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High Grade B-Cell Non Hodgkin's Lymphoma of Thyroid Gland Mimicking as Hashimoto's Thyroiditis: A Diagnostic Challenge

Dr. Shikha Jayesh Shah[1], Prof. Dr. Jasmin Jasani[2], Dr. Trupti R. Jansari[3], Dr. Simran Jain[4]

[1]2nd year Resident, Department of Pathology
[2]Professor, Department of Pathology
[3]Associate Professor, Department of Pathology
[4]3rd year Resident, Department of Pathology

ABSTRACT

Primary thyroid lymphoma (PTL) is a rare malignancy that has been estimated to constitute approximately 1%-5% of thyroid malignancies and 1%-2% of extranodal lymphomas, Different subtypes of lymphoma can present as primary thyroid lymphoma. Here we represent a case of a 57 years old female patient with complaints of midline neck swelling since 6 months which moves with deglutition and does not move with tongue protrusion. Sonography was suggestive of thyroiditis. FNAC report was given as Bethesda II: Features were suggestive of colloid goiter with nonspecific thyroiditis. Patient had undergone total thyroidectomy surgery and the specimen was received in our histopathology department. The representative sections were stained with hematoxylin and eosin (H & E) stain. Microscopic examination showed microfollicles and macro follicles filled with colloid. There was presence of lymphoid aggregates with prominent germinal center and diffusely infiltrating the thyroid parenchyma. Few follicles showed prominent hurthle cell changes and some of which showed atrophy.At places, the cells were arranged in discohesive pattern. The cells showed moderate pleomorphism irregular nuclear border and moderate amount of eosinophilic cytoplasm. At places, mitotic figures was seen. For further confirmatory IHC panel was kept and the tumours stained positive for CD45 and CD5 while the thyroid follicles stained positive for TTF-1 so the final diagnosis of high grade Non Hodgkins lymphoma was given.

Keywords: NHL, midline neck swelling, hashimoto's thyroiditis.

Introduction

Lymphoma is one of the most common hematological malignancies, but primary thyroid lymphoma (PTL) is very rare and accounts for 0.5-5% of all thyroid malignancies and about 2% of extranodal lymphomas. PTL is a rare extranodal lymphoma which is defined as lymphoma that involves just the thyroid or the thyroid and the regional lymph nodes, without metastasis to other areas at the time of diagnosis [1]. Lymphomas of the thyroid are almost exclusively of the non-Hodgkin's B cell type. The most common subtype of PTL is diffuse large B cell lymphoma (DLBCL) accounting for more than 50% of cases followed by mucosa associated lymphoid tissue (MALT) lymphoma which represents 10-23% cases. [2].

Hashimoto thyroiditis (HT) is the only well-known risk factor for the development of PTL. [3]

CASE REPORT

Here we present a case of 57 years old female patient, known case of hypothyroidism and on 50mcg thyroxine tablets presented with complaints of midline neck swelling since 6 months which moves with deglutition and does not move with tongue protrusion along with dysphagia, dyspnea, and dysphonia. Ultrasonography of the neck revealed an enlarged thyroid gland. Bilateral lobes of the thyroid appeared bulky and heterogeneous and showed raised vascularity on color Doppler. The FNAC was suggestive of colloid goiter with nonspecific thyroiditis.

Patient had undergone total thyroidectomy and we received the specimen in our histopathology department (figure 1).

Right and left lobe with isthmus measuring 10.5x7.0x4.0cm. Right lobe measuring 8.5x5.5x3.5cm, isthmus measuring 4.5cm and left lobe measuring 9.0x5.0x3.5cm. Outer surface was smooth, capsulated and bosselated. On cut section of thyroid whitish homogenous and at places hemorrhagic areas were seen.

