Case Report / Olgu Sunumu

Primer Tiroid Diffüz Büyük B Hücreli Lenfoma: Olgu Sunumu

Primary Thyroid Diffuse Large B Cell Lymphoma: Case Report

[1]Sinan Demircioğlu, [2]Melis Gülsar Çaycı, [3]Hasan Furkan Çaycı, [3]Fahriye Kılınç, [1]Atakan Tekinalp

[1] Necmettin Erbakan University Faculty of Medicine, Department of Hematology, Konya, Türkiye
[2] Necmettin Erbakan University Faculty of Medicine, Department of Internal Medicine, Konya Türkiye
[3] Necmettin Erbakan University Faculty of Medicine, Department of Pathology, Konya, Türkiye

Abstract: Primary thyroid lymphoma is a rare malignancy, accounting for approximately 5% of all thyroid malignancies and less than 2% of extranodal lymphomas. Diffuse B-cell lymphoma is the most common pathological subtype of primary thyroid lymphoma. It typically presents as a rapidly growing, painless thyroid mass and may cause compressive symptoms. Its treatment is similar to non-thyroid lymphoma.
Keywords: Primary thyroid lymphoma, diffuse large B-cell lymphoma, treatment

Özet: Primer tiroid lenfoması, tüm tiroid malignitelerinin yaklaşık %5'ini ve ekstranodal lenfomaların %2'sinden azını oluşturan nadir bir malignitedir. Diffüz B hücreli lenfoma, Primer tiroid lenfomalarının en sık görülen patolojik alt tipidir. Tipik olarak hızla büyüyen, ağrısız bir tiroid kitlesi olarak ortaya çıkar ve bası semptomlarına neden olabilir. Tedavisi tiroid dışı lenfomalara bezer şekilde yapılmaktadır.
Anahtar Kelimeler: primary thyroid lymphoma, diffuse large B-cell lymphoma, treatment

ORCID ID of the author: SD. 0000-0003-1277-5105, MGC. 0009-0003-1101-2496, HFC. 0009-0005-2551-5363, FK. 0000-0002-1202-8735, AT. 0000-0001-7937-4045

Received 04.05.2024 ***Accepted*** 02.07.2024 ***Online published*** 13.08 2024

Correspondence: Sinan DEMİRCİOĞLU - Necmettin Erbakan University Faculty of Medicine, Department of Hematology, Konya, Türkiye
e-mail: sinandemircioglumd@gmail.com

1. Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common histological subtype of non-Hodgkin lymphoma (NHL), accounting for approximately 25% of NHL cases. DLBCL is a clinically, pathologically and molecularly heterogeneous disease. As a reflection of heterogeneity, 5-year survival times vary widely, between 30% and 80% (1). The most commonly used prognostic tool in DLBCL patients is the International Prognostic Index (IPI) score. One of the factors included in the IPI score is the number of extranodal sites; Having more than one site of extranodal involvement is considered a poor prognostic indicator (2). In up to 40% of DLBCL cases, the disease occurs in extranodal tissues (3). The most common site of primary extranodal disease is the stomach/gastrointestinal tract. However, the disease can occur in almost any tissue, including testicles, bone, thyroid, salivary glands, tonsils, skin, liver, breast, adrenals, kidneys, nasal cavity, ocular adnexa, paranasal sinuses, cervix, vagina, and central nervous system (4–12). We presented our case of DLBCL arising in the thyroid, which we successfully treated with standard chemotherapy treatment.

2. Case

A sixty-four-year-old woman, who had been using L-thyroxine for Hashimoto's thyroiditis for five years, applied with complaints of swelling in the neck area, fatigue, weakness, cold intolerance, chills and constipation. The L-thyroxine dose was increased from 25 mcg to 75 mcg for the patient whose thyroid stimulating hormone (TSH) value was observed to be 26 mIU/L. It was determined that the patient had a previous history of thyroid nodule and in the ultrasonography (USG) examination, the size of the nodule in the right lobe increased and reached 3 cm. Total thyroidectomy was performed on the patient who was thought to have thyroid malignancy. Thyroid pathology bcl-6 (+) (> 30%), CD 20 and CD79a (+), Bcl-2, CD10, MUM-1, CD23, cyclin D1, CD3 and CD23 (-), Ki-67 index >%80 were detected and histopathological findings were found to be compatible with diffuse large B-cell lymphoma, germinal center subtype. (Figure-1). In pre-treatment PET-CT, opacities showing malignant FDG increases were observed in a larger area in the right lobe of the thyroid gland (SUVmax: 29.16) and in the left lobe (SUVmax: 6.16). A lymph node measuring 11 mm (SUVmax: 26.35) and showing malignant FDG increase was observed in the supraclavicular region, posterior to the left thyroid lobe. No lymphoma involvement was detected in the bone marrow biopsy. Stage 2E according to An Arbor classification, and IPI score was calculated low. The patient was started on a chemotherapy protocol of rituximab + cyclophosphamide + adriamycin + vincristine + prednisolone (R-CHOP) every 21 days. A complete metabolic response was achieved in the interim evaluation after three cycles of chemotherapy. The treatment was completed by giving three more cycles of R-CHOP chemotherapy. Informed consent form was obtained from the patient.

