

Unexpected Histological Finding of Diffuse Large B-Cell Lymphoma in a Patient with Long-standing Goiter and Hashimoto's Thyroiditis: A Case Report

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ABSTRACT

Primary thyroid lymphoma (PTL) is an uncommon malignancy, comprising less than 5% of all thyroid cancers. Hashimoto's thyroiditis (HT) is the most significant risk factor, increasing the risk of developing PTL by 40 to 80 times. Diffuse large B-cell lymphoma (DLBCL) is the most prevalent and aggressive histological subtype, accounting for over 50% of PTL cases. The diagnosis is challenging, as the clinical and sonographic features of PTL can mimic benign thyroiditis. A 60-year-old female with a three-year history of a progressively enlarging goiter and worsening compressive symptoms presented for surgical evaluation. Initial investigations revealed severe hypothyroidism and ultrasound findings of a nodular goiter with features of thyroiditis (TI-RADS 3). She underwent a total thyroidectomy for symptomatic relief. Postoperative histopathology unexpectedly revealed a DLBCL, confirmed by CD20 positivity, coexisting with a background of classic HT. The patient was subsequently treated with six cycles of R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) chemoimmunotherapy and achieved a complete clinical and radiological response. This case underscores the diagnostic challenge PTL presents, particularly in patients with pre-existing HT. A high index of suspicion is crucial for clinicians managing HT patients who present with a rapidly enlarging goiter or worsening compressive symptoms. While fine-needle aspiration has limitations, definitive diagnosis often requires a core needle or excisional biopsy to differentiate neoplastic infiltration from the benign lymphocytic infiltrate of HT.

Keywords: Primary thyroid lymphoma, hashimoto's thyroiditis, diffuse large B-Cell lymphoma

BACKGROUND

Primary thyroid lymphoma (PTL) is a rare neoplasm, accounting for 1-5% of all thyroid malignancies and approximately 2-7% of all

extranodal lymphomas.^{1,2,8} While papillary thyroid carcinoma is the most common thyroid cancer (85-90%), PTL represents a distinct and important clinical entity.⁹ The strongest known

Imaging Preoperative ultrasonography (US) demonstrated bilaterally enlarged thyroid glands containing a nodular goiter classified



Figure 2. Neck X-ray showing a large bilateral neck mass, more prominent on the left, which deviates the trachea to the right without causing significant airway constriction.

as TI-RADS 3. The thyroid parenchyma had an inhomogeneous echostructure, a finding consistent with the appearance of thyroiditis.

A cervical X-ray showed a bilateral neck mass causing a rightward deviation of the trachea but no evidence of critical airway obstruction.

Surgical Intervention and Histopathology Due to significant and worsening compressive symptoms, the patient underwent a total thyroidectomy. Postoperative histopathological examination of the specimen unexpectedly revealed a diffuse infiltration of the thyroid parenchyma by medium-to-large atypical lymphoid cells. The background thyroid tissue showed features characteristic of HT, including extensive lymphocytic infiltration with the formation of reactive germinal centers and Hürthle cell metaplasia.^{10,20} The immunohistochemical profile of the atypical lymphoid infiltrate was positive for CD20, confirming a diagnosis of DLBCL.¹²

Post operative Course and Treatment Postoperatively, the patient's TSH was 30.5 μ IU/mL and FT4 was 1.13 ng/dL.

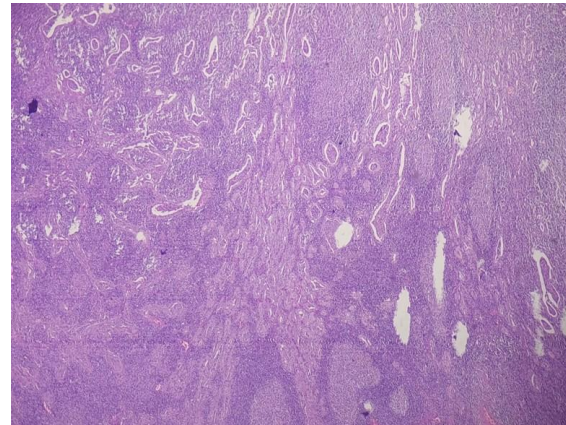


Figure 3. Histopathological Findings of the thyroidectomy specimen (H&E stain).

