

Non-Hodgkin's thyroid lymphoma associated with Hashimoto's thyroiditis

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Abstract

We report two cases of thyroid lymphoma. First was of a 54-year-old lady who presented with a 10 year history of goiter. Examination revealed an enlarged thyroid gland extending sub-sternally, with no palpable lymph nodes. She had been on thyroxine for 4 months, due to a high TSH with positive antibodies. Fine needle aspiration cytology of thyroid showed Hashimoto thyroiditis (HT). A total thyroidectomy was done because of pressure symptoms. Histopathology revealed HT in right lobe and Diffuse Large B-cell Non-Hodgkin's lymphoma (DLBCL) in left lobe. Second case was of a 30 year-old man who presented with dyspnoea secondary to rapidly enlarging thyroid. On examination, thyroid was diffusely enlarged together with palpable lymph nodes. His TSH was elevated & Anti-TPO antibodies were positive suggesting an autoimmune etiology. Ultrasound showed an ill-defined heterogeneous mass in the left lobe of thyroid gland with multiple enlarged lymph nodes. Ultrasound guided thyroid core biopsy revealed DLBCL.

Keywords: Thyroid lymphoma, Hashimoto thyroiditis, Non-Hodgkin's lymphoma.

Introduction

Thyroid non-Hodgkin's lymphoma is an uncommon tumour, representing 2-8% of thyroid malignancies and approximately 1-2% of extra nodal lymphomas. It occurs more frequently in elderly females and has been linked to Hashimoto's thyroiditis (HT) and prior therapeutic irradiation of the thyroid bed.¹

Case Report

We report two cases of thyroid lymphoma arising in a background of thyroiditis in 2012. The first was that of a 54-year-old lady who presented with a 10 year history of goiter which had started growing rapidly over the preceding 4 months. Physical examination revealed an enlarged thyroid gland which seemed to be extending sub-sternally, with no palpable lymph nodes. She was on Thyroxine 100 mcg daily for 4 months, as she had a low

FT4 and a high TSH with strongly positive thyroid antibodies. Fine needle aspiration (FNA) of the thyroid showed HT. She underwent total thyroidectomy because of pressure symptoms. Histopathology revealed HT in right lobe and Non-Hodgkin's Diffuse Large B-cell lymphoma (DLBCL) in left lobe. She was referred to Oncology for further management.

The second case was that of a 30 year-old gentleman who presented with dyspnoea secondary to rapid enlargement of thyroid over a period of one month. On examination thyroid was diffusely enlarged, hard in consistency and involving nearly half of the neck with enlarged lymph nodes on both sides. His TSH was elevated, FT4 was normal and Anti-TPO antibodies were

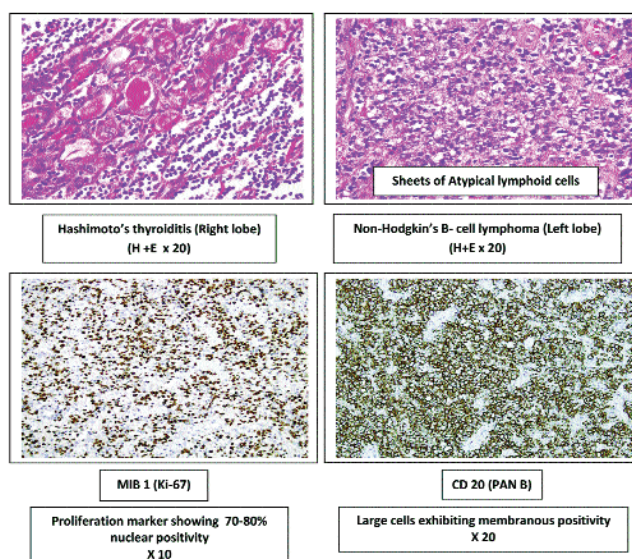


Figure-1: Case No. 1: Diffuse Large B-cell Non-Hodgkin's lymphoma (DLBCL).

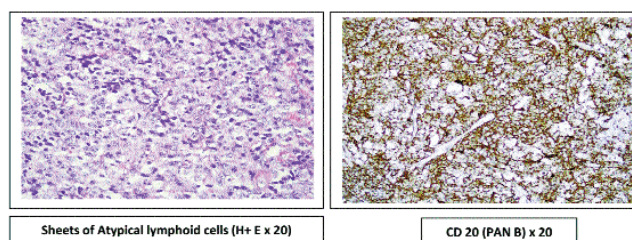


Figure-2: Case No. 2: Non-Hodgkin's Diffuse Large B-cell lymphoma (DLBCL).

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strongly positive. Ultrasound showed an ill-defined heterogeneous mass in the left lobe of thyroid gland extending to the isthmus and right lobe and infiltrating the trachea. Multiple enlarged lymph nodes were noted on both sides of the neck. Ultrasound guided thyroid core biopsy revealed DLBCL. He too was referred to oncology for further management.

Discussion

In our first case, there is clear evidence that the lymphoma developed in the setting of preexisting HT. In the second case however, thyroiditis is not confirmed histologically but raised TSH and strongly positive antibodies are both highly suggestive of an autoimmune etiology in the background.

