Documenta Haematologica -
Revista Romana de Hematologie | 2025, Vol. 3, Nr. 4

https://doi.org/10.59854/dhrrh.2025.3.4.207

– CASE PERPORT –

Dual Hematologic Malignancies: A Case of Concurrent Accelerated-Phase Chronic Myeloid Leukemia and Ann Arbor Stage III Follicular Lymphoma

Agus Jati SUNGGORO[1*], Henry Aldezzia PRATAMA[2], Kun SALIMAH[1], Ahmad NURDIANSYAH[3]

Abstract

Objectives: *To report an extremely rare case of concurrent accelerated-phase chronic myeloid leukemia (CML) and Ann Arbor stage III follicular lymphoma (FL) and to discuss the diagnostic and therapeutic challenges.*

Material and Methods: *We present the case of a 39-year-old male who presented with progressive lymphadenopathy and abdominal discomfort. The diagnostic workup included clinical evaluation, complete blood count, peripheral blood smear, bone marrow aspiration and analysis, BCR-ABL1 transcript quantification by PCR, contrast-enhanced computed tomography (CT), and nasopharyngeal biopsy with immunohistochemistry.*

Outcomes*: The patient was diagnosed with two synchronous hematologic malignancies: accelerated-phase CML, confirmed by the presence of the b3a2 BCR-ABL1 fusion transcript, and Ann Arbor stage III FL, confirmed by a nasopharyngeal biopsy revealing CD99+/Bcl-2+ germinal centers. Initial therapy with imatinib 400 mg/day and allopurinol led to a paradoxical improvement in both CML parameters and lymphoma-related symptoms, an atypical response for FL. The patient's clinical condition improved, with a reduction in lymphadenopathy and splenomegaly.*

Conclusions: *The co-occurrence of CML and FL presents significant diagnostic and management challenges. This case highlights an unexpected response of FL to a tyrosine kinase inhibitor (TKI) and underscores the importance of a comprehensive diagnostic evaluation when faced with complex clinical and radiological findings. Further investigation into the potential pathobiological interactions between these two malignancies is warranted.*

Keywords: *Chronic Myeloid Leukemia, Follicular Lymphoma, Dual Malignancy, Tyrosine Kinase Inhibitor, Case Report*

[1] Hematology-Oncology Division, Internal Medicine Department, Universitas Sebelas Maret, Surakarta, Indonesia

[2] Internal Medicine Department, Universitas Sebelas Maret, Surakarta, Indonesia

[3] Oncology Division, Otorhinolaryngology, Head and Neck Surgeon Department, Universitas Sebelas Maret, Surakarta, Indonesia

Corresponding author:
***Agus Jati SUNGGORO,** Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Sebelas Maret Jl. Ir. Sutami No.36A, Kentingan, Jebres, Surakarta, Central Java, Indonesia.
Email: agusjati@staff.uns.ac.id

Agus Jati SUNGGORO ORCID - 0000-0002-4410-6291

Introduction

The occurrence of dual malignancies in a single individual represents a rare clinical scenario. Hematologic malignancies, which include both leukemias and lymphomas, typically do not present concurrently in the same patient [1]. Chronic Myeloid Leukemia (CML) is a myeloproliferative neoplasm characterized by the presence of the Philadelphia (Ph) chromosome, resulting from the t(9;22)(q34;q11) translocation and the subsequent BCR-ABL1 fusion gene [2]. Follicular Lymphoma (FL), on the other hand, is an indolent B-cell lymphoid malignancy originating from follicular center B cells, typically characterized by the t(14;18) translocation involving the BCL2 gene [3].
The coexistence of CML and FL is exceptionally uncommon, with only a few cases reported in the literature [4, 5]. These rare presentations pose significant diagnostic and therapeutic challenges, as the clinical picture can be complex and treatment strategies must address both diseases simultaneously. Here, we report a case of a 39-year-old male diagnosed with concurrent accelerated-phase CML and Ann Arbor stage III FL, highlighting an unusual response to therapy and the complexities of managing dual hematologic neoplasms.