The micrograph illustrates the dual pathology present within the thyroid tissue. **(A)** A diffuse and infiltrative proliferation of large, atypical lymphoid cells is seen effacing the normal follicular architecture, consistent with Diffuse Large B-Cell Lymphoma. **(B)** The background stroma demonstrates features characteristic of Hashimoto's thyroiditis, including the formation of a prominent lymphoid follicle with a reactive germinal center.

She also developed mild hypocalcemia with a serum calcium level of 1.96 mmol/L (normal range: 2.15-2.5). She continued levothyroxine 100 mcg daily and started on calcium lactate 500 mg twice daily. Following her recovery from surgery, she was referred to for oncological treatment and completed six cycles of the R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) chemoimmunotherapy regimen. The patient tolerated the treatment well and has maintained a good quality of life with a complete clinical and radiological response.

DISCUSSION

This case highlights the unexpected diagnosis of DLBCL in a patient undergoing thyroidectomy for compressive symptoms attributed to a long-standing goiter in the setting of HT. PTL is a rare disease, but its incidence is significantly elevated in individuals with HT.^{3,4,11} Our patient's demographic profile—a female in her seventh decade of life—is consistent with the typical epidemiology of PTL, which predominantly

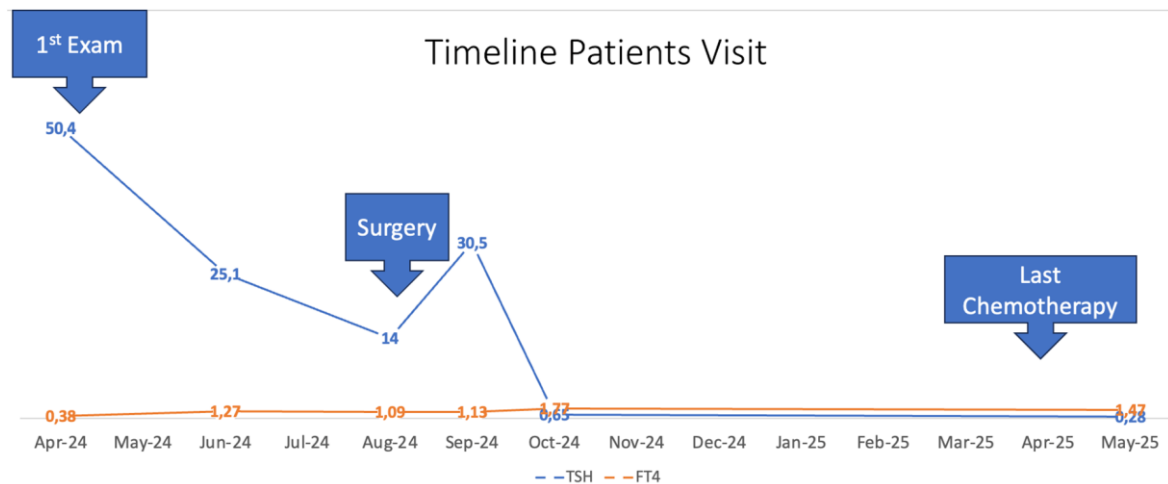


Figure 4. Timeline of patient's thyroid function tests and key clinical events. The line graph illustrates the changes in Thyroid-Stimulating Hormone (TSH, blue line) and Free Thyroxine (FT4, orange line) levels from the initial examination to post-treatment follow-up. At presentation in April 2024, the patient had severe primary hypothyroidism (TSH 50.4 µIU/mL, FT4 0.38 ng/dL). Following levothyroxine initiation, TSH levels decreased leading up to the total thyroidectomy in August 2024. A postoperative TSH spike was observed before stabilizing. The final measurement in May 2025, after completion of chemotherapy, shows a suppressed TSH (0.28 µIU/mL) and a normal FT4 (1.47 ng/dL), consistent with TSH-suppressive therapy.

affects middle-aged to older individuals, with a female-to-male ratio of approximately 3:1 and a mean age at diagnosis of 63–68 years.^{1,2,6}

