

Primary Thyroid Lymphoma Associated with Dyspnea in an Old Age Patient: A Case Report

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Primary thyroid lymphoma is a rare tumor which patients usually present an enlarging neck mass, often causing local obstructive symptoms. Hypothyroidism is seen in 30-40% of the patients with primary thyroid lymphoma. We report a 77-year-old man with history of hypothyroidism, presenting enlarging anterior neck mass which pathologically confirmed as thyroid lymphoma with literature review.

Key Words: Thyroid gland, Lymphoma, Dyspnea, Primary hypothyroidism

Introduction

Thyroid lymphoma is a rare disease, accounting for 0.5% to 5% of all thyroid malignancies and has been estimated to 2.5% to 7% of all extranodal lymphomas.^{1,2)} It usually occurs at middle-to-elder aged female group who have Hashimoto thyroiditis, and patients present rapidly growing thyroid mass which causes locally obstructive and infiltrative symptoms, such as dysphagia, dyspnea, and hoarseness.¹⁾ Most cases of thyroid lymphoma are non-Hodgkin's lymphoma with B cell origin and subtypes include diffuse large B-cell lymphoma (DLBCL), mucosa-associated lymphoid tissue (MALT) lymphoma, and mixed type.³⁾

Case Report

A 77-year-old man with hypothyroidism visited our department because of progressively enlarging anterior neck mass over 8 years. He complained of recent aggravation of dyspnea, odynophagia and palpable neck mass. He was taking levothyroxine 100 mcg

daily. He did not have any other disease except hypothyroidism. He denied any history of radiation to the head or neck. On physical examination, he had a palpable firm anterior neck mass sized about 10×10 cm without any tenderness (Fig. 1). The rest of the physical examination was unremarkable. Thyroid ultrasonography (US) showed two discrete hypoechoic thyroid nodules. There was a right thyroid hypoechoic nodule sized about 3.9×5 cm and another one sized about 5.5×7 cm which occupied left lobe, isthmus and right lobe mid portion. Neck computed tomography scan (CT) was done, and revealed marked enlargement of the thyroid gland (Fig. 2). Fine needle aspiration on both thyroid nodules was performed and raised possibility of the Hashimoto's thyroiditis or MALT lymphoma.

The patient was managed by total thyroidectomy (Fig. 3). Histopathology confirmed diffuse large B-cell lymphoma with MALT lymphoma component. There were numerous lymphoepithelial lesions with so called "MALT balls" (lymphoepithelial lesion which occupies thyroid follicle lumen) and aggregations of large lymphoma cells with frequent mitosis (Fig. 4). Immu-

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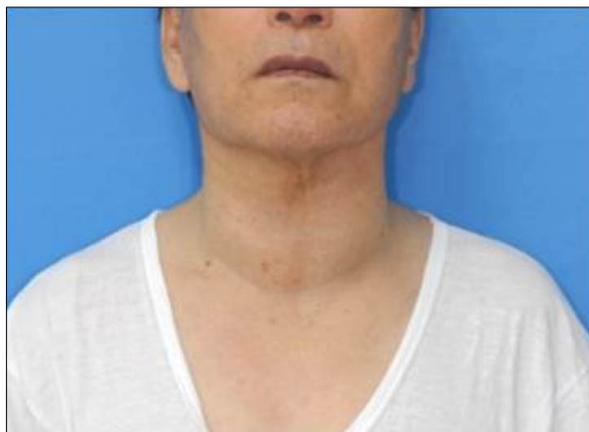


Fig. 1. The patient showed palpable, soft and non-tender anterior neck mass.

nohistochemical staining was performed, and CD20, bcl-6, bcl-2, CD21, Ki-67 were positive in tumor cells which was compatible with the diagnosis. After the surgery, PET CT, chest CT and abdominal CT were done. We could not find any pathogenic findings. The patient took 6 cycles of R-CHOP (Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) regimen followed by external beam radiation therapy. 2 years after the treatment, until now the patient did not show any recur sign.

Discussion

The head and neck is a common site of extra-nodal non-Hodgkin's lymphoma and most of them are B cell origin.⁴⁾ Primary Hodgkin's lymphomas in the head and neck are rare and are usually associated with nodal disease.⁵⁾ The treatment of head and neck region extra-nodal lymphoma is not different from the management of lymphoma in other sites which include chemotherapy followed by radiotherapy.⁴⁾

Thyroid lymphoma accounts for 0.5% to 5% of all thyroid malignancies and 2.5% to 7% of all extranodal lymphomas. Patient with chronic autoimmune thyroiditis (Hashimoto's disease) seem to have higher risk of developing thyroid lymphoma. It has been reported to be 40 to 80 times greater than in general populations.¹⁾ It shows a male preponderance that sex ratio is about 4-8 : 1 and the peak incidence is usually in 7th decade. This is probably due to middle and older