Case Presentation

A 39-year-old male presented with a two-month history of progressive, painless lumps in his neck, armpits, and groin, accompanied by abdominal discomfort and a feeling of fullness. Physical examination revealed pallor, multiple fixed and non-tender lymphadenopathies in the cervical, axillary, and inguinal regions, and significant splenomegaly, with the spleen palpable to Schuffner III.
Initial laboratory investigations showed severe normocytic normochromic anemia (Hemoglobin 6.7 g/dL), marked leukocytosis (White Blood Cell count 357,000/µL) with a left shift, and hyperuricemia (uric acid 13.0 mg/dL). The peripheral blood smear demonstrated granulocytosis with the presence of myeloblasts, promyelocytes, myelocytes, and metamyelocytes. A bone marrow aspiration revealed hyperactive granulopoiesis with 8.8% myeloblasts, 3.2% promyelocytes, and marked eosinophilia (7.4%), consistent with the accelerated phase of CML. This diagnosis was confirmed by a positive qualitative polymerase chain reaction (PCR) test for the b3a2 BCR-ABL1 fusion transcript.
To investigate the widespread lymphadenopathy and hepatosplenomegaly, a contrast-enhanced abdominal computed tomography (CT) scan was performed. The scan revealed multiple enlarged lymph nodes in the paraaortic, superior/inferior mesenteric, and internal/external iliac regions. Given the patient's nasopharyngeal symptoms, a biopsy of the nasopharyngeal mass was conducted. Histopathological examination and immunohistochemistry of the biopsy specimen revealed follicular lymphoma, with cells positive for CD99 and Bcl-2, and negative for CD56. Based on the involvement of lymph node regions on both sides of the diaphragm and the spleen, the FL was staged as Ann Arbor Stage III.
Thus, the patient was diagnosed with two concurrent hematologic malignancies: accelerated-phase CML and Ann Arbor Stage III FL. Initial therapy was commenced with imatinib 400 mg/day for the CML and allopurinol 300 mg/day for tumor lysis prophylaxis. The patient exhibited a paradoxical and favorable response. Over the following three months, his hematological parameters improved, with normalization of the leukocyte count and a significant increase in hemoglobin levels. Clinically, a marked reduction in the size of the peripheral lymphadenopathy and a decrease in spleen size were observed. The imatinib dose was temporarily adjusted due to a transient episode of anemia, but the patient's overall condition and both malignancies showed significant improvement with TKI monotherapy.

Table 1. Hematological Parameters During Imatinib Treatment.

Date	Hemoglobin (g/dL)	Leukocytes ($x10^3/\mu L$)	Thrombocytes ($x10^3/\mu L$)
12-Jul-2024	8.5	248.5	457
06-Aug-2024	6.1	357.0	357
09-Aug-2024	9.9	311.7	281
10-Aug-2024	11.3	336.1	257
19-Aug-2024	8.1	424.3	233
03-Sep-2024	7.7	246.7	229
28-Sep-2024	5.2	9.6	137
03-Oct-2024	9.6	4.1	247
10-Oct-2024	11.0	6.8	215

