CASE REPORT

DOI: 10.4274/nkmj.galenos.2025.84748
Nam Kem Med J 2026;14(1):95-99

A Case of Composite Lymphoma with Coexisting Papillary and Medullary Thyroid Carcinomas in a Patient with a History of Four Primary Malignancies

Dört Farklı Primer Malignite Öyküsü: Kompozit Lenfomaya Eşlik Eden Tiroid Papiller ve Medüller Kanser Olgusu

Zehra AKŞİT BOZKINA[1], Ajda GÜNEŞ[1], Derya DEMİR[2], Mine HEKİMGİL[2], Nur SOYER[1], Filiz VURAL[1]

[1]Ege University Faculty of Medicine, Department of Hematology, İzmir, Türkiye
[2]Ege University Faculty of Medicine, Department of Pathology, İzmir, Türkiye

ABSTRACT

Composite lymphoma refers to the simultaneous presence of two or more morphologically and immunophenotypically distinct lymphomas within the same tissue or organ. While cases of composite lymphoma consisting of classical Hodgkin lymphoma (cHL) and B-cell lymphoma have been reported, the combination of splenic marginal zone B-cell lymphoma (SMZL) and cHL is extremely rare. In this report, we present a case initially treated with insufficient response for SMZL, later experiencing recurrence, followed by a diagnosis of cHL. Additionally, thyroid tissue from the same patient revealed the presence of thyroid papillary and medullary cancers with a poor prognosis. This report presents a case of composite lymphoma involving four different primary malignancies occurring simultaneously.

Keywords: Hodgkin lymphoma, non-Hodgkin lymphoma, B-cell neoplasms

ÖZ

Kompozit lenfoma, aynı doku veya organda morfolojik ve immünofenotipik olarak farklı iki veya daha fazla lenfomanın eş zamanlı varlığına işaret eder. Klasik Hodgkin lenfoması (cHL) ve B-hücreli lenfoma içeren kompozit lenfoma olguları bildirilmiş olmasına rağmen, splenik marginal zon B-hücreli lenfoma (SMZL) ve cHL kombinasyonu son derece nadirdir. Bu raporda, başlangıçta SMZL için yetersiz yanıt ile tedavi edilen, daha sonra nüks eden ve ardından cHL tanısı konan bir olgu sunulmaktadır. Ayrıca, aynı hastanın tiroid dokusunda kötü prognozlu tiroid papiller ve medüller kanserleritespit edilmiştir. Bu rapor, aynı anda dört farklı primer malignitenin yer aldığı bir kompozit lenfoma olgusunu sunmaktadır.

Anahtar Kelimeler: Hodgkin lenfoma, non-Hodgkin lenfoma, B-hücreli neoplazmlar

INTRODUCTION

Composite lymphoma refers to the simultaneous presence of two or more lymphomas with different morphological and immunophenotypic features in the same tissue or organ[1]. Although cases of composite lymphoma consisting of classical Hodgkin lymphoma (cHL) and B-cell lymphoma have been reported, the combination of splenic marginal zone B-cell lymphoma (SMZL) and cHL is extremely rare[2]. This report presents a case where a patient initially treated for SMZL with inadequate response was later diagnosed with cHL following a repeat biopsy. Additionally, a biopsy of thyroid tissue from the same patient revealed a rare papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma (MTC).

Address for Correspondence: Zehra AKŞİT BOZKINA MD, Ege University Faculty of Medicine, Department of Hematology, İzmir, Türkiye
E-mail: zehraaksit1993@hotmail.com **ORCID ID:** orcid.org/0000-0003-3638-4491
Received: 12.12.2024 **Accepted:** 13.03.2025 **Publication Date:** 04.03.2026

Cite this article as: Akşit Bozkına Z, Güneş A, Demir D, Hekimgil M, Soyer N, Vural F. A case of composite lymphoma with coexisting papillary and medullary thyroid carcinomas in a patient with a history of four primary malignancies. Nam Kem Med J. 2026;14(1):95-99

Informed consent was obtained from the patient involved in this case report. They were informed about the medical procedures and the scientific purpose of this study.