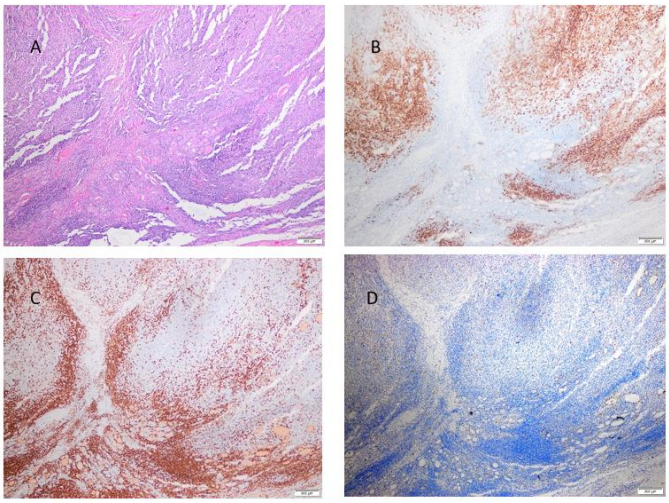

Figure 1. A: Hematoxylin-Eosin x4 B: x4, CD20: positive C: x4, CD 5: negative D: x4, CYCLIN D1: negative

3. Discussion

Primary thyroid lymphoma (PTL) is a rare neoplasm that accounts for 1-5% of thyroid malignancies and less than 2% of extranodal lymphomas. (13). PTL typically presents with a mass in the neck that grows rapidly and causes compressive symptoms. This clinical picture can be confused with anaplastic thyroid carcinoma. PTL is usually seen in people between the ages of 50 and 80 and is more common in women than in men (F:M, ~3–4:1) (14). Lymphoma of the thyroid gland is mainly non-Hodgkin lymphoma of B-cell origin. Diffuse large B-cell lymphoma (DLBCL) is the predominant histological subtype (70%), followed by mucosa-associated lymphoid tissue (MALT) lymphoma, follicular lymphoma (FL), Mantle cell lymphoma (MCL), Burkitt lymphoma (BL), and angioblastic lymphoma (15).

So far, the pathogenesis of PTL has not been fully elucidated. Normal thyroid tissue does not contain lymphoid tissue, and the appearance of lymphocytes promotes PTL formation. Sharma et al showed that 54.7% of PTL patients had a history of Hashimoto's thyroiditis (HT) (16). Antonio et al. reported that HT is the most important risk factor for PTL and increases the risk of PTL by 40-80 times (17). A larger study showed that 154 of 171 adult patients (90%) were diagnosed with Hashimoto's thyroiditis within 1-362 months before PTL diagnosis (18). Our case also had a history of Hashimoto's thyroiditis.

Clinical signs of PTL include rapid growth of neck masses or thyroid masses over a short period of time. Patients with large masses may have compression symptoms such as dysphagia, shortness of breath, and hoarseness. Typical symptoms of Horner syndrome, superior vena cava syndrome, and B-cell lymphoma, such as fever, night sweats, and weight loss, are relatively rare (19).

Ultrasonography has become a routine examination in the distinction between benign and malignant thyroid nodules. PTL tumor cells have uniform and dense growth, few interstitial components, and good acoustic permeability; This makes the capsule edge of the thyroid tumor clearer and the echo behind the gland stronger (20). Another study has shown that cases of PTL appear radiologically as a mass that is usually large, unilateral, in the center of the thyroid, hypoechoic by ultrasound, and spreads to adjacent soft tissues (16). Computed tomography (CT) has excellent sensitivity and specificity in clinical staging of DLBCL and extranodal metastasis. CT scan of PTL is usually isodensity or slightly lower density, with homogeneous parenchymal density and rare calcifications and cysts or necrotic foci (21). Fine needle aspiration (FNA) cytology is not a reliable method in the diagnosis of PTL, and the primary diagnostic method is ultrasound-guided needle biopsy or surgical excisional biopsy. Incisional biopsy or fine needle

aspiration biopsies are inadequate in the diagnosis of lymphoma, and choosing these procedures before excisional biopsy delays the diagnosis. In our case, total thyroidectomy was performed because thyroid cancer was considered as the preliminary diagnosis. If lymphoma had been considered in the preliminary diagnosis, the diagnosis could have been made only by excisional lymph node biopsy.

