Case Report / *Olgu Sunumu*

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Synchronous occurrence of chronic myeloid leukemia and chronic lymphocytic leukemia: An uncommon case

Kronik myeloid lösemi ve kronik lenfositik löseminin eşzamanlı görülmesi: Nadir bir olgu

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ABSTRACT

The aim of this study is to present a case involving the extremely rare coexistence of chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL), and to contribute to the identification of accurate diagnostic approaches and appropriate therapeutic strategies. A 55-year-old woman referred to our outpatient clinic for leukocytosis was found to have both marked neutrophilia and lymphocytosis on initial laboratory evaluation. Peripheral blood smear demonstrated mature lymphocytes along with an increased granulocytic series and myeloid precursor cells; no blasts were observed.

After exclusion of infectious etiologies, flow cytometric analysis revealed CD19, CD23, and CD5 positivity, consistent with CLL. Concurrent fluorescence in situ hybridization (FISH) analysis demonstrated the presence of the *BCR:ABL1* fusion. Subsequent bone marrow biopsy confirmed the concurrent presence of CML and CLL. The patient was started on imatinib therapy and remains under close hematologic follow-up.

Keywords: Chronic myeloid leukemia, chronic lymphocytic leukemia, concurrent leukemias

Note: *This study was presented as a poster at the 12th Aegean Hematology Oncology Symposium, held on September 25–28, 2025, at Royal Seginus Hotel, Antalya, Türkiye.*

ÖZ

Bu çalışmanın amacı, son derece nadir görülen kronik miyeloid lösemi (KML) ve kronik lenfositik lösemi (KLL) birlikteliğini içeren bir olguyu sunmak ve doğru tanısal yaklaşım ile uygun tedavi stratejilerinin belirlenmesine katkıda bulunmaktır. Lökositoz nedeniyle polikliniğimize başvuran 55 yaşındaki kadın hastanın başlangıç laboratuvar değerlendirmesinde belirgin nötrofili ve lenfositoz saptandı. Periferik kan yaymasında olgun lenfositler ile artmış granülositik seri ve miyeloid öncül hücreler izlendi; blastik hücre görülmedi.

Enfeksiyöz etiyolojiler dışlandıktan sonra yapılan akım sitometrisinde CD19, CD23 ve CD5 pozitifliği ile KLL ile uyumlu immünfenotip saptandı. Eş zamanlı olarak gerçekleştirilen floresan in situ hibridizasyon (FISH) analizinde BCR:ABL1 füzyonu gösterildi. Ardından yapılan kemik iliği biyopsisi, KML ve KLL birlikteliğini doğruladı. Hastaya imatinib tedavisi başlandı ve yakın hematolojik izleme alındı.

Anahtar Sözcükler: *Kronik miyeloid lösemi, kronik lenfositik lösemi, eşzamanlı lösemiler*

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Not: *Bu çalışma, 25–28 Eylül 2025 tarihlerinde Antalya, Türkiye'de düzenlenen 12. Ege Hematoloji Onkoloji Sempozyumu'nda poster olarak sunulmuştur.*

INTRODUCTION

Chronic myeloid leukemia (CML) is a clonal myeloproliferative neoplasm characterized by the *BCR:ABL1* fusion gene, resulting from the *t(9;22)(q34;q11)* translocation. It accounts for approximately 1–2 new cases per 100,000 individuals annually and represents about 10–15% of adult leukemia diagnoses (1). In contrast, chronic lymphocytic leukemia (CLL) is the most common leukemia in adults and is characterized by a clonal expansion of mature $CD5^{+}CD23^{+}$ B lymphocytes in the peripheral blood, bone marrow, and lymphoid organs (2).

The coexistence of CML and CLL in the same patient is exceedingly rare, with only a limited number of well-documented cases reported to date (3-5). Case series and literature reviews suggest that this association may arise through different biological mechanisms, including: (1) malignant transformation at the level of a common pluripotent hematopoietic stem cell capable of giving rise to both myeloid and lymphoid lineages, (2) the development of a second, independent malignant clone unrelated to the original neoplasm, and (3) therapy-related clonal evolution following targeted treatment of a primary hematologic malignancy (3-5).