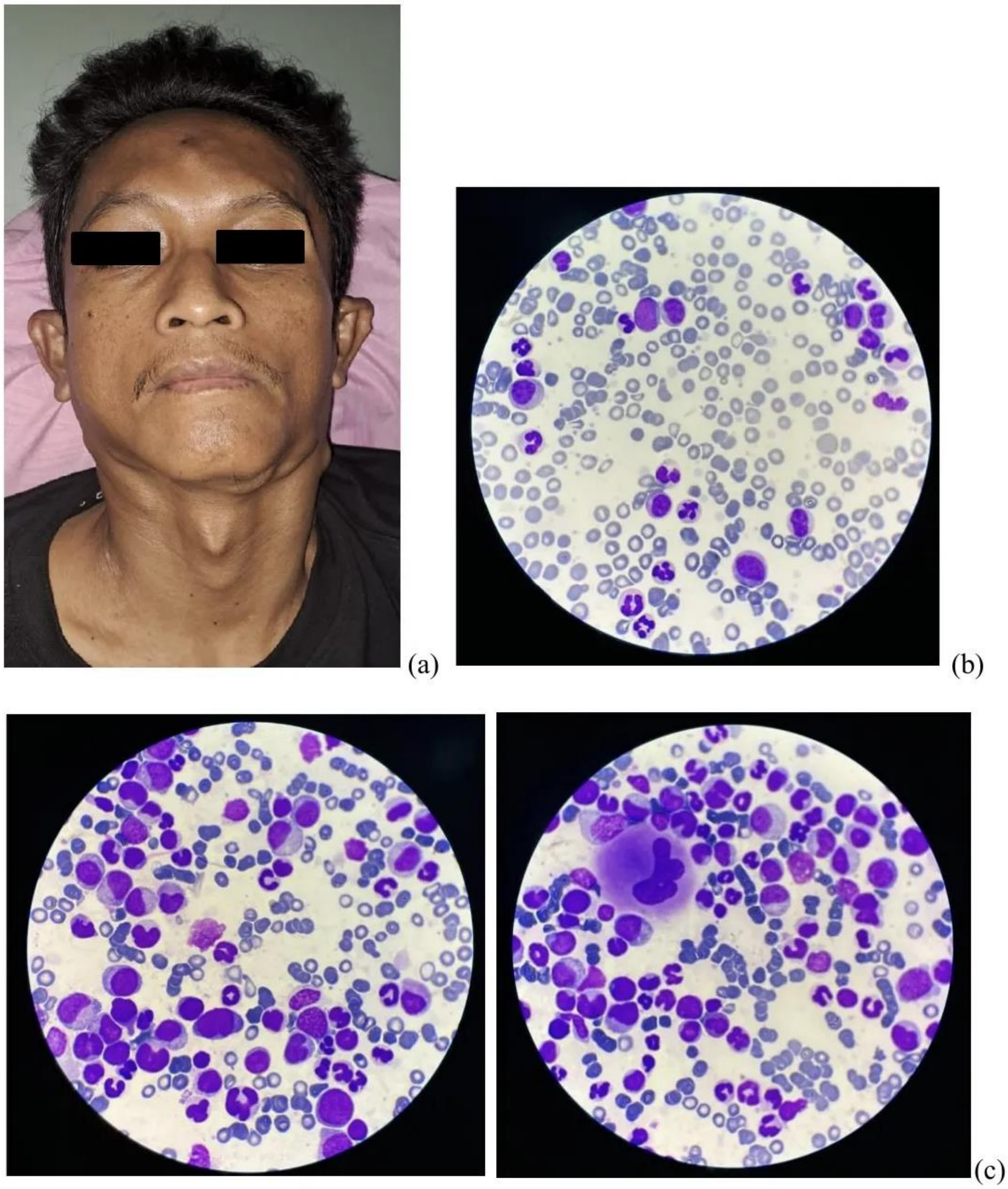
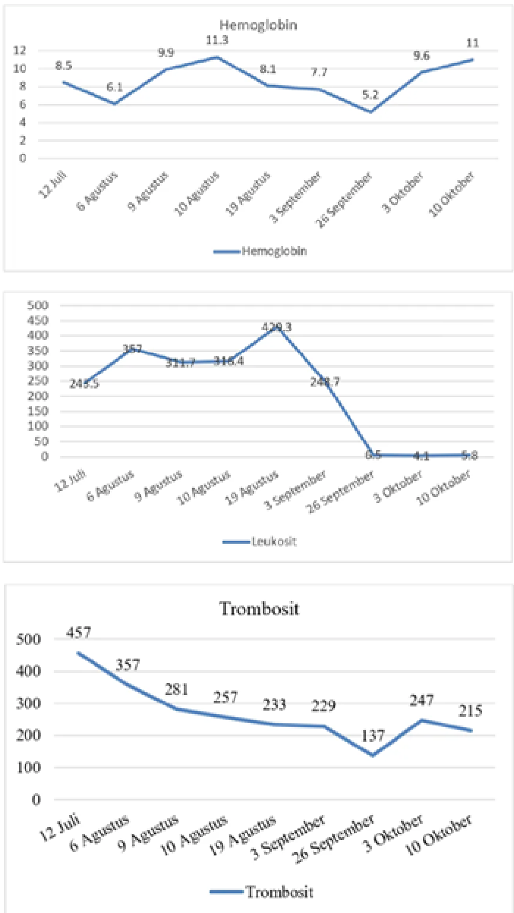


