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Primary Thyroid Lymphoma

ABSTRACT

Eight cases of primary thyroid lymphoma were reported in a tertiary government hospital from January 2005 to August 2011. All patients presented with a diffuse enlargement of both thyroid lobes with associated obstructive symptoms. Five of these cases were extranodal marginal zone lymphoma and three were diffuse large B-cell lymphoma. Clinical features that would favor a thyroid lymphoma include tumor size of greater than 7 cm, obstructive symptoms, clinical hypothyroidism or history of Hashimoto thyroiditis. Thus, these features must be considered in evaluating thyroid nodules during fine-needle aspiration biopsy. Histologically, extranodal marginal zone B-cell lymphoma shows vaguely nodular to diffuse infiltrates of small to intermediate size atypical lymphoid cells infiltrating the thyroid follicles while diffuse large B-cell lymphoma shows sheets of large atypical lymphoid cells infiltrating the thyroid follicular epithelium.

Keywords: *primary thyroid lymphoma, extranodal marginal zone B-cell lymphoma, diffuse large B-cell lymphoma*

Primary thyroid lymphoma is a rare neoplasm that comprises 1-5% of all thyroid malignancy and 1-7% of all extranodal lymphomas.[1-4] It usually occurs in older individuals with a mean age of 65.[1-2] It is more common in females with a ratio of 3-6:1.[1,4] A total of eight patients were diagnosed to have a primary thyroid lymphoma among 1,008 malignant thyroidectomy specimens seen by our department from January 2005 to August 2011 with an incidence rate of 0.8% of all thyroid malignancies in our institution. We review these cases.

CASES

There was one male and seven females with a ratio of 1:7. Their ages ranged from 37-86 years old with a median age of 56 years. Of the eight patients, only five had available clinical data. All five had a 1-3 year history of diffuse anterior neck mass and all had obstructive symptoms such as dyspnea and dysphagia. One patient each had weight loss and regional lymph node enlargement. Pre-operative thyroid function tests of 4/5 patients revealed hypothyroidism in one while three were euthyroid.

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Macroscopic examinations of all eight thyroidectomy specimens showed diffuse enlargement of both thyroid lobes with sizes ranging from 11 to 15 cm in widest diameter. Histopathologic diagnosis revealed diffuse large B-cell lymphoma *(Figure 1, A-D)* in three patients and extranodal marginal zone B-cell lymphoma in five patients. *(Figure 2, A-E)* Immunohistochemical staining with CD3, CD5 and CD20 confirmed the diagnosis.

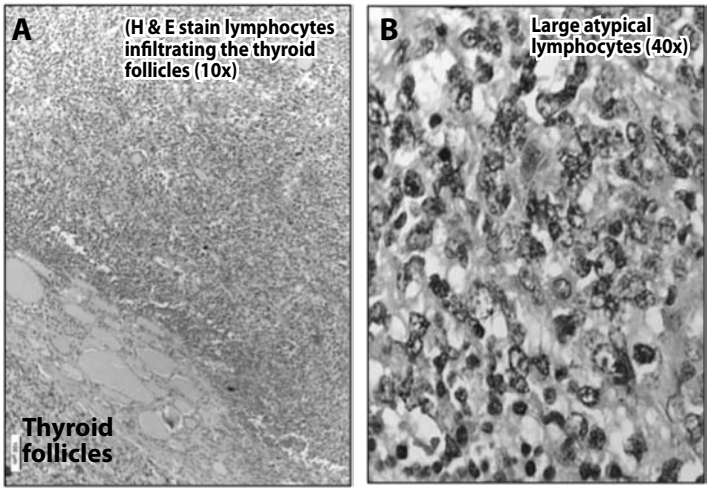

Figure 1. Diffuse large B-cell lymphoma. **A.** H and E stain shows large atypical lymphocytes infiltrating the thyroid follicles (10x). **B.** Large atypical lymphocytes (40x).

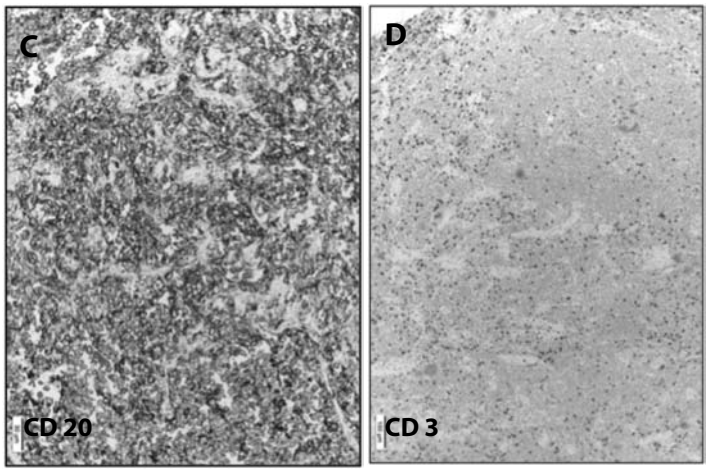

Figure 1. C,D. Immunohistochemical staining showed diffuse and strong cytoplasmic membrane staining for CD20 and negative for CD3.

