CASE REPORT

Thyroid Lymphoma: A Rare but Aggressive Disorder

Maryem Sarwar[1], Yumnah Babar[2*] and Sundas Saba[1]

[1]*Department of Histopathology, PAEC General Hospital, Islamabad, Pakistan*
[2]*School of Public Health, Nanjing Medical University, Nanjing, Jiangsu, China*

Abstract

Thyroid lymphoma is an uncommon insistent malignancy, often presenting unique diagnostic and therapeutic challenges in clinical practice. This case report describes a 49-year-old male with a previously unremarkable medical history, who presented in the surgical OPD with a progressively enlarging neck mass for approximately four to six months. Initially, there was an associated fever, which soon subsided. Upon clinical examination, a diffusely enlarged thyroid was observed with the enlargement predominantly involving the right lobe. Additionally, imaging revealed a 7x5 cm heterogeneous nodule. While the initial fine-needle aspiration cytology (FNAC) was inconclusive, subsequent cytology detected atypical cells. Due to the increasing discomfort, the patient opted for a right lobectomy but suffered intraoperative complications leading to his demise. Histopathological evaluation of the excised gland confirmed a diagnosis of diffuse large B-cell lymphoma, characterized by sheets of atypical lymphoid cells and extensive necrosis. This case highlights the aggressive nature of thyroid lymphoma and the need for timely diagnosis and management.

Keywords: *Thyroid lymphoma, lymphomatous conditions, Diffuse large B-cell lymphoma, fine needle aspiration cytology.*

INTRODUCTION

Thyroid lymphoma, although relatively rare, is a highly aggressive malignancy characterized by two primary forms: primary thyroid lymphoma (PTL) and secondary involvement of the thyroid by the systemic spread of terminal lymphoma [1]. PTL is mainly associated with autoimmune thyroid diseases especially Hashimoto's thyroiditis, where it frequently presents as a rapidly enlarging thyroid mass. Within this context, diffuse large B-cell lymphoma (DLBCL) is the most common subtype and is known for its aggressive nature, often leading to shorter durations of symptom onset compared to other lymphomatous conditions [2]. Common symptoms in patients having thyroid lymphoma include thyroid enlargement which may be diffuse or show unilateral preponderance, accompanied by systemic manifestations including fever, night sweats, and unexplained weight loss, as well as potential signs of hypothyroidism due to the infiltration of neoplastic cells in the thyroid [3].

Thyroid function test abnormalities in PTL are indistinguishable from other conditions of the gland making clinical diagnosis challenging. The cornerstone hence are imaging techniques such as ultrasound and ultrasound-guided fine needle aspiration cytology (FNAC) for evaluation indicating a possible diagnosis [4]. Although FNAC is a useful diagnostic tool, it is primarily the histological examination, typically done on core biopsy, that confirms the diagnosis [5]. Given the rare incidence of thyroid lymphoma and its clinical similarities to other thyroid disorders, early diagnosis can often be complicated. Despite these challenges, timely and effective treatment can lead to rapid symptom alleviation, particularly for complications like dyspnea caused by the mass effect. In some cases, effective medical management can even reduce the need for surgical intervention, demonstrating the importance of early detection and appropriate therapeutic strategies.

CASE REPORT

In March 2024, a 49-year-old gentleman with no past medical history presented to the surgical outpatient department at PAEC General Hospital, with a complaint of neck swelling persisting over the past 4 to 6 months. Initially, this swelling was accompanied by fever, which had now subsided. The patient did not experience any weight loss or difficulty in swallowing but reported increasing difficulty in breathing due to the swelling size. He was unable to lie down straight and the swelling was now interfering with his daily routine activities.