Figure 1. Clinical and Pathological Findings. *(A) Clinical manifestation at first admission (July 2024), showing cervical lymphadenopathy. (B) Peripheral blood smear showing leukocytosis with a left shift. (C) Bone marrow aspirate showing hypercellularity and increased granulopoiesis. (D) Endoscopic view of the nasopharyngeal mass. (E) Contrast-enhanced abdominal CT scan showing extensive lymphadenopathy. (F) Immunohistochemical staining of the nasopharyngeal biopsy showing Bcl-2 positivity.*

A

B

Pics 3. Clinical Manifestation after Imatinib 400mg/day (October 2024)



Pics 4. Complete Blood Count Lab Finding during Treatment with Imatinib

Figure 2. Clinical and Hematological Response to Imatinib. *(A) Clinical manifestation after three months of imatinib therapy (October 2024), showing significant resolution of lymphadenopathy. (B) Trends of hemoglobin, leukocyte, and thrombocyte counts during the first three months of imatinib treatment, showing normalization of leukocyte count and improvement in hemoglobin.*

Discussion

This case presents a rare and complex clinical challenge: the synchronous diagnosis of accelerated-phase CML and advanced-stage FL. The diagnosis of CML was established based on the characteristic peripheral blood and bone marrow findings, and confirmed by the detection of the BCR-ABL1 fusion gene, which is the molecular hallmark of the disease [2, 6]. The patient's blast percentage of 8.8% in the bone marrow placed him in the accelerated phase of CML, which carries a more aggressive course than the chronic phase [7].

The diagnosis of FL was confirmed through a nasopharyngeal biopsy. The immunophenotype, particularly the expression of Bcl-2 within the germinal centers, is a key diagnostic feature of FL, distinguishing it from reactive follicular hyperplasia [3, 8]. The widespread lymphadenopathy on both sides of the diaphragm led to the classification of Ann Arbor Stage III.

The simultaneous occurrence of CML and FL is an exceptionally rare event. While secondary malignancies are a known, albeit infrequent, complication in patients with CML, particularly after treatment, a synchronous presentation is highly unusual [4, 9]. The underlying pathobiological mechanism for this dual presentation is not well understood. It could represent two independent clonal hematopoietic diseases or, more speculatively, a common progenitor cell defect with divergent differentiation pathways.

One of the most striking aspects of this case is the patient's response to imatinib. Imatinib, a potent TKI targeting the BCR-ABL1 oncoprotein, is the standard first-line treatment for CML [6]. However, it is not a standard therapy for FL, which typically does not respond to this class of drugs [10]. The patient demonstrated a significant hematological response for his CML, as expected. Unexpectedly, he also experienced a marked regression of his lymphoma, evidenced by the reduction in lymphadenopathy and splenomegaly. This atypical response of FL to a TKI is intriguing. While some reports have described the development of lymphoma during TKI therapy [5], a therapeutic response of pre-existing FL to imatinib is not a recognized phenomenon. This observation suggests potential, yet-to-be-elucidated molecular pathways that might be sensitive to imatinib in this specific case of FL, or a complex interplay between the two malignancies that was disrupted by the TKI therapy.