DISCUSSION

The clinical features that would favour primary thyroid lymphoma include women in the sixth decade, a history of Hashimoto thyroiditis and rapid growth of a firm diffuse thyroid mass.[1,2,6] A study in the Philippines (1994-1998) showed a lower mean age than foreign data with 55% of cases occurring in the less than 60-year-olds (Range= 49-69 years) with a male to female ratio of 1:1.25.[6] The present series had 60%

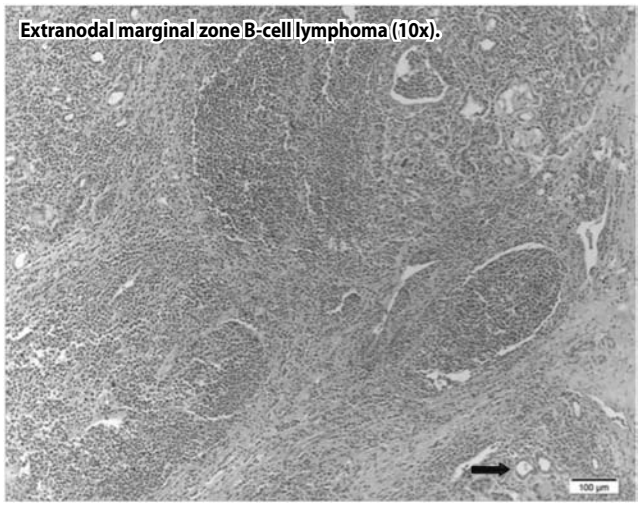

Figure 2. A. Extranodal marginal zone B-cell lymphoma (10x). There were nodular and diffuse proliferation of small to medium size lymphocytes infiltrating the thyroid follicle. In here, we can also appreciate the remnants of Hashimoto thyroiditis characterized by oncocytic changes of the follicular cells (arrow).

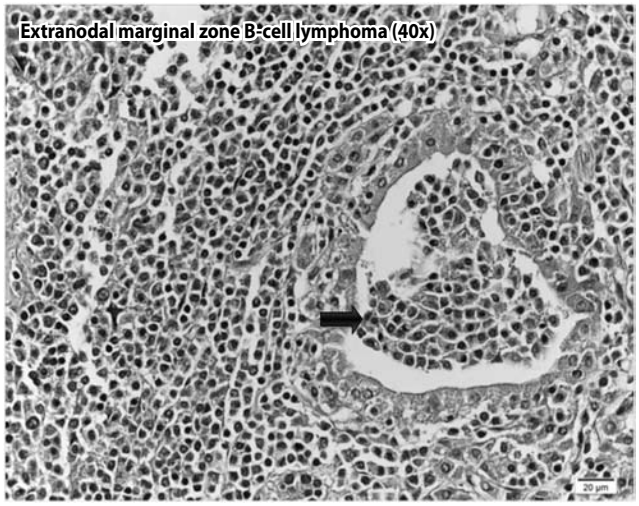

Figure 2. B. Extranodal marginal zone B-cell lymphoma (40x). Lymphoepithelial lesion showing neoplastic cells within the follicle (arrow).

of patients younger than 60 years old, comparable with the previous study done in the Philippines.

The tumor size is usually large at the time of diagnosis between 8-14 cm according to the previous Philippine study between 11-15 cm in our series and between 2-15 cm with a median size of 7 cm in other studies.[3,7] Due to the rapid growth of the tumor, compression of the adjacent organs causes obstructive symptoms such as dyspnea and dysphagia. Derringer *et al.* reviewed 108 cases of primary thyroid lymphoma with 72% having obstructive symptoms.[7]

Hypothyroidism is seen in up to 67% of cases of primary thyroid lymphoma.[3] A history of Hashimoto thyroiditis has a relative risk of