The prognosis of PTL patients largely depends on the histological subtype. MALT lymphoma is considered low grade with an indolent natural history. Previous studies have reported that disease-specific 5-year survival rates vary between 96% and 100%. DLBCL is considered a high-grade lymphoma with a more aggressive clinical course than MALT lymphoma, and the 5-year disease-specific survival rate for DLBCL is 71-75% (22–24). Graff-Baker et.al showed that older age, advanced stage, histological subtype, and lack of radiation/surgical treatment were associated with worse survival in PTL (23). The prognosis for early-stage PTL (stages IE and IIE) is excellent after current treatments. The 5-year survival rate has been reported as 100% in MALT type and mixed (MALT, DLBCL) type cases, and the 5-year survival rate in DLBCL type cases has been reported as 87.5% (25). In another study, the 5-year overall survival (OS) and event-free survival (EFS) rates of PTL patients were found to be 85% and 79%, respectively. Higher age and higher erythrocyte sedimentation rate (ESR) were significant risk factors for OS. Aggressive lymphomas had significantly shorter EFS than indolent lymphoma. This study showed that PTL responded well to radiotherapy and chemotherapy (18).

Since PTL is a rare disease, it is very difficult to conduct large-scale prospective studies for treatment. Current evidence shows that combined chemoradiotherapy treatment is effective in maintaining disease control and improving long-term outcomes. Researchers have shown that a combination of surgery and chemotherapy may provide more benefits to patients than surgery alone. The currently accepted chemotherapy regimen is CHOP or R-CHOP (26). It would be appropriate to treat primary thyroid DLBCL with standard DLBCL treatment recommendations. Current DLBCL treatment is planned considering the stage, presence of bulky disease, presence of extensive mesenteric disease, and risk scoring. Stage 1-2 patients who do not have bulky disease (<7.5 cm), do not have extensive mesenteric disease, and have a low stage-modified international prognostic index are treated with 3 cycles of R-CHOP chemotherapy. If a complete response is obtained in the interim evaluation, one more course of R-CHOP is given or involved-site radiation therapy (ISRT) is performed. Those with stage 1-2 bulky disease (>7.5 cm) and/or stage-modified international prognostic index of 0-1 are given 3-4 cycles of R-CHOP. If there is a complete response in the interim evaluation, 2-3 more cycles of R-CHOP±ISRT are given and the treatment is completed with 6 cycles. In stage 3-4 or stage 1-2 patients with extensive mesenteric disease, 2-4 cycles of R-CHOP chemotherapy are given and an interim evaluation is made. If complete and partial response is achieved, 6 cycles of treatment are completed. (27).

As a result, although thyroid cancers are common, thyroid lymphomas are rare. Rapidly growing thyroid lesions, especially in those with a history of Hashimoto's thyroiditis, should bring to mind thyroid lymphoma. Treatment is similar to non-thyroid lymphoma.

REFERENCES

1. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375-2390.
2. International Non-Hodgkin's Lymphoma Prognostic Factors Project. A Predictive Model for Aggressive Non-Hodgkin's Lymphoma. New England Journal of Medicine. 1993;329(14):987-994.
3. 3. Møller MB, Pedersen NT, Christensen BE. Diffuse large B-cell lymphoma: clinical implications of extranodal versus nodal presentation – a population-based