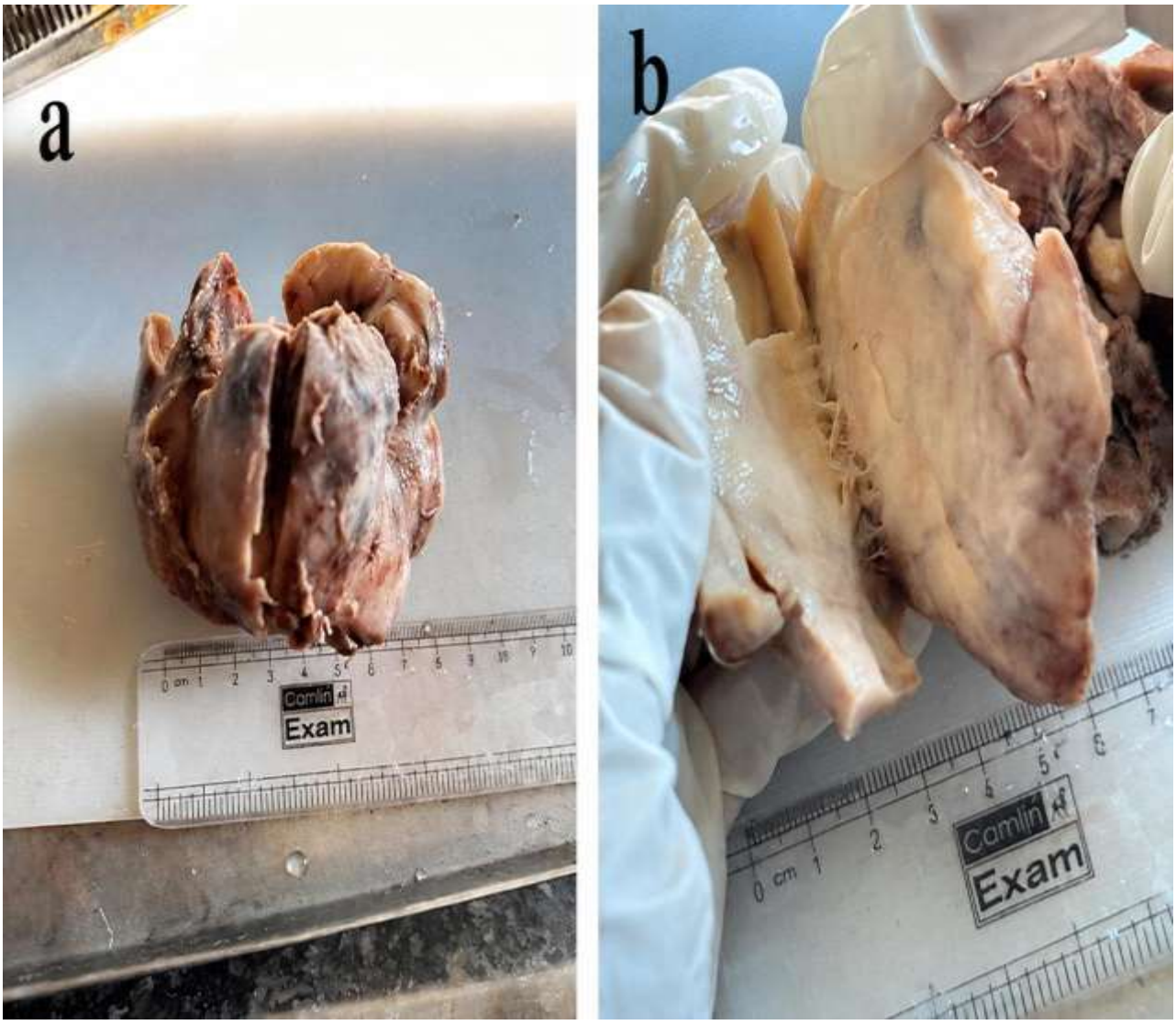

Figure 1: Grossing: a) outer surface of thyroid b) cut section of thyroid.

MICROSCOPY

The representative sections were given and the slides were stained with hematoxylin and eosin (H & E).
Microscopy in low power showed: Thyroid gland infiltered by discohesive infiltrates of atypical lymphoid cells (figure 2).
The cells showed moderate pleomorphism irregular nuclear border and moderate amount of eosinophilic cytoplasm in between them.
Microscopy in high power mode showed: Atrophied thyroid follicles and diffuse proliferation of atypical lymphoid cells. Mitosis was evident (figure 2).
Few follicles showed prominent hurthle cell changes and some of which showed atrophy.