On physical examination, the thyroid gland was found to be diffusely enlarged, with the right lobe showing greater involvement than the left. The consistency was firm to hard, and the mobility of the gland was limited. No cervical lymphadenopathy was palpated. Laboratory investigations revealed a hemoglobin level of 11.7 g/dL, an increased white blood cell count of 15,050 per microliter, and an elevated erythrocyte sedimentation rate (ESR) of 70 mm/hour (normal range 0-10 mm/hour). Significant serological markers included positive antithyroglobulin antibodies and elevated anti-thyroid peroxidase antibodies at 172.5 IU/mL (positive threshold >38.5 IU/mL), establishing a diagnosis of Hashimoto's thyroiditis. The patient had an ultrasound showing a normally outlined thyroid gland with normal vascularity and homogenous parenchymal echogenicity

**Corresponding author: Yumnah Babar, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu, China, Email: yumnahb@njmu.edu.cn*
Received: January 09, 2025; Revised: March 19, 2025; Accepted: April 03, 2025
DOI: https://doi.org/10.37184/jlnh.2959-1805.3.16

  ISSN: 2960-2963 (Online) *Journal of Liaquat National Hospital 2025; 3(2): 164-167*

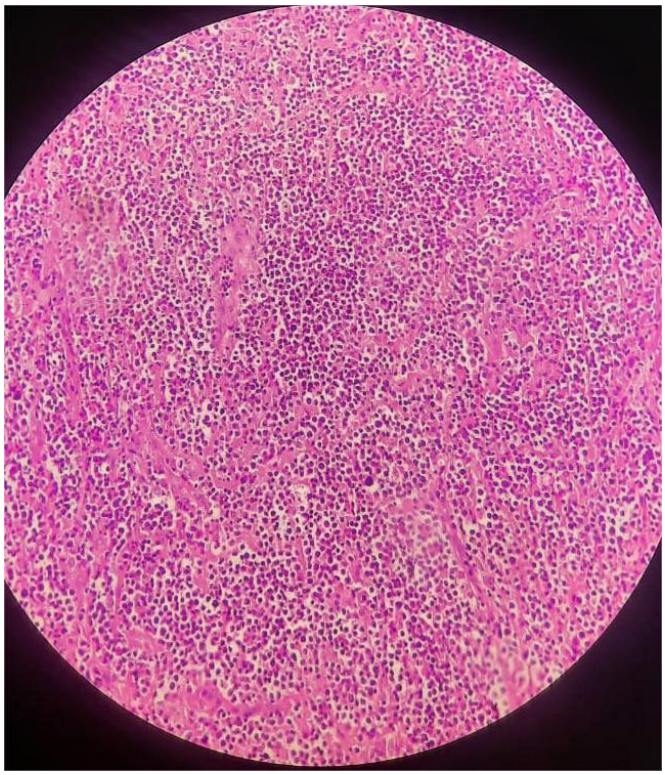

Fig. (1): H&E stained section showing diffuse sheets of medium to large lymphoid cells. No residual thyroid tissue is appreciated.

in both lobes, however, a large heterogeneous nodule was noted in the right thyroid lobe measuring 7x5 cm with normal vascularity. There were no other notable findings. Based on this an FNAC was planned.

The first attempt of FNAC was unsatisfactory, yielding hemorrhagic smears with scant thyroid follicular cells. A repeat FNAC a few weeks later demonstrated clusters of degenerating cells with high nuclear-to-cytoplasmic (N:C) ratios, leading to a diagnosis of atypia of undetermined significance (TBSRTC category 3), prompting a recommendation for a core biopsy. Due to the patient's preference, a right lobectomy was performed, during which intraoperative complications arose, resulting in the patient's demise.

Post-mortem, the excised thyroid gland was sent to the histopathology department for diagnostic assessment. A gross examination of the thyroid specimen revealed a grey-white cut surface with a fleshy appearance and areas of necrosis. Microscopic analysis (**Fig. 1**) showed sheets of large round blue cells with vesicular nuclei, distinct nucleoli, and notable mitotic activity, alongside extensive areas of coagulative tumour necrosis. Rare remnants of preserved thyroid tissue were noted, with no evidence of perithyroidal invasion. The differential diagnosis included anaplastic carcinoma and lymphoma. Immunohistochemical analysis yielded negative results for cytokeratin, PAX8 (**Fig. 2a**), and TTF1, while CD45 was positive (**Fig. 2b**). Additionally, CD20 demonstrated diffuse positivity, and CD3 was negative; the positivity of BCL6, MUM1, and CD10 confirmed the diagnosis of diffuse large B-cell lymphoma.