CASE REPORT

A 69-year-old male farmer with a known history of diabetes mellitus and cholelithiasis presented with fever, weight loss, night sweats, and left upper quadrant pain. This table summarizes key laboratory results from the patient's clinical report. Abdominal ultrasound revealed multiple lymphadenopathies in the liver hilum, with the largest node measuring 3.2 cm, and splenomegaly with a spleen size of 17 cm. A bone marrow biopsy was performed, and the immunohistochemical findings (positive for CD20, CD23, CD3, BCL 2) along with the morphological assessment were consistent with SMZL (Figure 1 presents the results of immunohistochemical staining). On the positron emission tomography/computed tomography (PET/CT) scan, the patient had a 47 mm [standardized uptake value (SUV) 6.2] nodular mass in the right lobe of the thyroid gland, a 12 mm (SUV 2.4) mass in the anterior mediastinum, 15 mm (SUV 2.1) bilateral axillary lymphadenopathy, multiple perisplenic lymphadenopathies with the largest being 20 mm, and splenomegaly with a spleen size of 19 cm. After 6 cycles of rituximab treatment, the PET/CT response evaluation showed no significant morphological changes in the hypermetabolic mass lesion in the right lobe of the thyroid gland (Figure 2a), with partial metabolic regression observed. Increased fluorodeoxyglucose (FDG) uptake was noted in the right axillary fossa (Figure 2b), subcutaneous tissue adjacent to the gluteal and paraspinal muscle planes, and bilateral inguinal regions. Complete regression was observed in lymph nodes in the periportal and perisplenic regions, while millimetric lymph nodes showing FDG uptake under mediastinal vascular structures were classified as Deauville score 2. Splenic size was found to be normal. Bone marrow biopsy did not show lymphoma infiltration. Due to a suspicious nodule, the patient underwent total thyroidectomy and an excisional lymph node biopsy from the right axilla. The thyroidectomy material showed MTC in the right lobe, PTC of the follicular variant with capsule invasion in the left lobe, and the right axillary lymph node biopsy revealed mixed cellularity type cHL. The lymph node biopsy showed positive results for CD30, CD15, MUM1, and PAX-5; while CD20, CD45, and EBER were negative (Figure 3 presents the results of immunohistochemical staining). The endocrinology team recommended monitoring with calcitonin and carcinoembryonic antigen every 3 months without treatment. A follow-up neck ultrasound revealed lymphadenopathy in the cervical chain, with the largest node

