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Case Report

A Tale of Two Leukemias

Sajjad A Bhatti* and Abdulraheem Yacoub

Fellow, Hematology and Oncology, University of Kansas Cancer Center, USA

***Corresponding Author:** Sajjad A Bhatti, Fellow, Hematology and Oncology, University of Kansas Cancer Center, USA.

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Abstract

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia [1], characterized by the accumulation of mature but functionally incompetent CD5+ monoclonal B cells. Chronic myelogenous leukemia (CML) is a myeloproliferative neoplasm characterized by a reciprocal translocation between chromosomes 9 and 22, leading to BCR-ABL1 fusion gene with constitutive tyrosine kinase activity resulting in dysregulated and uncontrolled proliferation of granulocytes.

Keywords: Chronic Lymphocytic Leukemia; Chronic Myelogenous Leukemia

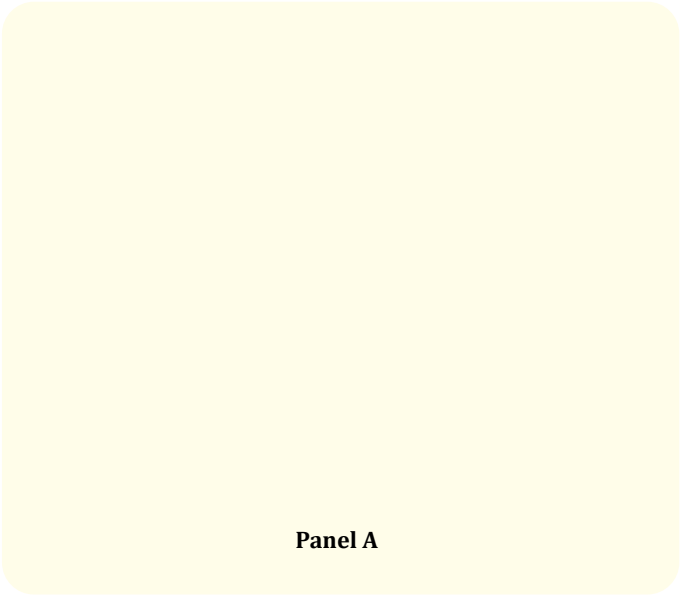
Observational studies suggest a higher incidence of secondary solid tumors in CLL as compared to the general population [2]. This phenomenon is postulated to be due to defects in host immune surveillance or result of the chemotherapy for CLL. The incidence of secondary hematological malignancies in CLL is rare. Only a few cases of CML and CLL in the same patient have been described in the literature [3-13]. In these cases, diagnosis of CLL usually precedes CML and simultaneous diagnosis of the two leukemias is an even rarer phenomenon.

It is crucial to understand clonality and molecular mechanisms underlying the simultaneous appearance of these hematological malignancies, which is important in designing a treatment plan for these patients. Here, we describe a patient case that we encountered in our clinical practice recently.

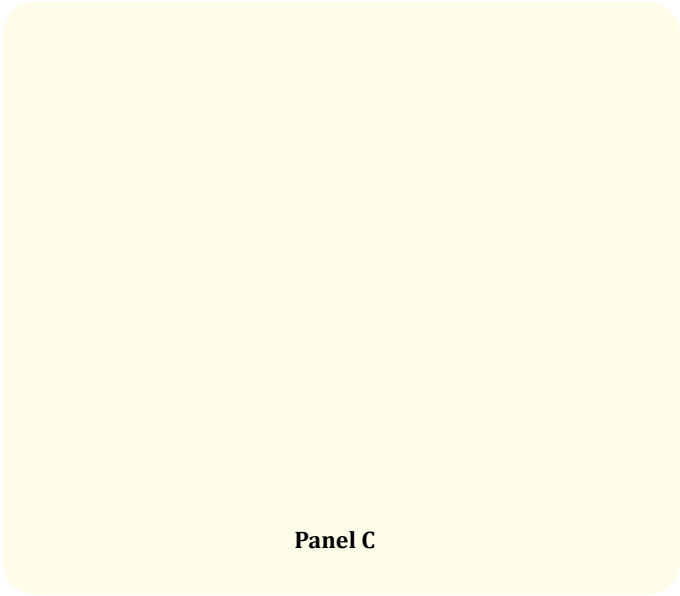
Case Report

A 70-year-old male presented to his primary care physician with chief complaint of fatigue and night sweats for several weeks. His CBC showed hemoglobin of 13.4, platelets of 344 and WBC of 161,000. Differential count was as of follows: 13% lymphocytes, 30% segmented neutrophils, 13% bands, 7 % metamyelocytes, 11% myelocytes,6 % promyelocytes, 5 % basophils. Peripheral smear showed neutrophilic leukocytosis with left-sided shift and basophilia (panel A; Wright-Giemsa stain, original magnification ×100). Bone marrow biopsy showed hypercellular marrow with marked granulocytic, megakaryocytic hyperplasia and 2% blasts consistent with the diagnosis of Chronic Myeloid Leukemia, chronic phase. (panel B; Wright-Giemsa stain, original magnification ×100). The diagnosis was confirmed with the FISH assay for BCR-ABL rearrangement, which was positive in 82.5% of the interphase nuclei. Conventional cytogenetics showed BCR-ABL translocation in 20 out of 20 metaphase nuclei with an absence of other cytogenetic abnormalities.