Given its rarity, the clinical presentation, diagnostic work-up, and optimal therapeutic strategy for the coexistence of CML and CLL remain poorly defined. Reporting additional cases with detailed morphologic, immunophenotypic, and cytogenetic characterization is therefore essential to improve our understanding of the underlying biology and to inform future diagnostic and management approaches.

CASE REPORT

In April 2024, a 55-year-old woman was referred to our hematology outpatient clinic for evaluation of leukocytosis detected on routine laboratory testing. On admission, she was clinically asymptomatic. Complete blood count showed hemoglobin 13.1 g/dL and leukocytosis of 23.8 × 10^9/L, with neutrophilia (13.5 × 10^9/L), lymphocytosis (5.7 × 10^9/L), monocytosis (3.05 × 10^9/L), eosinophilia (0.8 × 10^9/L), basophilia (0.7 × 10^9/L), and thrombocytosis of 464 × 10^9/L.

On physical examination, the patient was in good general condition and vital signs were stable. No hepatosplenomegaly was detected, and there was no palpable peripheral lymphadenopathy. Systemic examination was otherwise unremarkable. Abdominal ultrasonography confirmed normal liver and spleen size.

Peripheral blood smear demonstrated increased granulocytic precursors alongside mature lymphocytes consistent with a CLL-like morphology; blasts were not observed. Given the coexistence of myeloid and lymphoid abnormalities, further immunophenotypic and cytogenetic evaluation was performed. Peripheral blood fluorescence in situ hybridization (FISH) analysis revealed a BCR:ABL1 fusion pattern with a minor 9q34 deletion associated with *t(9;22)(q34;q11),* detected in approximately 7% of interphase nuclei. Concurrent flow cytometry identified a clonal B-cell population expressing CD19 (100%), CD23 (93%), and CD5 (85%), consistent with a CLL immunophenotype.

The patient was classified as RAI stage 0 CLL. Bone marrow aspiration demonstrated an 83% *BCR:ABL1* fusion-positive cell population harboring *t(9;22)(q34;q11.2),* confirming a Philadelphia chromosome–positive myeloproliferative neoplasm. Bone marrow biopsy revealed hypercellularity with dysplastic megakaryocytes compatible with CML, along with interstitial infiltration by small mature lymphocytes expressing CD5 and CD23, diagnostic of CLL (Figure-1).

Based on the integration of morphologic, immunophenotypic, and cytogenetic findings, a concurrent diagnosis of chronic myeloid leukemia and chronic lymphocytic leukemia was established. The patient was started on imatinib therapy. The *BCR:ABL1* transcript level on the International Scale (IS) was 13.92% prior to treatment. At 3, 6, and 9 months after initiation of imatinib, IS values were 3.5%, 0.35%, and 0.043%, respectively. The patient achieved a major molecular response (MMR).

During follow-up, hematologic parameters normalized, no lymphadenopathy or splenomegaly developed, and the CLL component remained clinically indolent without treatment requirement. Imatinib therapy was continued, and the patient remains under regular hematologic follow-up with no evidence of disease acceleration or progression.

