EJCRIM
European Journal
of Case Reports
in Internal Medicine

FROM SOLID ORGAN MALIGNANCIES TO DUAL LEUKAEMIAS: SEQUENTIAL CLL AND CML IN A CANCER SURVIVOR

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Received: 20/04/2026
Accepted: 30/04/2026
Published: 21/05/2026

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Written informed consent for the publication of this case was obtained from the patient's next of kin- (his wife) because the patient is deceased.
Acknowledgments: Grateful to the learning opportunity at Department of Haematology and Medical Oncology, University of Connecticut.
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How to cite this article: Sidhu S, Hamouche R, Forbes V. From solid organ malignancies to dual leukaemias: sequential CLL and CML in a cancer survivor. *EJCRIM* 2026;**13**:doi:10.12890/2026_006813

ABSTRACT

Introduction: Chronic lymphocytic leukaemia (CLL), the most common adult leukaemia is known to undergo Richter's transformation. However, transformation into myeloid neoplasms is extremely rare with no established pathogenetic mechanisms. Management of coexisting haematological neoplasms becomes more complex in the presence of prior solid organ malignancies, potential therapy-related complications, and immunosuppression.

Case description: An 83-year-old man with prior history of invasive bladder cancer (s/p chemotherapy and cystectomy in 2013) and pancreatic adenocarcinoma treated with Whipple's procedure in 2015 was diagnosed with CLL in 2015 without 17p deletion. He began treatment with Ibrutinib in 2018 due to bulky symptomatic adenopathy and later switched to acalabrutinib due to arthralgias. Following a hospitalization in 2022 for coronavirus disease 2019, he was found to have chronic myeloid leukaemia (CML), confirmed by BCR-ABL positivity and bone marrow biopsy. Imatinib was started for CML but due to potential drug-induced pulmonary toxicity, switched to asciminib. His BCR-ABL transcript was undetectable, and therapy was discontinued due to multiple hospitalizations with organizing pneumonia. His course was further complicated by neutropenic fever and hypogammaglobulinemia and he transitioned to hospice care for better quality of life. Thus, both CLL and CML were treated with targeted oral agents.

Conclusion: This report highlights concurrent CLL and CML in a patient with multiple prior malignancies treated with chemotherapy and surgical interventions. It also adds to the limited literature on the CLL to CML overlap, suggesting vigilant long-term surveillance in cancer survivors. Coexisting management of haematological malignancies need careful weighing of individual toxicity profiles of medications tailored to individual patient.

KEYWORDS

CLL, CML, cancer survivorship

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

LEARNING POINTS

- Chronic lymphocytic leukaemia (CLL) most commonly transforms into aggressive lymphoma; development of chronic myeloid leukaemia (CML) in a patient with CLL should prompt evaluation for an independent myeloid clone rather than presumed transformation.
- Myeloid neoplasms in patients with CLL may arise from therapy-related leukemogenesis or divergent evolution from a shared hematopoietic progenitor, highlighting the importance of molecular characterization.
- Management of coexisting CLL and CML requires individualized risk–benefit assessment, particularly in elderly patients with prior solid tumours and immune dysfunction.

INTRODUCTION

Chronic lymphocytic leukaemia (CLL) is now widely recognized as the most common adult leukaemia in Western countries. It is characterized by clonal neoplastic expansion of mature B lymphocytes in the blood, bone marrow and lymphoid tissues[1]. The course of the disease is varied ranging from highly indolent asymptomatic patients to an aggressive malignancy requiring targeted therapy. It is well known to transform into diffuse large B cell lymphoma (DLBCL), a phenomenon called Richter's transformation in up to 20% of all cases[2]. The natural history of CLL has not been demonstrated to predispose to myeloid neoplasms. There have only been a few reports of an association of CLL with chronic myeloid leukaemia (CML)[3–7].

CML is defined by the presence of BCR-ABL1 fusion gene and the resultant Philadelphia chromosome. This leads to progressive accumulation of mature monoclonal myeloid cells that is usually managed with tyrosine kinase inhibitors (TKIs). The introduction of these medications has improved outcomes in CML over the past years with evidence of molecular remission in many patients[8]. Given widely different morphology and pathogenesis of CML and CLL, coexistence in the same patient raise important questions regarding clonal evolution, therapy related leukemogenesis and the possibility of two independent hematopoietic clones rising in a susceptible host. Here, we present an elderly patient with prior solid organ malignancies who developed sequential CML after CLL, highlighting the diagnostic and pathogenetic considerations of underlying clones in these different haematological neoplasms.

CASE DESCRIPTION

An 83-year-old man with a complex oncologic history was followed for recurrent infections and progressive haematological abnormalities. In 2013, he was diagnosed with invasive bladder cancer and underwent neoadjuvant chemotherapy followed by radical cystectomy with ileal conduit diversion. In 2015, he underwent the Whipple procedure for pancreatic intraductal papillary mucinous neoplasm with high-grade intraepithelial carcinoma. There was no evidence of recurrence of either malignancy.

In November 2015, he was diagnosed with CLL without 17p deletion and observed. In 2018, due to symptomatic bulky lymphadenopathy, ibrutinib therapy was initiated. In 2020, treatment was transitioned to acalabrutinib because of significant arthralgias. His disease course was complicated by hypogammaglobulinemia requiring monthly intravenous immunoglobulin replacement and recurrent respiratory infections. In 2022, following hospitalization for coronavirus disease 2019 infection, laboratory evaluation revealed leucocytosis and BCR-ABL1 positivity. Bone marrow biopsy confirmed chronic-phase CML and imatinib was initiated. Given concern for drug-related pulmonary toxicity in the setting of organizing pneumonia, therapy was transitioned to asciminib. Subsequent BCR-ABL1 transcripts became undetectable, consistent with molecular remission.