study of 1575 cases. Br J Haematol. 2004;124(2):151-159.
4. Castillo JJ, Winer ES, Olszewski AJ. Sites of extranodal involvement are prognostic in patients with diffuse large B-cell lymphoma in the rituximab era: An analysis of the Surveillance, Epidemiology and End Results database. Am J Hematol. 2014;89(3):310-314.
5. Guastafierro S, Tedeschi A, Criscuolo C, et al. Primary Extranodal Non-Hodgkin's Lymphoma of the Vagina: A Case Report and a Review of the Literature. Acta Haematol. 2012;128(1):33-38.
6. Shikama N, Ikeda H, Nakamura S, et al. Localized aggressive non-Hodgkin's lymphoma of the nasal cavity: a survey by the Japan Lymphoma Radiation Therapy Group. International Journal of Radiation Oncology*Biology*Physics. 2001;51(5):1228-1233.
7. Domchek SM, Hecht JL, Fleming MD, Pinkus GS, Canellos GP. Lymphomas of the breast. Cancer. 2002;94(1):6-13.
8. Ferrucci PF, Zucca E. Primary gastric lymphoma pathogenesis and treatment: what has changed over the past 10 years? Br J Haematol. 2007;136(4):521-538.
9. Avilés A, Neri N, Huerta-Guzmán J. Large bowel lymphoma: An analysis of prognostic factors and therapy in 53 patients. J Surg Oncol. 2002;80(2):111-115.
10. Güngör S, Vural Ö, Çerçi M. Primer Mide Lenfoması. Selçuk Tıp Dergisi. 1992;8(1):143-146.
11. Demircioglu S, Telci U, Ozcelik M, Dogan A, Bayram İ. Renal involvement in diffuse large B-cell lymphoma: A case report. Marmara Medical Journal. 2019;32(3):144-146.
12. Tekinalp A, Demircioğlu S, Karakuş V, Çeneli Ö, Turgut B. Yaygın Büyük B Hücreli Lenfoma (YBBHL) Tanılı Olguların Retrospektif Değerlendirmesi. Namık Kemal Tıp Dergisi. 2020;8(3):383-390.
13. Pavlidis ET, Pavlidis TE. A Review of Primary Thyroid Lymphoma: Molecular Factors, Diagnosis and Management. Journal of Investigative Surgery. 2019;32(2):137-142.
14. Derringer GA, Thompson LDR, Frommelt RA, Bijwaard KE, Heffess CS, Abbondanzo SL. Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases. Am J Surg Pathol. 2000;24(5):623-639.
15. Graff-Baker A, Sosa JA, Roman SA. Primary thyroid lymphoma: a review of recent developments in diagnosis and histology-driven treatment. Curr Opin Oncol. 2010;22(1):17-22.
16. Sharma A, Jasim S, Reading CC, et al. Clinical Presentation and Diagnostic Challenges of Thyroid Lymphoma: A Cohort Study. Thyroid. 2016;26(8):1061-1067.
17. Travaglino A, Pace M, Varricchio S, et al. Clinical features associated with high pathological grade in primary thyroid lymphoma. Pathol Res Pract. 2020;216(3):152819.
18. Watanabe N, Noh JY, Narimatsu H, et al. Clinicopathological features of 171 cases of primary thyroid lymphoma: a long-term study involving 24 553 patients with Hashimoto's disease. Br J Haematol. 2011;153(2):236-243.
19. Katna R, Shet T, Sengar M, et al. Clinicopathologic study and outcome analysis of thyroid lymphomas: Experience from a tertiary cancer center. Head Neck. 2013;35(2):165-171.
20. 20. Wei X, Li Y, Zhang S, Li X, Gao M. Evaluation of primary thyroid lymphoma by ultrasonography combined with contrast-enhanced ultrasonography: A pilot study. Indian J Cancer. 2015;52(4):546.
21. Li XB, Ye ZX. Primary Thyroid Lymphoma: Multi-Slice Computed Tomography Findings. Asian Pacific Journal of Cancer Prevention. 2015;16(3):1135-1138.
22. Hancock B. Primary thyroid lymphoma: The 40 year experience of a UK lymphoma treatment centre. Int J Oncol. Published online February 22, 2012.
23. Graff-Baker A, Roman SA, Thomas DC, Udelsman R, Sosa JA. Prognosis of primary thyroid lymphoma: Demographic, clinical, and pathologic predictors of survival in 1,408 cases. Surgery. 2009;146(6):1105-1115.
24. Derringer GA, Thompson LDR, Frommelt RA, Bijwaard KE, Heffess CS, Abbondanzo SL. Malignant Lymphoma of the Thyroid Gland. Am J Surg Pathol. 2000;24(5):623-639.
25. Chai YJ, Hong JH, Koo DH, et al. Clinicopathological characteristics and treatment outcomes of 38 cases of primary thyroid lymphoma: a multicenter study. Ann Surg Treat Res. 2015;89(6):295.
26. Mian M, Gaidano G, Conconi A, et al. High response rate and improvement of long-term survival with combined treatment modalities in patients with poor-risk primary thyroid diffuse large B-cell lymphoma: an International Extranodal Lymphoma Study Group and Intergruppo Italiano Linfomi study. Leuk Lymphoma. 2011;52(5):823-832.
27. Dwyer, Mary. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines ®) B-Cell Lymphomas NCCN.Org NCCN Guidelines for Patients ® Available at Www.Nccn.Org/Patients.; 2024. www.nccn.org/patients

Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.
Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

Peer-review: Internally peer-reviewed.
Authorship Contributions: Surgical and Medical Practices: HFÇ, FK. Concept: SD, MGÇ. Design: SD, MGÇ. Data Collection or Processing: MGÇ, HFÇ. Analysis or Interpretation: AK, FK, HFÇ. Literature Search: AK, MGÇ, SD. Writing: SD, MGÇ
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study received no financial support