Thyroid lymphoma: diagnostic pitfalls on pre-operative ago-biopsy

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BACKGROUND: Thyroid cancer has the highest prevalence of all endocrine malignancies. Malignancy can be of thyroid or non-thyroid origin. Sarcomas and primary thyroid lymphomas (PTL) are rare and surgery is treatment of choice in the former but not in latter.

OBJECTIVE: To describe thyroid lymphomas histological types of thyroid cancer found in a reference center.

METHODS: Medical chart review from admitted patients diagnosed with thyroid cancer in the period from January 2007 to June 2012. Demographic, diagnostic, therapeutic and histopathological information were collected.

RESULTS: 1604 records of patients admitted with thyroid disease were reviewed. Among 307 thyroid cancer, the cases diagnosed with rare tumors were: 10 cases of anaplastic carcinoma (3.5%), followed by 4 cases of medullary carcinoma (1.3%), 1 case of teratoma (0.03%), 2 cases of lymphoma (0.06%). The most frequent clinical presentation was a palpable thyroid nodule. All patients with lymphoma died.

CONCLUSION: Thyroid lymphomas are uncommon and tend to worse outcomes.

KEY WORDS: FNC, Surgery, Thyroid lymphoma

Introduction

Thyroid cancer is the most common neoplasia of the head and neck, representing 1% of all malignant tumors in the age range between 30 and 74 years, with a three fold higher prevalence in women, when compared to men, although such difference drops after 48 years of age 1. In a North-American statistics, it corresponds to 3% of all the neoplasia affecting women, there were estimates of 48,020 cases of thyroid cancer in both genders in 2011. Inherited and sporadic medullary thyroid cancer (MTC) is uncommon, accounting 1-5% of thyroid cancer 2,3. The B-type Raf kinase (BRAFV600E) mutation in exon 15 of the BRAF gene has been noted to be a putative prognostic marker of the most prevalent form of thyroid cancer, papillary thyroid cancer (PTC) - a tumor type with high proclivity for recurrence or persistence 5,6.

Primary thyroid lymphoma (PTL) is a very rare tumors, and accounts for 0.6–5% of all thyroid malignancies and 1–2% of all extra-nodal lymphomas 7. PTL typically presents as a rapidly enlarging, painless thyroid mass, which may cause pressure symptoms of the aerodigestive tract. It is more common in women and the median age of presentation is in the seventh decade 8. There is an association between chronic lymphocytic thyroiditis (Hashimoto's thyroiditis) and primary thyroid lymphoma. There is a clinical past of Hashimoto thyroiditis in 27% to 100% of the cases. This evolution from Hashimoto's thyroiditis to lymphoma [typically a
mucosa-associated lymphoid tissue (MALT) lymphoma occurs in 0.5% of cases and is generally characterized by an indolent course. There may be Hodgkin and Non-Hodgkin lymphoma, and the B-cell Non-Hodgkin is the most prevalent. A large study from Japan calculated the incidence of thyroid lymphoma among patients with Hashimoto's thyroiditis to be 0.56%.

Preoperative diagnosis can be difficult and, although preparations from fine needle aspiration are improving in specificity and sensitivity, they are not yet reliable enough to replace core needle or surgical biopsy. This is due to the histopathological similarities between primary thyroid lymphoma and Hashimoto's thyroiditis. Ultrasound is frequently used in the diagnosis of thyroid lymphoma after which staging computed tomography of the neck, chest, abdomen and pelvis is required. Open (surgical) biopsy may be indicated to confirm the diagnosis and identify the subtype of PTL.

This paper aims at doing a descriptive analysis of the PTL histological types of thyroid cancer in a reference center. Two cases of primary thyroid lymphoma are hereby presented.

Methods

We carried out a retrospective study of a series of cases, studying 1604 charts from patients with thyroid disease submitted to a surgical procedure between January 2007 and June 2012. We collected demographic information associated with the diagnosis, treatment and histopathological results. This paper was approved by the Ethics Committee of the Institution where it was done.