The management of such dual malignancies is not standardized and requires an individualized, multidisciplinary approach. In this case, the decision to start with a TKI was driven by the life-threatening nature of the accelerated-phase CML. The favorable response of the lymphoma to this initial therapy was a fortunate and unexpected outcome, which deferred the need for immediate, more intensive chemotherapy like R-CHOP, the standard for advanced-stage FL [11]. This case underscores the necessity for comprehensive diagnostic evaluations, including molecular and histopathological analyses, when clinical and radiological findings are complex.

Conclusion

We report an extremely rare case of concurrent accelerated-phase CML and Ann Arbor stage III FL. The case was notable for its diagnostic complexity and the unexpected, favorable response of the follicular lymphoma to imatinib therapy. This presentation highlights the challenges in managing dual hematologic malignancies and suggests that there may be unknown biological interactions between CML and FL that could be therapeutically exploited. Further research is needed to understand the pathophysiology of such rare co-occurrences and to establish optimal treatment strategies.

Acknowledgements

This research received no specific grant. The authors express their sincere gratitude to the patient and his family for their cooperation and consent to publish this case. The authors also acknowledge the Departments of Clinical Pathology, Anatomical Pathology, and Radiology of Dr. Moewardi General Hospital for their valuable support in providing diagnostic resources.

Ethics Statement and Conflict of Interest Disclosures

Financial support and sponsorship: All authors have declared that no financial support was received from any organization for the submitted work.

Ethics Consideration: The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national laws. Written informed consent was provided by the participant in this study.

Conflict of interest: No known conflict of interest correlated with this publication.

Availability of data and materials: The data used and/or analyzed throughout this study are available from the corresponding authors upon reasonable request.

Competing interests: The authors declared that they have no competing interests.

The use of generative AI and AI-assisted technologies: The authors did not use in this article generative AI and AI-assisted technologies.

References

1. Starr A, Jonna S, Chahine J. Concurrent Diagnosis of Chronic Myeloid Leukemia and Follicular Lymphoma: An Unreported Presentation. Case Rep Hematol. 2018;2018:7493601.
2. Kantarjian H, Jabbour E, Cortes J. Chronic myeloid leukemia. In: Loscalzo J, Kasper D, Longo D, eds. Harrison's principles of internal medicine. 21st ed. McGraw-Hill; 2022.
3. Dreyling M, Ghielmini M, Rule S, et al. Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(3):298-308.
4. Hoti M, Morina S, Elezi D, et al. CML-096: Dual Hematologic Malignancies: A Case of Chronic Myelogenous Leukemia and Follicular Lymphoma With Paraneoplastic Neurological Manifestation. Clin Lymphoma Myeloma Leuk. 2025;25(Supplement 1):S552.
5. Geelani SA, Rathod SG, Dhar A, Atri P, Bhat J. Follicular Lymphoma Secondary to Chronic Myeloid Leukemia During Treatment With Imatinib. Cureus. 2022;14(11):e31884.
6. Hochhaus A, Saussele S, Rosti G, et al. Chronic Myeloid Leukaemia: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017;28(suppl_4):iv41-iv51.
7. Shanmuganathan N, Hughes TP. Accelerated-phase CML: de novo and transformed. Hematology Am Soc Hematol Educ Program. 2023;2023(1):459-468.
8. Kaseb H, Babiker HM. Follicular Lymphoma. In: StatPearls. StatPearls Publishing; 2024.
9. Sahu KK, Malhotra P, Uppin MS, et al. CML as Part of Dual Malignancies—A Retrospective Analysis. Indian J Hematol Blood Transfus. 2016;32(4):423-428.
10. Fujiwara SI, Shirato Y, Ikeda T, et al. Successful treatment of follicular lymphoma with second-generation tyrosine kinase inhibitors administered for coexisting chronic myeloid leukemia. Int J Hematol. 2018;107(6):712-715.
11. Reksodiputro AH, Irawan C. Limfoma non Hodgkin. In: Setiati S, Alwi I, Sudoyo AW, Simadibrata M, Setyohadi B, Syam AF, eds. Buku ajar ilmu penyakit dalam. VI. Jakarta: Interna Publishing; 2014.