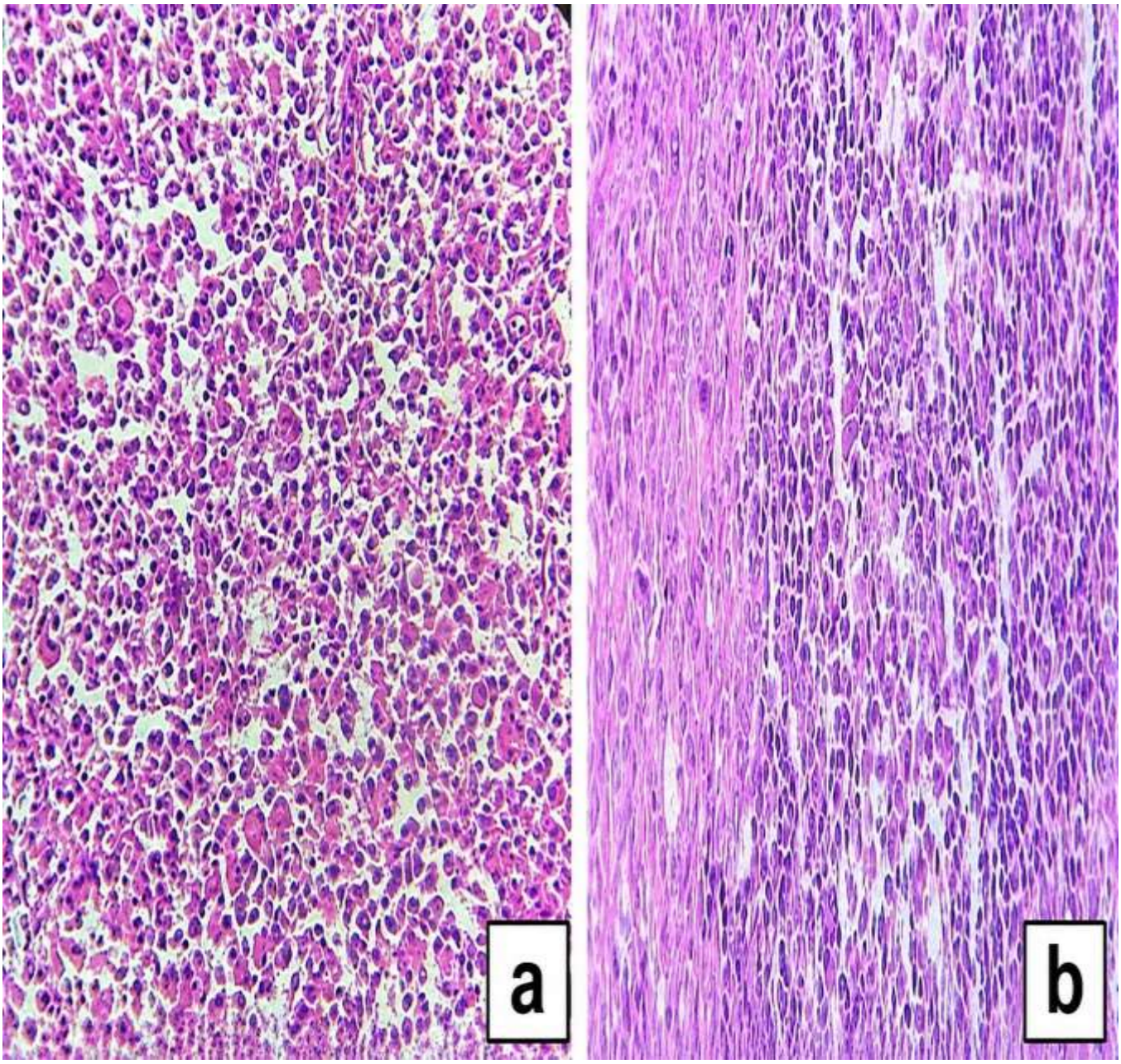

Figure 2: Microscopy: a) Atypical lymphoid cells (10x); b) Atrophied thyroid follicles and atypical lymphoid cells (40x).

IMMUNOHISTOCHEMISTRY STUDY

- For further confirmation immunohistochemistry study was done.