Results

We studied the surgical causes of thyroid disease, encompassing a total of 1604 cases (Table I). Of these, we found histological benign disease in 81% of the cases, the most prevalent was colloid goiter; 19% of the cases were thyroid cancer. Among 307 thyroid cancer, we found 78.17% papillary thyroid cancer and 15.30% follicular thyroid cancer. The cases diagnosed with rare tumors were: anaplastic carcinoma 10 cases (3.5%), followed by 4 cases of medullary carcinoma (1.3%), 3 cases of Hurte cell carcinoma, 2 cases of lymphoma (0.06%), and 1 case of teratoma (0.03%). The most frequent clinical presentation was a palpable thyroid nodule. All patients with lymphoma and anaplastic carcinoma died. In particular, case 1 was a 66 years old male patient presented with thyroid enlargement and hypothyroidism. He was operated in the surgical department for total thyroidectomy. Histopathology of the surgical specimen revealed it to be diffuse large non-Hodgkin lymphoma, type MALT; associated to histiocytosis X foci; on immunohistochemistry CD 20 CD3, CD5, CD10 e Bcl2 and CD 43 were positive (Fig. 1). There was no history of B symptoms (fever, weight loss, increased sweating). Case 2 was a 46 years old female patient with history of rapid increase in size of mass in front of neck causing pressure symptoms of dysphagia and dyspnea. She was operated for total thyroidectomy and tracheostomy to relieve pressure symptoms. Histopathology of the surgical specimen revealed it to be Hodgkin lymphoma, positive on immunohistochemistry for CD30 e CD15 (Fig. 2).

![Fig. 1: Non-Hodgkin lymphoma, type MALT, associated to histiocytosis X foci. (0144) Langerhans' cells with typical nuclear grooves. Note: Inflammatory background with eosinophils (EE 400 x).](image1)

![Fig. 2: Hodgkin lymphoma. (0147) Typical Hodgkin cells in inflammatory background (EE 400 x).](image2)
Primary thyroid lymphoma: a rare finding in thyroid cancer. Our results call for a more accurate and proper evaluation of aspirates. The use of appropriate diagnostic tools is needed to avoid unnecessary and armful surgical trauma in these cases.

## Discussion

After assessing 1604 charts of thyroid disease cases operated, we had 17.8% of the patients submitted to surgical treatment for thyroid cancer, with histology reports of well-differentiated thyroid carcinoma and only 0.12% of the patients were diagnosed with lymphoma of the thyroid gland, and such data match those published in the literature. Since PTL is a rare disease, it is difficult to carry out prospective randomized trials to evaluate prognostic factors and optimal treatment combinations. PTL continues to produce diagnostic and therapeutic dilemmas. Flow cytometry, etc. are of particular importance in differentiating PTL from anaplastic thyroid carcinoma; this is an important consideration given that management and anaplastic carcinoma. PTL should be differentiated from lymphomas at other sites. This is especially important given the rarity of PTL. In this case, lymphoma of the thyroid gland could be the result of secondary involvement of the gland by the tumor. Moreover, PTL should be differentiated from Hashimoto’s thyroiditis and from poorly differentiated (undifferentiated or anaplastic) thyroid carcinomas. Adjunctive techniques (immunohistochemistry, flow cytometry, etc.) are of particular importance in differentiating PTL from anaplastic thyroid carcinoma; this is an important consideration given that management and prognosis of these two diseases is totally different. Ultrasound is frequently used in the diagnosis of thyroid lymphoma after which staging computed tomography of the neck, chest, abdomen and pelvis is required. Moreover, several reports in the literature have documented an association of Langerhans’ cell granulomatosis (LCG) with malignant lymphoma. In conclusion our data confirm that thyroid lymphoma is a rare finding in thyroid cancer. Our results call for a more accurate and proper evaluation of aspirates. The use of appropriate diagnostic tools is needed to avoid unnecessary and armful surgical trauma in these cases.

### References