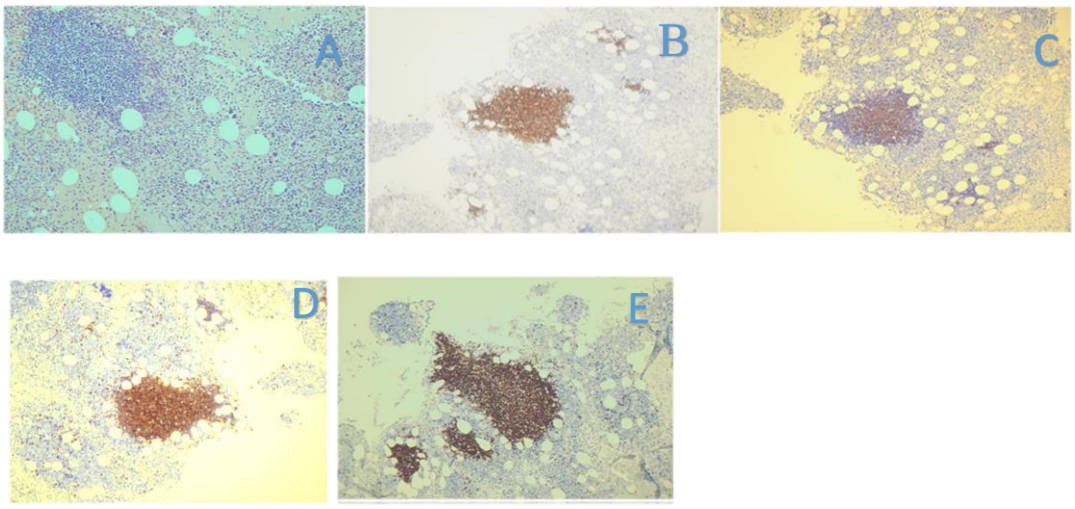

Figure-1: Hematoxylin and eosin (H&E), 20×: Hypercellular bone marrow demonstrating dysplastic megakaryocytes consistent with CML and interstitial infiltration by monotonous small lymphoid cells with non-paratrabecular distribution amid increased granulopoiesis and eosinophilic precursors (A)
BCL-2, IHC, 10×: Diffuse positivity in infiltrating lymphoid cells (B)
CD23, IHC, 10×: Focal positivity in lymphoid cells (C)
CD5, IHC, 10×: Diffuse positivity in lymphoid cells (D)
PAX5, IHC, 10×: Diffuse nuclear positivity in lymphoid cells, confirming B-cell lineage (E)

DISCUSSION

The coexistence of CML and CLL in the same patient is exceptionally rare, with only a limited number of well-documented cases reported to date (3-5). In our patient, both malignancies were detected at initial presentation, making it difficult to determine whether one neoplasm preceded the other or whether they arose independently. This highlights the importance of considering dual clonal hematologic processes in patients whose laboratory or morphologic findings cannot be fully explained by a single disease entity.

Several pathogenetic mechanisms have been proposed to explain the coexistence of CML and CLL. One hypothesis suggests transformation at the level of a common pluripotent hematopoietic stem cell, giving rise to both myeloid and lymphoid malignant clones (3-4). Another proposes the development of two independent neoplastic clones evolving in parallel (4-5). In addition, therapy-related clonal evolution has been described in hematologic neoplasms, although this mechanism is more relevant when one disease develops after treatment of the other.[6] Our case, however, represents a de novo concurrent presentation.

The presence of two distinct hematologic malignancies creates both diagnostic and therapeutic complexity. CML typically shows a predictable response to tyrosine kinase inhibitor therapy, whereas CLL often follows an indolent course in its early stages and may be monitored without immediate treatment unless iwCLL criteria are met (1,2). In our patient, the myeloproliferative component, including marked neutrophilia, basophilia, and dominant *BCR:ABL1* fusion, was the main driver of disease burden; therefore, imatinib therapy was initiated. The CLL clone, although clearly demonstrated immunophenotypically, remained clinically silent and was managed with observation, consistent with previously reported cases (3-5).

Management may become particularly challenging when both malignant clones show activity or progression, as treatment strategies for CML and CLL differ substantially. Reported cases emphasize the importance of individualized decision-making based on the dominant clone, cytogenetic and molecular features, patient comorbidities, and overall disease course (4-6). Our case reinforces the diagnostic value of integrating morphology, immunophenotyping, and cytogenetics, and underscores the need for careful long-term follow-up in patients with concurrent dual hematologic malignancies.

CONCLUSION

The coexistence of chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL) represents an exceptionally rare clinical entity. This case underscores the importance of considering dual clonal hematologic processes when clinical, morphologic, or laboratory findings cannot be sufficiently explained by a single malignancy. Accurate diagnosis requires careful integration of cytogenetic, molecular, and immunophenotypic data, including the identification of the *BCR:ABL1* fusion, to avoid misclassification and to ensure appropriate therapeutic decision-making.

Because the biological behavior and treatment strategies of CML and CLL differ substantially, management should be individualized and guided by the dominant clone, disease kinetics, molecular characteristics, and patient-specific clinical factors. In this context, recognizing the distinct yet coexisting disease components is essential for optimal care, and careful long-term follow-up remains crucial, as each malignancy may evolve independently over time.

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