



## CD30 positive (non-anaplastic) peripheral T cell lymphoma of the thyroid gland

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### Abstract

**Primary non-Hodgkin's lymphoma of the thyroid gland are infrequent tumors. They almost exclusively derive from B cells of mucosa-associated lymphatic tissue and only a very small minority of them are T cell lymphomas. CD30 molecule, other than in Hodgkin's and Reed-Sternberg cells, is strictly associated with anaplastic large cell lymphoma and ALK lymphomas, the latter being identified by the monoclonal antibody ALK1. We report a case of CD30-positive non-anaplastic (ALK1-negative) peripheral T cell lymphoma of the thyroid gland and speculate on aspects concerning diagnosis and the morphologic and immunohistochemical findings.**

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Key words: thyroid, NHL, ALK1, CD30, non-anaplastic

Primary thyroid lymphomas are rare, almost always of B-cell origin and derive from mucosa-associated lymphatic tissue.<sup>1</sup> Very few, less than 2% of all primary thyroid lymphomas,<sup>2,3</sup> are of T cell origin. We report here the first case, to our knowledge, of a CD30<sup>+</sup> non-anaplastic T-cell lymphoma of the thyroid gland well documented from morphologic and immunohistochemical points of view. Aspects concerning the diagnosis are discussed and the peculiar morphologic and immunohistochemical pattern of this lymphoma is commented upon.

### Case Report

A 39-year-old Caucasian woman was seen because of marked goitre. No other symptoms or signs at physical examination were present. Laboratory values were normal except for the presence of serum antibodies against hepatitis C virus. An ultrasonography of the thyroid revealed the presence of a 20-mm diameter solid nodule localized in the isthmus. Concomitantly, a scintigraphy of the thyroid with radioactive technetium (<sup>99m</sup>TcO<sub>4</sub><sup>-</sup>) showed uneven distribution of the radionuclide which was prevalently present in the right lobe and absent in the area corresponding to the nodule. Two fine needle biop-

sies were performed in two different centers and on both occasions a diagnosis of chronic thyroiditis was made. Since the patient had no symptoms or signs of disease, the chosen management was no therapy but only observation.

However, after 4 weeks, the goitre enlarged and the patient developed fever, dysphonia and severe dysphagia that required admission to hospital, parenteral alimentation and steroid treatment. A computerized tomographic scan of the neck and the chest revealed a huge enlargement of the right thyroid lobe in which a 4 cm diameter nodular lesion with a wide necrotic central component was present. In addition, the mass extended to the superior mediastinum with involvement of lymph nodes which compressed and displaced the trachea, the esophagus and the superior arterial vessels. Laboratory examinations showed: Hb 10.7 g/dL; Hct 35%; MCV 84.1 fL; WBC 9.9×10<sup>9</sup>/L; Plt 111×10<sup>9</sup>/L; TSH 3.16 μU/mL (normal: 2-10 μU/mL); fT<sub>4</sub> 21.16 pg/mL (normal 8-24 pg/mL); fT<sub>3</sub> 3.95 pg/mL (normal 2.6-4.8 pg/mL). Anti-peroxidase, anti-thyroglobulin and anti-TSH receptor antibodies were absent in the serum and thyroglobulin serum concentration was 47.8 ng/mL (normal 3-50 ng/mL). β<sub>2</sub>-microglobulin was 2.1 ng/mL (normal 0.81-2.2 ng/mL) and lactate dehydrogenase was 260 IU/L (normal 230-460 IU/L). C-reactive protein and erythrocyte sedimentation rate were increased to 7.8 mg/dL and 84 mm/h, respectively. Since a carcinoma or a lymphoma was suspected, open biopsy of the thyroid mass and supraclavicular lymph nodes was made.

Histomorphologic analysis of the specimens revealed an infiltrate of lymphoid elements of variable size with focal aggressive tendency towards some follicles in the thyroid, and an infiltrate of variably sized lymphoid cells in the lymph nodes. In neither site was cell morphology characteristic of an anaplastic large cell form of lymphoma. Immunohistochemical studies revealed that lymphomatous cells of the thyroid gland and lymph node were CD30<sup>+</sup>, CD45RO<sup>+</sup>, CD3<sup>-</sup>, CD20<sup>-</sup>, CD79a<sup>-</sup>, CD21<sup>-</sup>, BCL2<sup>-</sup>, thyrocalcitonin<sup>-</sup>, thyroglobulin<sup>-</sup>, ALK1<sup>-</sup>, and CD43<sup>-</sup>. The CD45RO positivity of the lymphomatous cells was consistent with a T-phenotype (Figures 1, 2 and 3).

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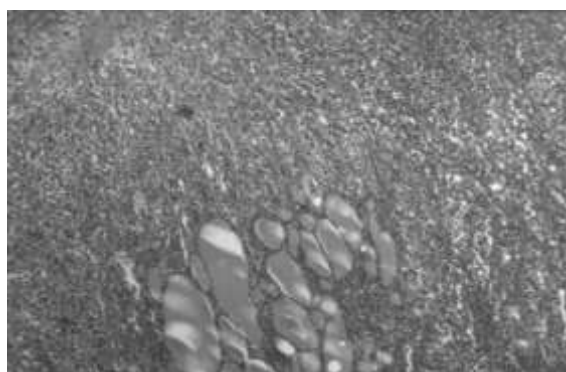


Figure 1. Residual thyroid follicles surrounded by lymphoid cells of variable size. H&E,  $\times 100$ .