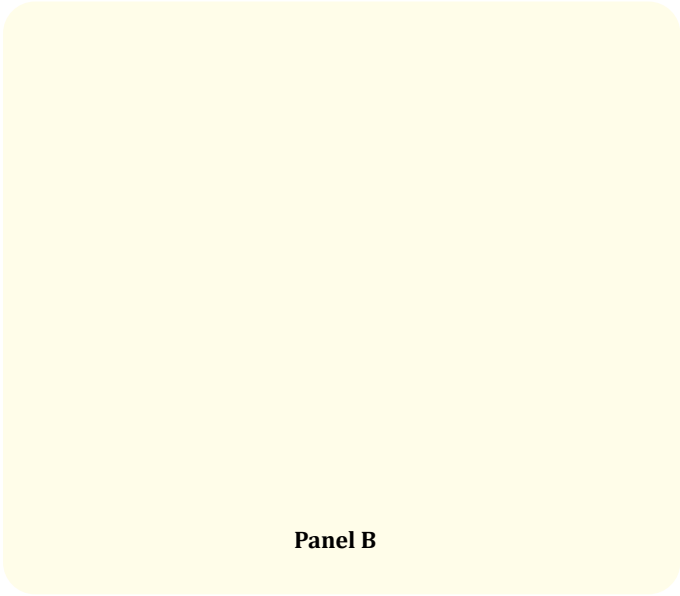
The patient was started on Imatinib 400mg PO daily and achieved a complete hematological response and BCR-ABL<10% on 3 months follow up. At his 6 months follow up, his BCR-ABL was <1%. However, his WBC had increased to 22,000 with an absolute lymphocyte count of 18,000. A peripheral smear showed absolute lymphocytosis and smudge cells. (panel C; Wright-Giemsa stain, original magnification ×100). Flow cytometry on peripheral blood



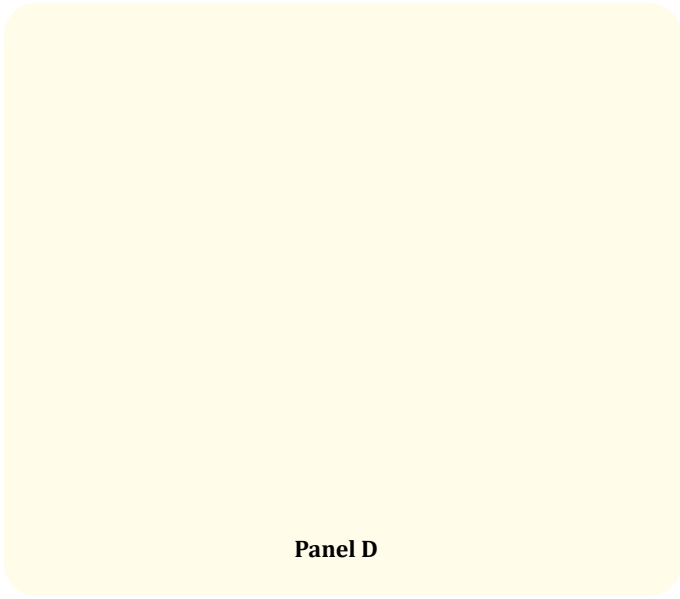
Panel A



Panel C



Panel B



Panel D

showed evidence of CD5+ neoplasm with 69% of the cells expressing CD5, CD19, CD20, CD23, CD 200, and monoclonal surface lambda chain. A repeat bone marrow biopsy showed 70% hypercellular marrow with 50% involvement with B cell chronic lymphocytic leukemia. (panel D; Wright-Giemsa stain, original magnification ×100). FISH detected the presence of del 13q in 69% of the cells. Conventional cytogenetics were normal in 11 metaphases; seven metaphases show del 13q and two cells showed t(9,22).

Retrospective review of his first bone marrow biopsy did show the presence of several small lymphoid aggregates composed of small, mature lymphocytes (panel E; Wright-Giemsa stain, original magnification ×100) confirmed with CD 20 staining. (panel F; CD20 stain, original magnification ×100). This finding is consistent with the presence of simultaneous CML and CLL with CLL being masked by marked CML presence at the time of his initial bone marrow biopsy.

Panel E

Panel F

The patient currently does not meet criteria for treatment for CLL per the iwCLL criteria. He continues on imatinib while his CLL is under active surveillance.

Discussion

The presence of CML and CLL in the same patient is a rare condition.

In most of the case reports, the diagnosis of CLL precedes CML. Defective immune surveillance and prior chemotherapy are thought to be the plausible reasons for this phenomenon. Simultaneous diagnosis is even rarer with only a handful of case reports which begs the questions if there is a common stem cell to blame. In our case report, we showed that 13q deletion and BCR-ABL translocation were mutually exclusive on conventional cytogenetics, which was consistent with the argument that the two leukemia populations arose from different stem cells. The clonal origin of these neoplasms was investigated in some other case reports, all of which suggested the independent origin of the two diseases [3,10-12].

There is not enough data to inform the prognosis for these patients given the rarity of the condition. The largest series of patients with co-existent CLL/MPN had a total of 8 CML patients [13]. The study reported mostly indolent nature of the CLL in these patients and MPN therapy with imatinib or hydroxyurea having no effect on the CLL course [13]. None of these patients were treated with dasatinib.

Current literature addressing the management and outcome of concomitant CML and CLL is limited. As mentioned above, imatinib did not affect the CLL in the Italian series [13]. A phase II study of patients with relapsed and refractory CLL treated with dasatinib showed a partial response rate of 20% suggesting single-agent activity of dasatinib in CLL thought to be due to inhibition of lyn and syk kinase [14]. Two case reports of patients with concomitant CML/CLL showed PR of CLL in these patients [9,10].

Conclusion

Our case report adds to the limited literature available on the topic of concomitant CML/CLL. In our case, conventional cytogenetics provided evidence of independent origin of the two neoplasms consistent with previously reported literature. Although data on management strategies is limited for these patients with concomitant CML/CLL, dasatinib can be considered as a treatment option due to activity in both cancers.

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