DISCUSSION

Primary thyroid lymphoma (PTL) is an exceptionally rare thyroid cancer, representing approximately 5% of thyroid malignancies and 2% of extranodal lymphomas [6]. Whereas the occurrence of thyroid involvement in patients with malignant lymphoma is reported to range between 11% and 27% [7]. It usually manifests as a rapidly enlarging mass in the neck, with compressive symptoms. Other presenting complaints include signs of hypothyroidism such as fatigue, cold intolerance,

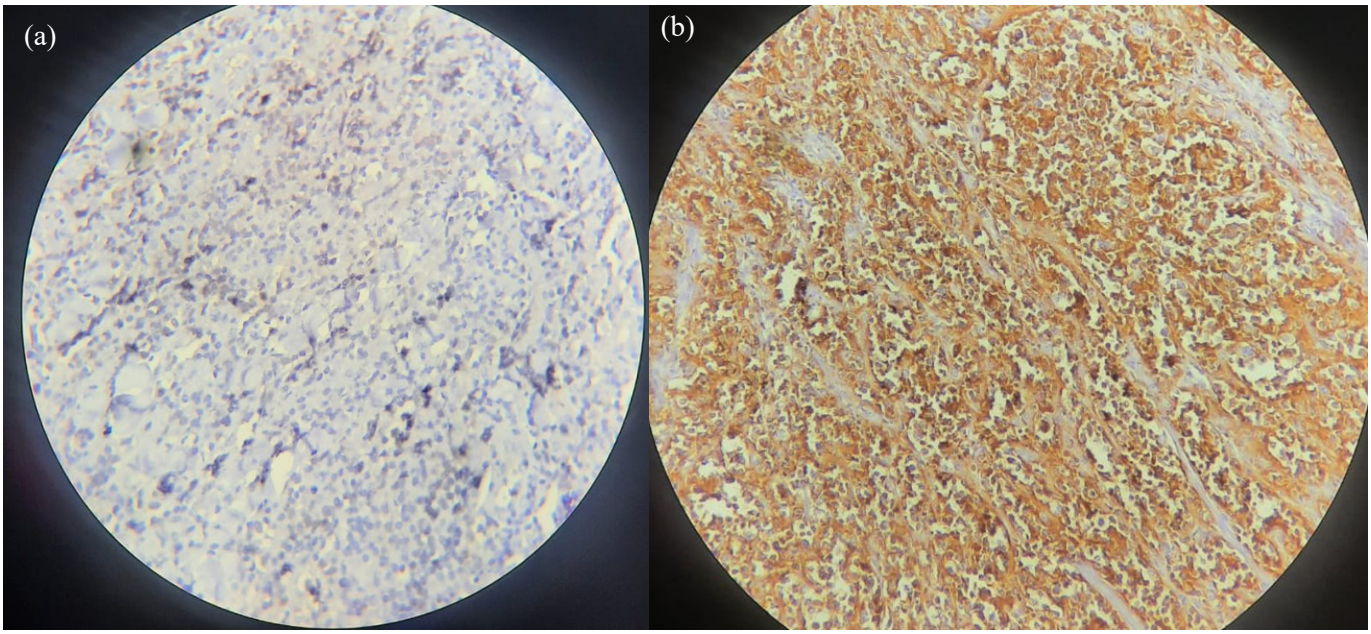

Fig. (2): (a) Negative staining with PAX8 immunohistochemical marker, **(b)** Positive staining with CD45 immunohistochemical marker.

constipation, dry skin and hair, hoarseness, menstrual irregularities or fever, night sweats, and weight loss. A known risk factor for the development of thyroid lymphoma is Hashimoto thyroiditis, as in our patient, however only 0.5% of patients with this autoimmune condition go on to develop the condition [8].

Previous reports indicate that patients with PTL typically present with an enlarging neck mass, (the primary complaint of the patient in our case) accompanied by cervical lymphadenopathy. Compressive symptoms like dyspnea, dysphagia, stridor, and hoarseness are also found in some patients, while B-symptoms such as weight loss, fever, and night sweats are less common. Our patient had dysphagia and a history of fever. Physical examination often reveals a hard, smooth-surfaced neck mass while a diffusely enlarged thyroid was present in our patient. Ultrasonography is commonly used for initial evaluation, with findings helping classify PTL as nodular, diffuse, or mixed. Fine-needle aspiration (FNA) is essential despite some variability in results, with improved accuracy due to immunophenotypic analysis. Staging of the tumour is done through CT scans based on the Ann Arbor system, however, this was not done in our patient and he was operated upon. Further treatment could not be ensued as the patient expired however in usual reported cases treatment depends on histology and stage, with chemotherapy and radiation being the primary options. Surgery has a limited role, and combined chemo-radiation therapy has shown promising results. Prognosis is generally good, with a median all-cause survival of 11.6 years and five- and ten-year survival rates of 75% and 59%, respectively [9].