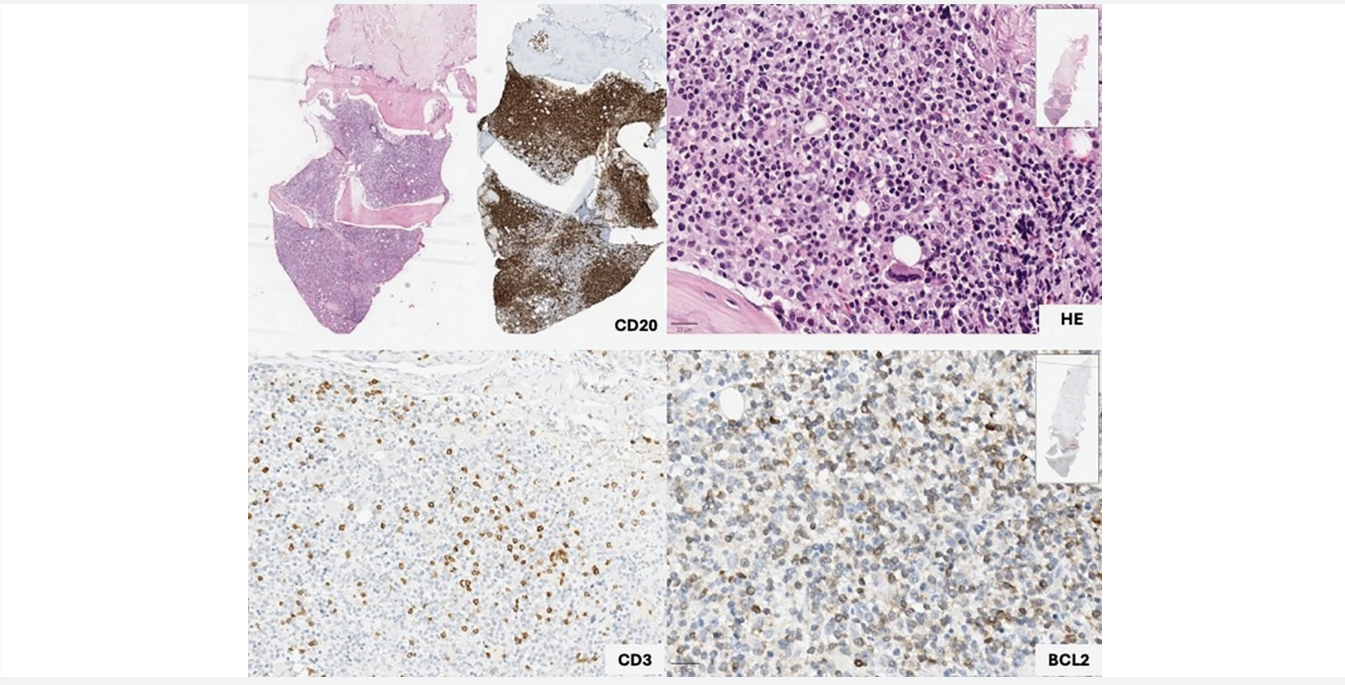

Figure 1. Bone marrow involvement by low-grade B-cell lymphoma/leukemia. Top left: H&E staining shows lymphoid infiltration in the bone marrow with diffuse CD20 positivity. Top right: High-magnification view reveals infiltration of small to medium-sized atypical B-lymphocytes. Bottom left: CD3 immunohistochemical staining highlights sparsely scattered accompanying T lymphocytes. Bottom right: BCL2 immunohistochemical staining shows weak but positive expression in the neoplastic B-cells

H&: Hematoxylin and eosin

measuring 15x6 mm in the right supraclavicular region, and additional nodes in the right parotid cortex. The patient was diagnosed with stage 3A cHL and began doxorubicin (adriamycin), bleomycin, vinblastine, dacarbazine therapy. Genetic testing from the lymph node biopsy using next-generation sequencing (NGS) panel identified possible pathogenic variants: CIITA p.C83fs (loss-of-function) with a variant allele frequency (VAF) of 10% and TCF3 p.R525W with a VAF of 2.9%. After two cycles, the patient achieved a complete response on PET/CT but unfortunately passed away due to pneumonia during the course of treatment.

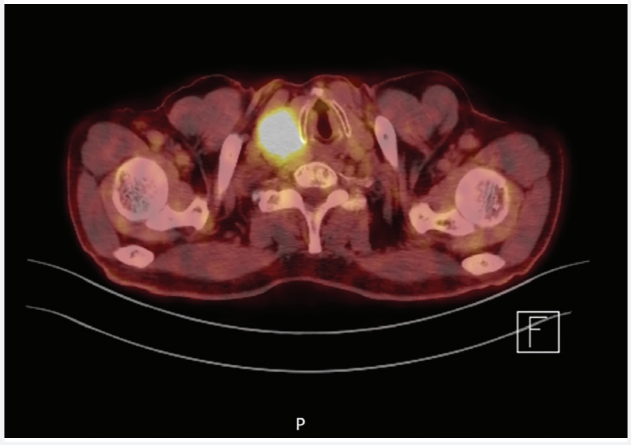

Figure 2a. PET/CT findings: There is a hypermetabolic mass lesion in the right lobe of the thyroid gland, hypodense in nature, measuring 4.6x3.5 cm at its widest, with heterogeneous characteristics (SUV_{max}: 7.7)

SUV_{max}: Maximum standardized uptake value, PET/CT: Positron emission tomography/computed tomography

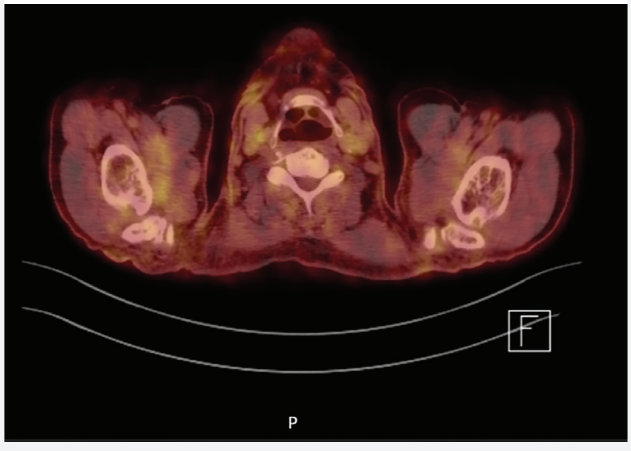

Figure 2b. PET/CT findings: There is a reticulonodular density in the right axillary fossa showing increased FDG uptake (SUV_{max}: 4.9)

SUV_{max}: Maximum standardized uptake value, PET/CT: Positron emission tomography/computed tomography, FDG: Fluorodeoxyglucose