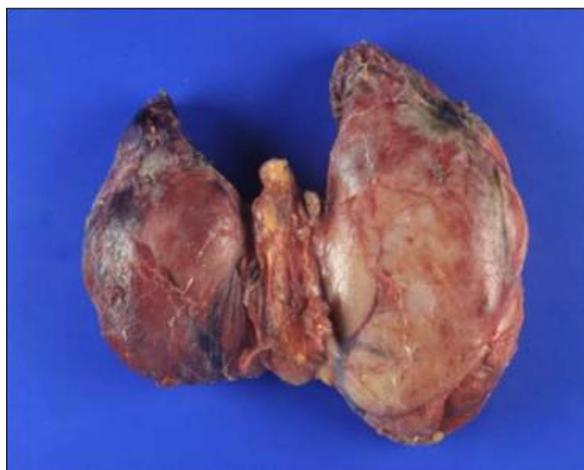


Fig. 3. Gross finding of the enlarged thyroid gland.

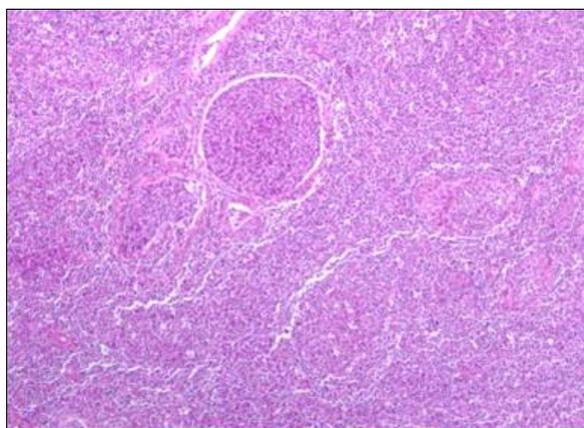


Fig. 4. Lymphoepithelial lesions with MALT balls (lymphoepithelial lesion that occupies thyroid follicle lumen). (H&E stain, original magnification $\times 100$)

aged females have higher incidence of Hashimoto's disease. The thyroid gland does not contain any lymphoid tissue. The lymphoid tissue is accrued during chronic inflammation or an autoimmune process such as chronic autoimmune thyroiditis.⁶⁾

Patient usually present rapidly growing neck mass over 1 to 3 months from starting symptoms.⁷⁾ In case of DLBCL, mass tends to grow more rapidly than MALT lymphoma.⁸⁾ Enlarging mass can cause locally obstructive symptoms such as dysphagia, dyspnea and hoarseness.⁹⁾ Classic B symptoms of fever, night sweat and weight loss are less common.⁷⁾

The diagnosis is made with patient's symptom, radiologic and pathologic evaluation. Thyroid US and

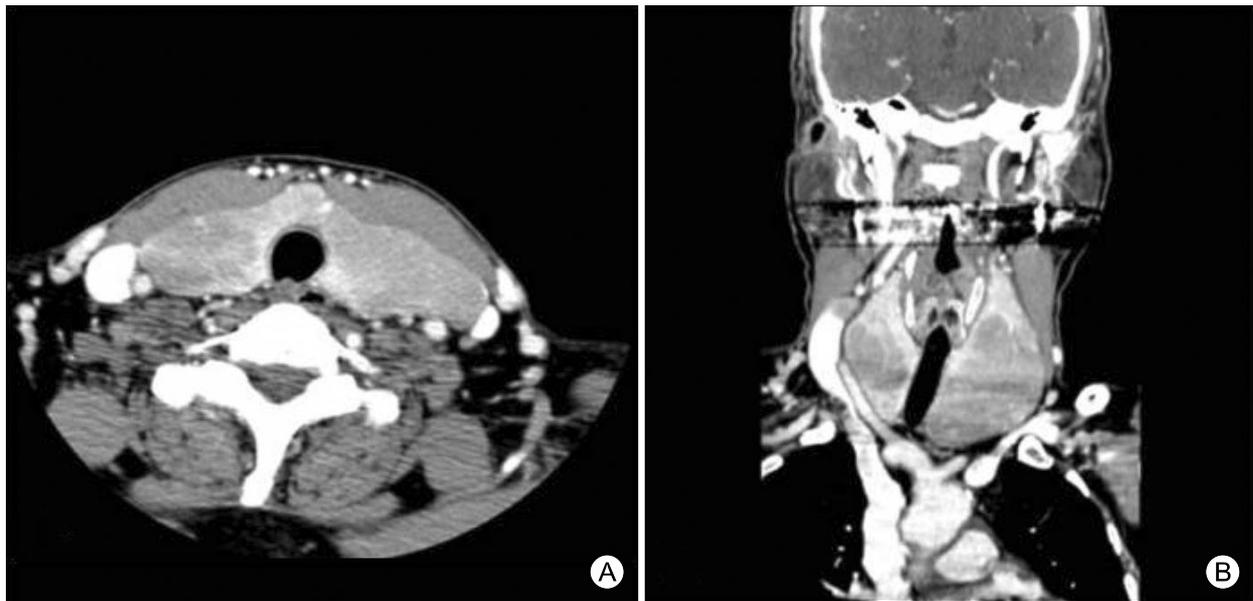


Fig. 2. Preoperative CT scan shows a diffusely enlarged thyroid gland (A) with tracheal deviation (B).