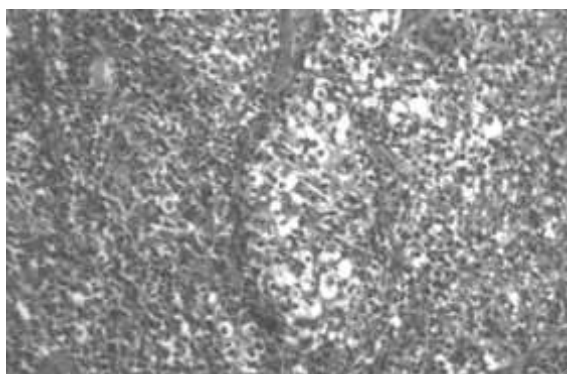


Figure 2. At a higher magnification, some lymphoid cells of large size and irregular nuclear shape, sometimes surrounded by a dim halo, can be seen. H&E,  $\times 250$ .

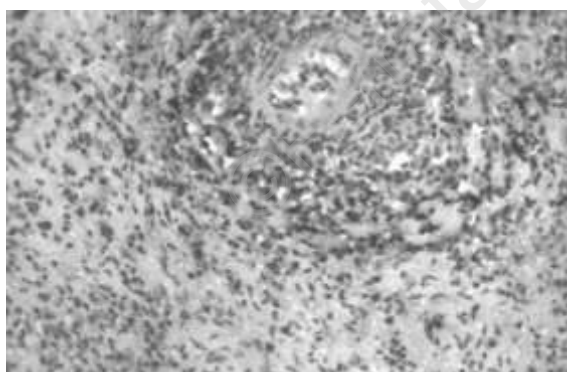


Figure 3. Immunostaining of CD30 molecule (Ber-H2): this shows the faint positivity of the larger lymphoid cells.  $\times 250$ .

A diagnosis of peripheral T CD30<sup>+</sup> cell lymphoma, large-cell, unspecified according to the REAL classification, was made.<sup>4</sup> Staging was completed with a CT scan of the abdomen and a bone marrow biopsy, both of which resulted negative. The patient was, therefore, considered to be in clinical stage IIA with *bulky* disease.

The patient was treated with 8 courses of MACOP-B regimen which produced a partial response and then with high-dose chemotherapy with BCNU, etoposide, cytosine-arabioside, cyclophosphamide, followed by reinfusion of autologous peripheral hemopoietic progenitor cells. Despite complete disappearance of the mass, the patient received additional irradiation (3600 cGy) to the involved sites at the time of diagnosis.

One year from the completion of therapy the patient remains well with no evidence of recurrence.

## Discussion

Thyroid lymphomas are infrequent tumors: they represent 2 to 5% of all thyroid neoplasms<sup>5,6</sup> and 2-3% of all extranodal lymphomas.<sup>7-9</sup> Isaacson and Wright<sup>10</sup> have suggested that primary non-Hodgkin's lymphomas (NHL) of the thyroid gland should be grouped with NHL derived from the mucosa-associated lymphatic tissue, since they tend to have the same morphology. According to one of the latest reclassifications of thyroid lymphomas,<sup>2</sup> 17% of patients had a low-grade pattern of disease and 83% a high-grade one. Although histologic grade may be differently distributed in different investigations, all published studies concur that almost all primary NHL of the thyroid gland are of B-phenotype,<sup>11-17</sup> with a single exception, in a study of a limited number of patients in which 10% of the cases were documented to have a T-phenotype.<sup>13</sup>

Apart from a single case observed after Hashimoto's thyroiditis,<sup>18</sup> T-cell lymphomas developed after thyroiditis have not been described; however, histology of fine needle aspiration biopsy samples may lead to misinterpretation between thyroiditis and T-cell lymphomas. In fact the sensitivity of this technique is not absolute and varies from 70 to 90%<sup>19,20</sup> and, as in our case, sometimes it may even become misleading.<sup>21</sup> Thus, to confirm the diagnosis, open biopsy of the thyroid should always be performed.

CD30 molecule, other than on Hodgkin's and Reed-Sternberg cells, is strictly associated with anaplastic large cell lymphoma (ALCL)<sup>4,22,23</sup> and with ALK lymphoma, a new clinical and pathologic entity which shows mostly, but not constantly, anaplastic morphology and is characterized by the presence of the fusion protein P80 resulting from the t(2;5) translocation.<sup>24-26</sup>

In 1990, the CD30 molecule was also demonstrated on non-anaplastic lymphomas such as peripheral T-cell lymphomas, histiocytic lymphomas and pleomorphic lymphomas and since then the CD30<sup>+</sup> pattern has no longer been considered *synonymous* of ALCL.<sup>27</sup> However, the REAL classification group does not yet consider CD30<sup>+</sup> non-anaplastic lymphomas as a separate immunohistologic pattern. These lymphomas have been identified in nodal and extranodal sites such as the skin, subcutaneous tissue and stomach,<sup>28-30</sup> but to our knowledge, never in the thyroid.

Our case report demonstrates that CD30<sup>+</sup> non-anaplastic (ALK1-negative) T-cell lymphomas can involve other extranodal sites, namely the thyroid.

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FF was the principal investigator, contributed to the conception of the study, data handling and interpretation and wrote the paper. MB, SM, MM, GF-O contributed to data handling and interpretation. FL was responsible for direct supervision and critical revising of the final version of the manuscript. The criteria for the order is: 1<sup>st</sup> name: principal investigator and writer; 2<sup>nd</sup> to 5<sup>th</sup> name: data handling and interpretation; last name: senior author, direct supervisor and revisor of the manuscript.

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