DISCUSSION

In this report, we present a case of composite lymphoma with four different primary malignancies occurring simultaneously. The coexistence of SMZL and cHL is rare, given that cHL typically presents in lymph nodes[2]. To our knowledge, there are very few reported cases of cHL developing in a patient with SMZL. In one case study, PCR and sequencing analyses revealed that amplified rearranged immunoglobulin genes originated from the same clone[3]. In another case, where both cHL and mantle cell lymphoma were present, the findings were clonally unrelated[4]. According to a published review, more than 70% of patients with composite lymphoma are ≥55 years old, and the majority are male. The most commonly associated lymphomas are cHL with follicular lymphoma or diffuse large B-cell lymphoma, with over 130 cases reported. The cHL group is frequently of the mixed cellularity type, and compared to other types, it often shows focal/weak CD20 expression, suggesting a distinct pathophysiology. Both groups can share similar IgH/IgK rearrangements and the same pathogenic variants, which supports the hypothesis of a common clonal origin. Thus, composite lymphomas appear to support a common clonal origin and transdifferentiation process during lymphoma pathogenesis[5]. A study of 20 cases with both HL and non-HL (NHL), including three cases diagnosed with SMZL, found that the HL that developed later was usually more aggressive and at a more advanced stage[6]. In most of these cases, malignant clones develop separately from a common precursor cell, often a germinal center B-cell. Thus, this suggests a scenario where malignant precursor cells undergo transformation resulting in the development of two different lymphomas through distinct and repeated transformation events within the germinal center microenvironment. Molecular findings support this view[7]. PTC is the most common endocrine malignancy. The simultaneous occurrence of HL and MTC has been rarely reported. The coexistence of MTC and PTC in the same thyroid gland is classified into two forms. The first form consists of two distinct tumors separated by non-neoplastic thyroid tissue. The other form is a mixed tumor. Our case fits the first form. In thyroid cancers, metastases are usually observed as lymph nodes in the cervical and anterior mediastinal regions, similar to the widespread involvement seen in HL[8]. HL treatment was initiated after total thyroidectomy in our case. In our case, NGS of the lymph node revealed a significant loss-of-function mutation in CIITA p.C83fs with a VAF of 10%. Hematopoietic cancer cells can also present antigens in the context of HLA class II. It has been shown that CIITA methylation can lead to transcriptional down regulation of *HLA II* genes, allowing these cells to evade antigen presentation. The *CIITA* gene often breaks and fuses in some lymphomas, playing a key role in how these cancers evade

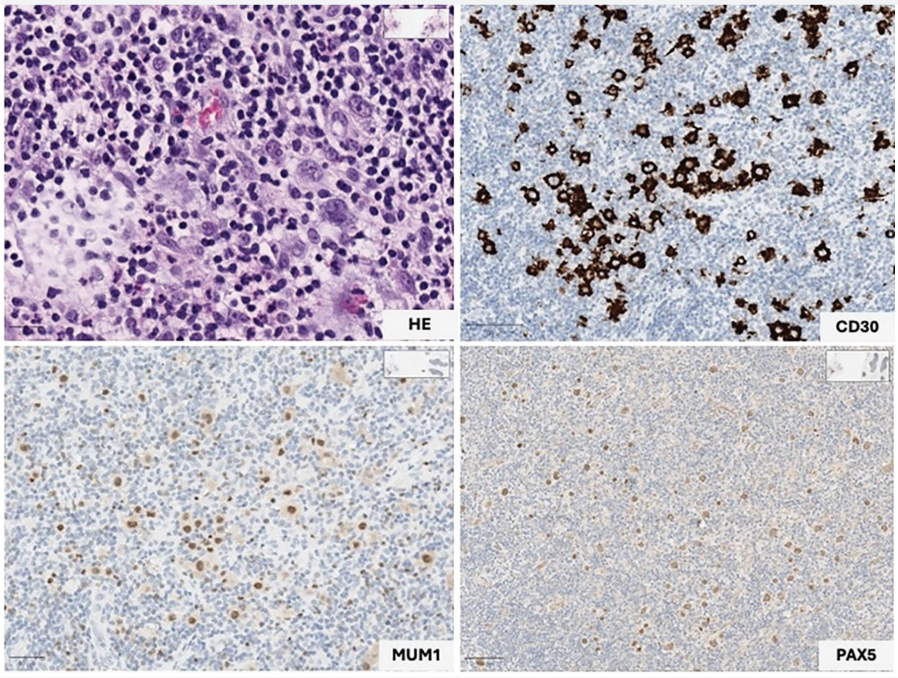

Figure 3. Lymph node involvement by classical Hodgkin lymphoma in the same patient. Top left: H&E staining shows a characteristic nodal architecture with scattered large atypical Reed-Sternberg cells in an inflammatory background. Top right: CD30 immunohistochemical staining highlights strong membranous and Golgi-associated positivity in Reed-Sternberg cells. Bottom left: MUM1 immunohistochemical staining shows moderate positivity in neoplastic cells. Bottom right: PAX5 immunohistochemical staining demonstrates weak but detectable nuclear expression in Hodgkin cells