- The following markers stained positive: TTF-1

CD 45
CD 5
CD 19
CD 20

- The following markers stained negative: BCL- 6 Cyclin D1 CD 10

Ki67	50-60 % in tumor cells.
TTF-1	Positive in thyroid follicles.
CD 45	Positive in tumor cells.
CD 5	Positive in tumor cells.
CD 20	Positive in tumor cells.
CD 19	Positive in tumor cells
Cyclin D1	Negative in tumor cells.
CD 10	Negative in tumor cells.
BCL 6	Negative in tumor cells

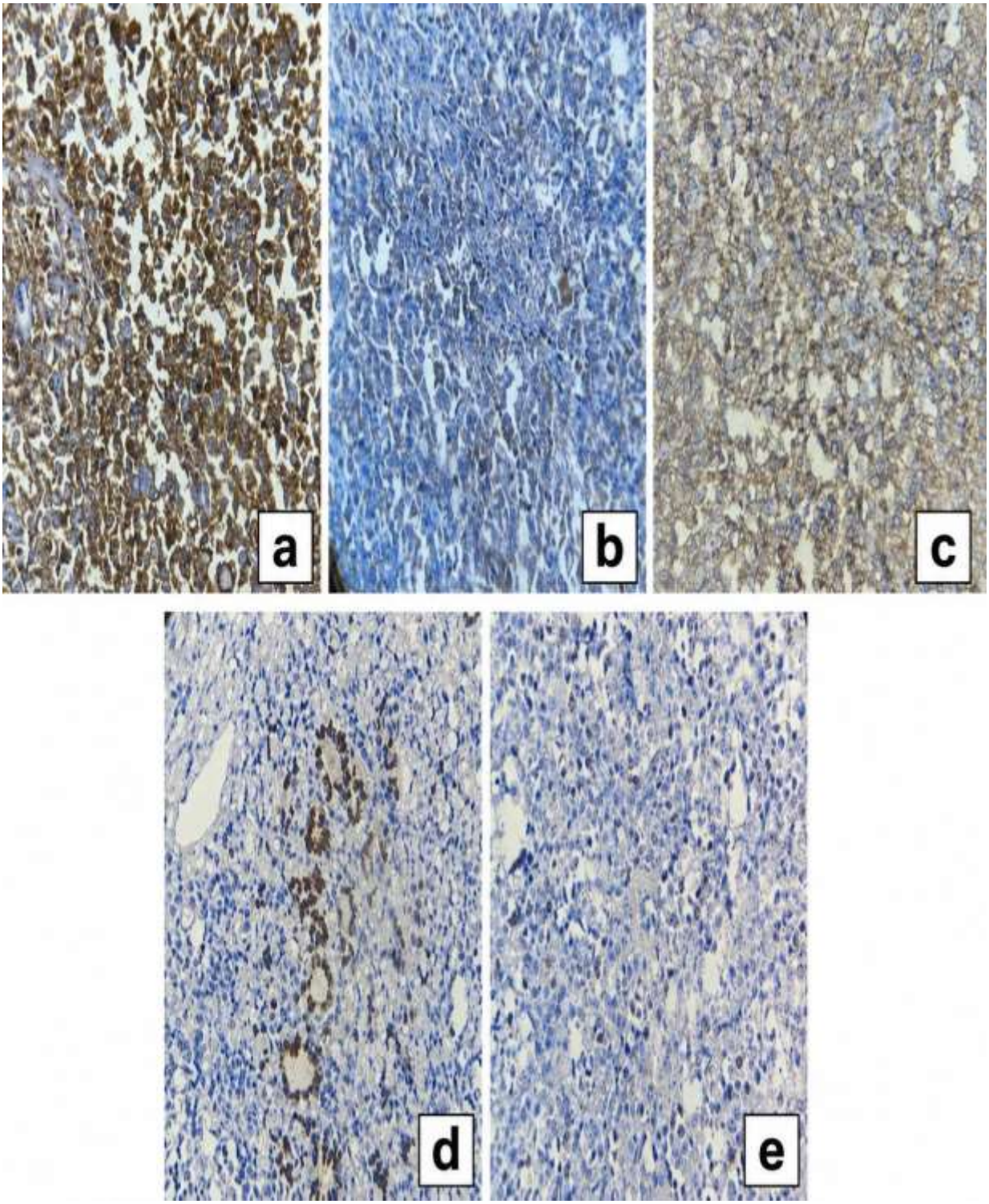

Figure 3; immunohistochemistry: a).CD 20 and b).CD 19: positive; c).CD 45 positive in tumor cells; d).TTF 1 Positive in thyroid follicles; e). Ki 67 :50-60 % in tumor cells respectively.

