8 22%, CD3–CD19 46%, CD10 negative, CD19-kappa 54%, and CD19-lambda 45%).

Left thyroid lobectomy was performed and a firm mass was found, partially adhered to deep tissues, with small but multiple homolateral lymph nodes which were also resected for further histopathological analysis. The left hemithyroid specimen was a 5 cm × 4 cm × 2 cm firm white mass, with a single nodule of 4.5 cm at its largest diameter. Microscopically, a polinodular pattern, with lymphoid aggregates delimited by thick fibrous septa, was seen. These nodules showed a variegated cellularity: while most of them were part of a typical lymphoid thyroiditis (with few remaining thyroid follicles, oncocytic metaplasia, dense T and B cells infiltrate and reactive BCL2− germinal centers), some of them showed a complete loss of thyroid epithelium, and a predominant CD4 cell population admixed with polyclonal plasma cells and some eosinophils, surrounding large clear cells with bilobated nuclei and prominent eosinophilic nucleoli, typical of Reed–Sternberg cells. Immunohistochemistry revealed: CD30+, CD15+, CD20−, MUM1+, EBER+, LMP1+, CD3− in the RSC, whereas the small lymph cell population was CD3+, CD5+, CD4+ in the nodules and CD3+, CD20+ in the rest of the tissue (Fig. 1). The gene-rearrangement assay resulted polyclonal for both IgH and TCR.

The cervical lymphadenectomy was integrated by five firm, whitish lymph nodes varying from 0.5 to 1.5 cm. Microscopically (Fig. 2), there was a predominant diffuse B cell small size population (CD20+, CD10−, CD5−, CD43−), which partially erased the follicular architecture although some reactive germinal centers BCL2− remained. IgD and IgM were negative except for IgM positivity at the follicular mantle. We could not find typical RSC in the infiltrate although there were some reactive immunoblasts CD20+, CD30+, EBER+. The gene-rearrangement assay results were polyclonal for both IgH and TCR but the presented polymorphism was not congruent with those of the thyroid. This pointed to a different cellular origin.

Fluorescence in situ hybridization (FISH) for MALT lymphoma was negative when applied both to the thyroid and the lymph nodules. We used the MALT1 (mucosa-associated lymphoid tissue) lymphoma translocation gene at chromosome 18 band q21 (*MALT1 FISH DNA Probe, Split Signal, Dako, Denmark A/S*).