H&E: Hematoxylin and eosin

the immune system. In a study of 263 patients with B-cell lymphoma, 15% of those with cHL showed recurring genomic breakages in CIITA[9]. Inactivating CIITA mutations are found in cancers including mediastinal large B-cell lymphoma, cHL, and gastric and colorectal cancers[10]. Loss of CIITA function can lead to impaired antigen presentation due to reduced MHC-II expression[11]. CIITA rearrangements can result in the loss of CIITA function, deletion of tumor suppressors, or overexpression of oncogenic fusion partners[9].

CONCLUSION

This case provides clinical experience in the management of both HL and NHL when occurring simultaneously, demonstrating appropriate treatment strategies for both. Further research is needed to elucidate the molecular mechanisms that lead to the simultaneous occurrence of multiple malignancies. To the best of our knowledge, this appears to be the first reported case of composite lymphoma coexisting with two distinct primary thyroid carcinomas, resulting in four synchronous primary malignancies.

Ethics

Informed Consent: Informed consent was obtained from the patient involved in this case report. They were informed about the medical procedures and the scientific purpose of this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.A.B., A.G., D.D., M.H., N.S., F.V., Concept: Z.A.B., A.G., D.D., F.V., Design: Z.A.B., F.V., Data Collection or Processing: Z.A.B., A.G., F.V., Analysis or Interpretation: Z.A.B., A.G., D.D., M.H., N.S., F.V., Literature Search: Z.A.B., A.G., D.D., M.H., N.S., F.V., Writing: Z.A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Kim H, Hendrickson R, Dorfman RF. Composite lymphoma. Cancer. 1977;40:959-76.
2. Harada S, Kalla H, Balasubramanian M, Brodsky I, Gladstone D, Hou JS. Classical Hodgkin lymphoma concurrently evolving in a patient with marginal zone B-cell lymphoma of the spleen. Ann Diagn Pathol. 2008;12:212-6.
3. Rosenquist R, Roos G, Erlanson M, Küppers R, Bräuninger A, Hansmann ML. Clonally related splenic marginal zone lymphoma and Hodgkin lymphoma with unmutated V gene rearrangements and a 15-yr time gap between diagnoses. Eur J Haematol. 2004;73:210-4.
4. Caleo A, Sánchez-Aguilera A, Rodríguez S, Dotor AM, Beltrán L, de Larrinoa AF, et al. Composite Hodgkin lymphoma and mantle cell lymphoma: two clonally unrelated tumors. Am J Surg Pathol. 2003;27:1577-80.
5. Trecourt A, Donzel M, Fontaine J, Ghesquières H, Jallade L, Antherieu G, et al. Plasticity in classical Hodgkin composite lymphomas: a systematic review. Cancers (Basel). 2022;14:5695.
6. Fogazzi S, Tucci A, Bottelli C, Ungari M, Facchetti F, Rossi G. Association of Hodgkin lymphoma and non-Hodgkin lymphoma in the same patient. Clinicopathologic characteristics and outcome in a series of 20 cases. Blood. 2010;116:3886.
7. Küppers R, Dührsen U, Hansmann ML. Pathogenesis, diagnosis, and treatment of composite lymphomas. Lancet Oncol. 2014;15:e435-46.
8. Liu S, Zhao Y, Li M, Xi J, Shi B, Zhu H. Simultaneous hodgkin lymphoma and BRAFV600E-positive papillary thyroid carcinoma: a case report. Medicine (baltimore). 2019;98:e14180.
9. Steidl C, Shah SP, Woolcock BW, Rui L, Kawahara M, Farinha P, et al. MHC class II transactivator CIITA is a recurrent gene fusion partner in lymphoid cancers. Nature. 2011;471:377-81.
10. Son HJ, Choi EJ, Yoo NJ, Lee SH. Inactivating mutations of class II transactivator (CIITA) gene in gastric and colorectal cancers. Pathol Res Pract. 2020;216:153110.
11. León Machado JA, Steimle V. The MHC class II transactivator CIITA: not (quite) the odd-one-out anymore among NLR proteins. Int J Mol Sci. 2021;22:1074.