DISCUSSION

Primary malignant lymphoma of thyroid is uncommon and comprises less than 2% of thyroid malignancies. Present as a rapidly growing mass and is predominantly a disease of elderly females They constitute 2.5-7% of all extranodal lymphomas [2].

The great majority of primary thyroid lymphoma are B cell lymphomas which may be associated with

Hashimoto's thyroiditis [2].

The most common clinical presentation of PTL is rapid enlargement of a mass in the neck which, in about 30% of patients, may cause compression symptoms such as dysphasia, dyspnea, coughing, and hoarseness (3),B-cell lymphoma symptoms, such as fever, night sweats, and weight loss, occur in 10–20% of patients Most commonly, ultrasound (US) of PTL shows a hypoechoic mass, with the echogenicity less than that of the adjacent neck musculature, combined with hypervascularity and a characteristically undifferentiated outline (3).

The case was reviewed by 2 experienced pathologists. The specimens were subjected to histopathologic examination as well as immunohistochemistry analysis using a panel of monoclonal antibodies(3).

Microscopically, DLBCL appears as large, atypical lymphocytes with frequent mitosis.[4].

Immunohistochemistry, the process whereby antibodies are used to detect antigens in biological tissues has improved the accuracy of cytology in diagnosing lymphoma. This technique allows for specification of lineage and developmental stage of lymphoma [2].

The presence of antibodies against the B cell antigens CD19 and CD 20 for example identifies a B cell lineage to the lymphoid cells. Although CD10 is present in most follicular lymphoma, it is typically negative in both DLBCL and MALT lymphoma.

Ann Arbor staging system, originally developed for Hodgkin's lymphoma, is presently applied to non-Hodgkin's lymphoma as well, for staging the disease. The suffix A and B are used for presence or absence of constitutional symptoms respectively whereas the suffix E and S are used for extra-nodal and splenic involvement. (5).

The prognosis for thyroid lymphoma depends on the histopathological 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 favorable prognosis. [2].

PLT is a rare tumor, histologically the most common subtype is a diffuse large B-cell lymphoma (DLBCL), which has a more aggressive clinical course and is usually diagnosed at a disseminated stage [4].

Unlike the most common types of thyroid cancer, irradiation is not a factor in the disease, but long-standing Hashimoto's thyroiditis is a frequent predisposing cause [3]. Currently the role of Hashimoto's thyroiditis in the pathogenesis of PLT remains unclear, in fact some authors demonstrate that the risk of Hashimoto's thyroiditis patients developing PTL is 40 to 80 times greater than that of the general population, while the others have found that it is associated with over 90% of the PTL [4].

FNA under US guidance can confirm the diagnosis for 70–80% of patients, but for low-grade lymphomas, especially when the distinction between MALT and HT is quite difficult, the distinguishing features may be the abundance of lymphoid tissue and a high proportion of intermediate centrocyte-like cells in low-grade PTL compared to HT (3).

Ann Arbor Classification for PTL

Stage IE: Involvement of thyroid gland only.

Stage IIE: Involvement of thyroid gland and regional lymph nodes on the same side of the diaphragm.

Stage IIIE: Involvement of thyroid gland and regional lymph nodes on both sides of the diaphragm.

Stage IVE: Disseminated disease.

Modifiers (Constitutional Symptoms):

- A: Absent
- B: Present (fever > 38°C, weight loss > 10% in 6 months, night sweats

LIMITATIONS OF STUDY

In our study, the diagnosis of MALT lymphoma was often difficult because there were no specific immunohistochemical markers that could be used to clearly identify this type of tumor. A characteristic pathological feature was the presence of an interstitial infiltrate, which mainly consisted of lymphocytes organized into true lymphoid follicles. (3).

CONCLUSION

It is challenging to diagnose primary thyroid lymphomas because of their rare occurrence. For this reason, it should be kept in mind that patients with chronic lymphocytic thyroiditis should be evaluated carefully when they have symptoms like a rapidly growing thyroid gland or cervical lymphadenopathy.

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