The diagnosis of thyroid lymphoma is confounded not only by the nonspecific clinical picture but also inconclusive serological analysis, thyroid function tests, and radiological findings. Laboratory findings associated with hypothyroidism include raised thyroid stimulating hormone (TSH) with low T3, and T4, while those associated with Hashimoto thyroiditis include raised antithyroglobulin or the presence of antithyroid peroxidase antibodies [3]. The favoured imaging modality, ultrasound may suggest the diagnosis, with increased posterior echoes, hypoechoic features, lack of internal calcifications, enhanced vascularity and variable edge characteristics.

FNA is a simple enough procedure to aid in the workup. A study performed by Lee *et al.* in Korea indicated out of nine patients, the diagnosis of lymphoma was suggested in four patients, was benign (with Hashimoto's thyroiditis) in three patients, indicated benign intrathyroidal lymph nodes in one patient, and atypia of undetermined significance, as in our case, in one patient [1] and the sensitivity of FNAC alone was 50-80%. The FNAC results may be enhanced with the use of flow cytometry and immunohistochemistry, however, the utilization of these techniques might be based on the available medical facilities. In our case, the initial immunohistochemical panel included PAX8, TTF1 and cytokeratin. TTF1, a transcription factor crucial to thyroid development known to have a high sensitivity and specificity for cells of thyroid origin. Studies indicate PAX8 is also useful for scenarios [10] where the differential includes anaplastic thyroid carcinoma and other carcinomas as presented in our case. Cytokeratin (CKAE1/AE3) negativity ruled out metastatic carcinoma. As thyroid cells and other carcinoma were excluded, a CD45 stain was applied. The positivity indicated the diagnosis of lymphoma. A further panel was applied to determine the subtype. Tissue diagnosis with core biopsy remains most useful. The cores obtained contain an adequate amount of tissue, demonstrate architectural features, allow differentiation between a benign (thyroiditis) and malignant process, and allow for the subtyping of the malignancy [11]. Open surgical biopsies are rarely indicated, lesser still, surgical excisions, unless a strong suspicion of anaplastic thyroid carcinoma cannot be ruled out.

It is important to rule out the possibility of an anaplastic thyroid carcinoma, with the help of immunohistochemistry when needed. Where lymphomas would show negative staining for PAX8, TTF1 and Cytokeratin, and positive staining for CD45, anaplastic carcinomas would stain positively for cytokeratin and negative for CD45. The characteristics of the lymphoma coincide with the subtype, regardless of primary or secondary origin. The most common subtypes of primary thyroid lymphoma are non-Hodgkin lymphomas, particularly large B cell types, followed by MALT lymphomas. Follicular lymphomas, classic Hodgkin lymphomas and T-cell lymphomas are less common [6]. Surgery, which used to be the cornerstone of treatment for this disease, now plays a minor role. Treatment recommendations vary, after appropriate staging using the Ann Arbor classification. Primary thyroid lymphomas are generally treated with radiation, with or without chemotherapy, whereas secondary thyroid lymphomas, due to the already disseminated nature of the disease may not respond equally well [12].

CONCLUSION

In conclusion, thyroid lymphomas, while uncommon and challenging to diagnose, necessitate heightened awareness among clinicians due to their aggressive nature and varied presentations. A thorough understanding of the disease characteristics is essential, as early recognition can significantly impact patient outcomes. Clinicians are encouraged to approach the evaluation of thyroid lymphoma on a case-to-case basis, considering each patient's unique clinical history, symptomatology, and laboratory findings. This individualized approach enables more accurate diagnosis and tailored treatment strategies, ultimately optimizing management outcomes. Furthermore, interdisciplinary collaboration in diagnostics incorporating advanced imaging, fine-needle aspiration cytology (FNAC), and histopathological examination can enhance diagnostic accuracy. As thyroid lymphomas may mimic other thyroid disorders, ongoing education and awareness are critical for improving diagnostic efficacy and ensuring timely, effective intervention, thereby contributing to better prognoses for affected patients.