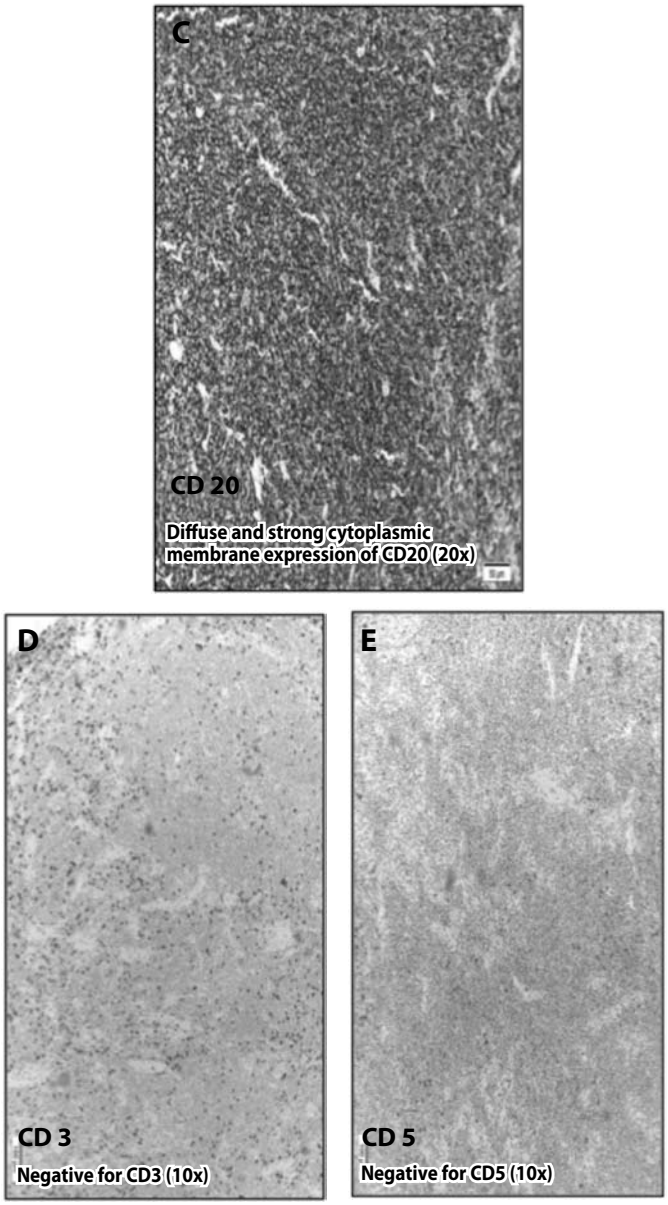

Figure 2, C-E. Extranodal marginal zone B-cell lymphoma. Diffuse and strong cytoplasmic membrane expression of CD20 (20x). Negative for CD3 (10x). Negative for CD5 (10x).

up to 80x compared to the general population in developing primary thyroid lymphoma.[4] Extranodal marginal zone B-cell lymphoma is the morphologic variant associated with Hashimoto thyroiditis. In our series, only one patient was hypothyroid out of four for whom clinical data was available.

Fine needle aspiration has become the procedure of choice for the initial pathological diagnosis of thyroid nodules. In one series, a correct diagnosis with FNAB was made in 70-80% of patients with thyroid lymphoma,[8] but in others, FNAB was suggestive but not diagnostic in only 50-60% of patients.[9-10] In the present series, only one out of five cases of PTL was correctly diagnosed by FNAB. Data was not available for the three other cases. The sensitivity of FNAB in the diagnosis of primary thyroid lymphoma in our institution is lower compared to the foreign literature. Ancillary procedures such as immunohistochemical staining and molecular genetic testing can increase diagnostic accuracy, especially in cases of Extranodal Marginal Zone B-cell lymphoma since it resembles a reactive lymph node in cytology specimens.

Cytologically, diffuse large B-cell lymphoma shows a cellular aspirate which consists of large atypical lymphoid cells (2-3x larger than mature small lymphocyte) with scattered small cytoplasmic fragments of lymphocytes in the background. There are scanty to absent follicular cells. Extranodal marginal zone B-cell lymphoma shows cellular aspirate which consists of small to intermediate-size lymphoid cells. Some cells show abundant, pale cytoplasm (monocytoid appearance). This cytologic features overlap with chronic lymphocytic thyroiditis. However, the absence of tangible body macrophages, activated follicle-center cells and spectrum of lymphocytes in all stages of maturation favor extranodal marginal zone B-cell lymphoma. Immunophenotyping is often required to aid in the definitive diagnosis.

Clinical features that would favor a thyroid lymphoma include tumor size of greater than 7 cm, obstructive symptoms, clinical hypothyroidism or a history of Hashimoto thyroiditis. Thus, these features must be considered in evaluating thyroid nodules during FNAB. Immunohistochemistry and molecular techniques can be used as adjunct in these cases when cytology specimens are equivocal for lymphoid malignancy.

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