However, his clinical course was complicated by recurrent organizing pneumonia, neutropenic fever, and progressive cytopenias. TKI therapy was ultimately discontinued because of repeated hospitalizations and declining functional status. Despite molecular remission of CML, he experienced cumulative morbidity related to immunosuppression and recurrent infections. After multidisciplinary discussions and goals-of-care conversations, he elected to transition to hospice care to prioritize quality of life.

DISCUSSION

This case highlights the rare coexistence of CLL and CML and raises some critical concerns regarding clonal biology and therapy-related risk. Our patient received therapy with Bruton tyrosine kinase (BTK) inhibitors for CLL but no fludarabine or alkylator-based regiments that are more strongly associated with therapy related myeloid malignancies. He did have exposure to cytotoxic chemotherapy for bladder cancer about nine years prior to diagnosis of CML. The latency makes a direct causal relationship difficult to establish. Notably, CML which is defined by the presence of BCR-ABL1 fusion gene represents a different molecular entity suggesting an independent myeloid clone rather than transformation of lymphoid neoplasm like CLL[8].

There have been reports of genomic studies demonstrating that haematological malignancies can arise from early hematopoietic stem cell clones that harbour pre-leukemic mutations[9]. These can subsequently diverge into lymphoid or myeloid lineages. This makes a biological framework

in which multiple haematological neoplasms emerge from a shared ancestral clone a possibility. It is easy to establish clonal relatedness between CLL and DLBCL by demonstrating immunoglobulin heavy chain sequencing with Richter's transformation in CLL[10]. However, this is in sharp contrast to CML, where it is difficult to derive such an association with no molecular comparisons for early clonal mutations across the lymphoid and myeloid lineages. It thus remains only speculative whether our patient's CLL and CML shared a clonal progenitor. Three potential pathogenetic possibilities that can explain the association include an independent de novo development of CML in a patient with CLL, therapy related leukemogenesis after solid organ malignancies and divergent evolution from a shared hematopoietic stem cell clone.

CLL is associated with immune dysregulation and hypogammaglobulinemia that renders patients susceptible to infection. This was demonstrated in our patient through recurrent infections and pulmonary complications. Additionally, the management of CML with CLL becomes challenging with both BTK inhibitors and TKIs having their heterogenous adverse effect profiles. In our patient, the pulmonary toxicity and recurrent infections ultimately limited therapy. Disease control as evidenced by BCR-ABL 1 transcript does not necessarily lead to improved functional outcomes especially in elderly patients with significant comorbidities. The combination of prior solid organ malignancies, exposure to cytotoxic chemotherapy, immunocompromise, targeted therapies and age-related clonal haematopoiesis could have all played a role in paving the way for a second hematologic malignancy. It highlights the vigilance for additional neoplasm after successful management of one malignancy as cancer survivorship continues.

REFERENCES

1. Eichhorst B, Robak T, Montserrat E, Ghia P, Hillmen P, Hallek M, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2015;**26**:v78-84. doi: 10.1093/annonc/mdv303
2. Ding W. Richter transformation in the era of novel agents. *Hematology Am Soc Hematol Educ Program* 2018;**2018**:256-263. doi: 10.1182/asheducation-2018.1.256
3. Selene I, Jacob A, El-Amir ZM, Sathe S, Taj A. A Tale of Two Hematological Malignancies: CML Followed by CLL in the Same Patient. *Ann Intern Med Clin Cases* 2023;**2**:e220116. doi: 10.7326/aimcc.2022.0116
4. Matutes E, Polliack A. CLL and CML sometimes meet and circulate together. *Leuk Lymphoma* 2019;**60**:1352–1353. doi: 10.1080/10428194.2018.1564050
5. Boddu P, Gibbons J, Burger J, Sivina M, Thakral B, Kanagal-Shamanna R, et al. Co-occurrence of chronic myeloid leukemia with chronic lymphocytic leukemia: a report of two cases. *Leuk Lymphoma* 2019;**60**:1568–1571. doi: 10.1080/10428194.2018.1547902
6. Luedke C, Zhao Y, McCracken J, Maule J, Yang LH, Jug R, et al. Myeloid neoplasms in the setting of chronic lymphocytic leukaemia/chronic lymphocytic leukaemia-like disease: a clinicopathological study of 66 cases comparing cases with prior history of treatment to those without. *J Clin Pathol* 2022;**75**:292–301. doi: 10.1136/jclinpath-2020-207334
7. Abdalla E, Fadul A, Osman AE, Mohamed G, Soliman DS, Shawayli H, et al. Review of Rare Association between Chronic Lymphocytic Leukemia and Chromic Myeloid Leukemia. *Blood* 2024;**144**:6805–6805. doi: 10.1182/blood-2024-205929
8. Senapati J, Sasaki K, Issa GC, Lipton JH, Radich JP, Jabbour E, et al. Management of chronic myeloid leukemia in 2023 – common ground and common sense. *Blood Cancer J* 2023;**13**:58. doi: 10.1038/s41408-023-00823-9
9. Ferrando AA, López-Otín C. Clonal evolution in leukemia. *Nat Med* 2017;**23**:1135–1145. doi: 10.1038/nm.4410
10. Wierda WG, Brown J, Abramson JS, Awan F, Bilgrami SF, Bociek G, et al. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Version 2.2024. *J Natl Compr Canc Netw* 2024;**22**:175–204. doi: 10.6004/jnccn.2024.0018