CONSENT FOR PUBLICATION

Written informed consent was taken from the patient.

CONFLICT OF INTEREST

The authors declare that no known financial or personal conflict of interest could affect or influence the presented work.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the Department of Histopathology, Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad, Pakistan for the provision to publish this case report.

AUTHORS' CONTRIBUTION

Maryem Sarwar and Sundus Saba provided the details of the case history, the radiological reports and performed the histology and immunohistochemistry. Yumnah Babar organized the information, completed the write-up and the relevant literature search and finalized the manuscript.

REFERENCES

1. Lee JS, Shin SJ, Yun HJ, Kim SM, Chang H, Lee YS, *et al.* Primary thyroid lymphoma: A single-center experience. Front Endocrinol (Lausanne) 2023; 14: 1064050. 2023/02/28.
DOI: https://doi.org/10.3389/fendo.2023.1064050 PMID: 36843586

2. Halouani C, Mesfar R, Mhamed RB, Akkari K, Bouomrani S. Dysphagia revealing primary large B-cell thyroid lymphoma. Arch Gastroenterol Hepatol 2019; 1: 108.
DOI: https://doi.org/10.29011/AGEH-108/100008

3. Sharma A, Jasim S, Reading CC, Ristow KM, Bisneto JCV, Habermann TM, *et al.* Clinical presentation and diagnostic challenges of thyroid lymphoma: a cohort study. Thyroid 2016; 26(8): 1061-7.
DOI: https://doi.org/10.1089/thy.2016.0095 PMID: 27256107

4. Jayaprakash Ks, Kishanprasad HI, Hegde P, Chandrika R. Hashimotos Thyroiditis with Coexistent Papillary Carcinoma and Non-hodgkin Lymphoma-thyroid. Ann Med Health Sci Res 2014; 4(2): 268-70.
DOI: https://doi.org/10.4103/2141-9248.129061 PMID: 24761251

5. Sun XS, Bay JO, Marcy PY, Hammoud Y, Lacout A, Michels JJ, *et al.* Treatment of primary thyroid lymphomas. Bull Cancer 2013; 100(10): 1031-42.
DOI: https://doi.org/10.1684/bdc.2013.1820 PMID: 24077086

6. Ansell SM, Grant CS and Habermann TM. Primary thyroid lymphoma. Semin Oncol 1999; 26(3): 316-23.
PMID: 10375088

7. Willis RA. Metastatic tumours in the thyreoid gland. Am J Pathol 1931; 7(3): 187-208.3.
PMID: 19969962

8. Watanabe N, Noh JY, Narimatsu H, Takeuchi K, Yamaguchi T, Kameyama K, *et al.* Clinicopathological features of 171 cases of primary thyroid lymphoma: a long-term study involving 24553 patients with Hashimoto's disease. Br J Haematol 2011; 153(2): 236-43.
DOI: https://doi.org/10.1111/j.1365-2141.2011.08606.x PMID: 21371004

9. Khanal P, Lageju N and Adhikari B. Diffuse Large B-Cell Lymphoma of Thyroid: A Case Report and Review of Literature. Indian J Otolaryngol Head Neck Surg 2022; 74 (Suppl2): 2287-90.
DOI: https://doi.org/10.1007/s12070-020-02088-1 PMID: 36452532

10. Nonaka D, Tang Y, Chiriboga L, Rivera M, Ghossein R. Diagnostic utility of thyroid transcription factors Pax8 and TTF-2 (FoxE1) in thyroid epithelial neoplasms. Mod Pathol 2008; 21(2): 192-200.
DOI: https://doi.org/10.1038/modpathol.3801002 PMID: 18084247

11. Pavlidis ET and Pavlidis TE. A review of primary thyroid lymphoma: molecular factors, diagnosis and management. J Invest Surg 2019; 32(2): 137-42.
DOI: https://doi.org/10.1080/08941939.2017.1383536 PMID: 29058491

12. Takashima S, Takayama F, Momose M, Shingu K, Sone S. Secondary malignant lymphoma which simulated primary thyroid cancer. Clin Imaging 2000; 24(3): 162-165. 2001/01/11.
DOI: https://doi.org/10.1016/s0899-7071(00)00195-9 PMID: 11150685