Hashimoto thyroiditis, first described by Hashimoto in 1912, is an autoimmune inflammation of the thyroid commonly affecting middle-aged women.¹ Histologic features of HT include diffuse infiltration of lymphoid cells usually with formation of lymphoid follicles, varying degrees of fibrosis, oxyphilic change or squamous metaplasia in the epithelial cells.¹ When the presence of focal lymphocytic infiltration is assumed to be an adequate criterion for diagnosis of HT, the incidence appears to be as high as 16-23% in elderly females.¹

In HT, the antithyroid immune response begins with activation of thyroid antigen-specific helper T cells. There are two theories regarding what serves as an antigen in this immune reaction. According to one theory, the antigen triggering the reaction is a viral protein with molecular mimicry to a thyroid protein, although clear evidence for a viral etiology is lacking. According to the other theory, thyroid epithelial cells present their own intracellular proteins to T cells.²

A variety of thyroid autoantibodies have been identified in the sera of patients with HT. Thyroid antiperoxidase antibodies (TPOAbs) and antithyroglobulin antibodies are demonstrated in the sera of 90% of patients with HT. Thyrotropin receptor-blocking antibodies are also frequently present.

The thyroidal lymphoid infiltrate in HT represents the substrate from which thyroid lymphoma may arise.³ Primary thyroid gland lymphomas are uncommon tumours more frequently seen in older women. They represent around 2-8% of thyroid malignancies and approximately 1-2% of extra nodal lymphomas.² They have been described to occur in the setting of HT in almost all cases suggesting a role of chronic antigen stimulation in the development of the disease.⁴ In this condition a distinction between an inflammatory

lymphoid infiltrate and a low grade lymphoma may be extremely difficult and precise criteria are necessary for a correct diagnosis.⁵ Most reported cases have a short history of an enlarging thyroid or a neck mass causing compressive symptoms very similar to our patients.⁶

There are several case reports which illustrate common etiology of the thyroid lymphoma and HT.

Kapadia SB et al reviewed 21 cases of thyroid lymphoma diagnosed between 1969 and 1980. The thyroid gland was the primary site in all but two cases. Associated HT was found histologically in 57% of the cases.⁶

In another study, Hadzic B et al reported 49 cases, out of which histologic diagnosis of chronic diffuse lymphocytic thyroiditis was established in 9 (18%) patients. The frequency of the appearance of this autoimmune disease might well be greater because a relatively small number of patients underwent the operation.⁷ Simultaneous or previous evolution of HT into malignant lymphoma has been described by several authors. On the basis of this extensively reported data, HT should be regarded as a prelymphomatous state which has great histological importance.⁷

Moshynska et al worked on the clonal relationship between HT and thyroid lymphoma. He reported that 12/20 patients with primary thyroid lymphoma had a previous history and histological diagnosis of HT and there was clonal similarity between HT and thyroid lymphoma.⁸

Although thyroid lymphoma is very rare, one study has reported the increased risk of lymphoma by a factor of 67 in patients with HT. They recommend that patients with HT and a dominant thyroid nodule should undergo fine-needle aspiration biopsy to rule out lymphoma and thyroid carcinoma.²

Ultrasonography (US) is the single-most valuable imaging modality in the evaluation of the thyroid gland.⁵ In the hands of experienced operators this investigation is by far the most sensitive and economical technique for a comprehensive diagnostic evaluation of the thyroid nodules, differentiating not only between benign and malignant pathology but also helping plan initial management of the issue.^{9,10} Furthermore, it is still the most simplified and non-invasive modality for pre and post treatment follow up of thyroid nodules.¹⁰

Other imaging modalities like computed tomography (CT) and magnetic resonance imaging (MRI) are not very reliable in differentiating between malignant and benign nodules. These tests are rarely indicated in the evaluation of thyroid

pathology. An exception is in the diagnosis and evaluation of substernal goiters. Independent of morphology, fine-needle aspiration (FNA) provides the most direct and specific information about a thyroid nodule. FNA has diagnostically useful results in about 80 percent of cases, typically with two to four passes of the needle. The yield increases if the biopsy is guided by ultrasonography.¹¹

If FNA is non diagnostic, core needle biopsy or open biopsy should be considered depending on the level of suspicion. If the diagnosis is confirmed, additional evaluation includes neck, chest and abdominal CT or MRI to assess for extrathyroidal spread.¹¹

The prognosis for thyroid lymphoma depends on the histopathologic type and stage of the disease. Treatment consists of chemotherapy and radiation therapy. Surgery may be warranted in some patients to relieve local pressure symptoms. It should be recognized that early diagnosis and correct treatment lead to favourable prognosis.^{4,12}

Conclusions

Thyroid lymphoma is a rare condition. However, the incidence is higher in patients with a history of HT. A relatively rapid growth in size of the thyroid gland in these patients should alert the physicians to the possibility of a thyroid lymphoma. Diagnosis can be missed on FNA and a core needle biopsy should be carried out. Chemotherapy and radiation is the mainstay of treatment. Thyroidectomy is occasionally required for compressive symptoms.

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