The link between HT and PTL is well-established, with chronic antigenic stimulation of lymphocytes within the thyroid gland thought to be the driving pathogenetic mechanism.^{10, 11} This process can be considered a form of acquired MALT.¹⁰ A recent meta-analysis of 38 studies found that 78.9% of PTL cases had evidence of HT, with 64% confirmed on pathology.³ This strong association suggests a progression model where chronic inflammation in HT leads to the development of MALT lymphoma, which can subsequently transform into the more aggressive DLBCL.^{10,13} It is hypothesized that persistent stimulation of B-cells by autoantigens increases the probability of cumulative genetic events, potentially involving the activation of the nuclear factor-κB (NF-κB) pathway.

However, the same meta-analysis also found that the prevalence of HT was significantly lower in pure DLBCL compared to MALT lymphoma ($p=0.007$) and in mixed DLBCL/MALT cases ($p=0.002$). This suggests that while

many DLBCLs arise from pre-existing MALT lymphoma, a subset of thyroid DLBCL may arise de novo, without a MALT precursor.³

The question of whether the lymphocytic infiltrate in HT merely provides fertile ground for lymphoma growth or if the chronic activation directly predisposes lymphocytes to malignant transformation remains a subject of investigation.

A primary challenge in managing these patients is diagnostic difficulty. The most common presenting symptom of PTL is a rapidly enlarging neck mass with compressive features, as seen in our patients.^{1,14,15} However, these symptoms can also be attributed to a benign enlarging goiter. Furthermore, the sonographic features of diffuse PTL and HT demonstrate significant overlap, including a markedly hypoechoic and heterogeneous parenchyma, which complicates diagnosis by imaging alone.^{7,6,21} Advanced imaging techniques, such as contrast-enhanced ultrasound (CEUS) and ultrasomics, are being investigated to better differentiate benign from malignant processes in the setting of HT but are not yet standard practice.^{21,22}

Fine-needle aspiration (FNA) is often the initial diagnostic test for thyroid nodules, but its accuracy for PTL is notoriously poor, with sensitivities sometimes as low as 60%.^{1,17,23} The cytological similarity between the reactive lymphoid infiltrate of HT and the neoplastic cells of low-grade lymphoma makes a definitive diagnosis challenging on FNA alone.^{1,17,23}

Consequently, a core needle biopsy (CNB) or an excisional surgical biopsy is often necessary to obtain sufficient tissue for accurate histological and immunophenotypic analysis. CNB is considered superior to FNA for diagnosing PTL, with accuracy rates reported as high as 94.3%. In our case, the diagnosis was not established until after total thyroidectomy, which, while not standard for PTL treatment, was clinically indicated for the management of severe compressive symptoms.^{7,14}

The standard of care for thyroid DLBCL is systemic chemoimmunotherapy with a regimen like R-CHOP, which has demonstrated high response rates.^{1,11,12} Radiotherapy may be used as an adjunct, and dual-modality therapy has been shown to improve survival benefits over single-modality treatment. The excellent response of our patients to R-CHOP is consistent with the known chemosensitivity of this lymphoma subtype.^{1,14}

Prognosis in PTL is variable and depends on factors such as histological subtype, disease stage, and patient age. MALT lymphomas generally have a more favorable prognosis than DLBCL.

Although some literature reports poor outcomes, with 50% of reviewed cases resulting in death with the disease within a year, modern multi-modal therapy has significantly improved survival rates, especially for localized disease (Stage I-IIe), which accounts for the majority of presentations. The time interval from a diagnosis of HT to the development of PTL is often long, on the order of 9-10 years, reinforcing the need for long-term vigilance in this patient population.

CONCLUSION

PTL, though rare, is an important differential diagnosis in patients with HT who present with a rapidly growing neck mass or worsening compressive symptoms. The significant overlap in clinical and imaging findings between PTL and benign thyroiditis complicates early detection. This case demonstrates that a definitive diagnosis of PTL may be an unexpected finding following surgery for what is presumed to be a benign goiter. A high index of suspicion and a low threshold for obtaining a core needle or excisional biopsy are essential for timely and accurate diagnosis, allowing for the prompt initiation of appropriate, primarily non-surgical, oncologic therapy.

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