neck CT are used for radiologic evaluation and fine needle aspiration cytology (FNAC), tissue biopsy and other cytomorphologic, immunophenotypic, molecular techniques are used as pathologic evaluation. Thyroid US classified into 3 types based on internal echoes, borders, and posterior echoes: nodular, diffuse, and mixed types. US findings show hypoechoic internal echoes which is due to severe chronic thyroiditis has a fibrous structure after the destruction of follicular cells by lymphocyte infiltration.²⁾ Thyroid scan shows cold nodule. Thyroid lymphoma has been reported to have a low frequency of necrotic degeneration and calcification.¹⁰⁾ Neck CT scan shows multiple, well demarcated and homogeneous mass with homogeneous expansile growth pattern and peripheral high attenuating residual thyroid tissue.¹¹⁾ However Hashimoto's thyroiditis also present homogeneous pattern with high attenuating residual thyroid tissue which makes hard to differentiate thyroid lymphoma from Hashimoto's thyroiditis.¹²⁾ Fine needle aspiration is a relatively non-invasive screening diagnostic tool, however because of the pathologic similarities between the thyroid lymphoma and Hashimoto's thyroiditis, the diagnostic accuracy is about 40% to 50%. Nowadays supportive studies of cytomorphologic, immunophenotypic and molecular techniques are available. For example, most

of the DLBCL are CD19-, CD20-, and CD45-positive whereas MALT lymphomas express surface immunoglobulin and are CD5-, CD10-, and CD23-negative.¹³⁾ Tissue biopsy or surgery is recommended when primary thyroid lymphoma is suspected using FNAC with adjuncts and for subclassify it into MALT versus DLBL or mixed type.^{1,13)} Although Matsuzuka et al.⁹⁾ diagnosed thyroid lymphoma in 78.3% cases, the authors do recommend open biopsy in all cases in order to subtype and grade the thyroid lymphoma.

Most of the primary thyroid lymphomas are non-Hodgkin's lymphomas with B-cell origin and extranodal marginal zone B cell lymphoma of MALT lymphoma are common subtype and follicular lymphoma, Hodgkin's lymphoma, small lymphocytic lymphoma and T cell lymphoma are relatively rare subtypes.¹⁴⁾ DLBCL is the most common subtype (70%) and are aggressive with almost 60% diagnosed with dissemination whereas MALT lymphomas (6-27%) have relatively indolent course.³⁾ Up to 40% of all DLBCL appear to have undergone transformation from a MALT lymphoma.¹⁵⁾

Current treatment modalities of thyroid lymphoma include radiotherapy, chemotherapy, surgery, and combined chemoradiotherapy. Although there are no

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definite treatment guidelines for the thyroid lymphoma, can best managed with chemoradiotherapy.^{4,6,7,13–16} In early-stage MALT lymphoma of thyroid (IE), single use of locoregional therapy with either surgery alone or radiotherapy is preferred.⁶ However, currently there is no randomized or prospective trials for single modality therapy for early stage thyroid lymphoma.¹⁶ Surgery is generally used for palliation or diagnosis of thyroid lymphoma. When the mass rapidly grows, the compressive symptoms as dysphagia, dyspnea and pain can managed with prompt surgery. But there is only one retrospective trial addresses the use of palliative surgery.¹⁷ Furthermore, combination chemoradiation with or without tracheal stent insertion would also promptly impact on compression symptoms.⁹ Nowadays, biological agents such as rituximab which is a monoclonal antibody against B-cell specific antigen CD20 would be added to whatever chemotherapy regimen is used.⁶

The Ann Arbor stage classification is most widely used for primary thyroid lymphoma. The overall 5-year survival for stage IE (confined to the thyroid gland) is 80%, stage IIE (locoregional lymph nodes positive, addition to the thyroid) 50%, stage IIIE (additional disease in nodes located on both sides of the diaphragm), and stage IVE (with disseminated disease) less than 36%.¹³

When a patient present progressively enlarging neck mass, the thyroid lymphoma should be considered. Although there are no retrospective studies of palliative surgery, surgery can promptly salvage the patient with dyspnea, because the diagnosis process will somehow takes time.

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