

A 'double-hit' bone marrow rare co-occurrence of 2 different pathologies

Adham Jurdi, MD, Koyamangalath Krishnan, MD, and Kanishka Chakraborty, MD

Division of Hematology/Oncology, Department of Internal Medicine, East Tennessee State University, Johnson city, Tennessee

A patient is diagnosed with chronic lymphocytic leukemia 6 months after he was diagnosed with chronic myeloid leukemia for which he initially received imatinib.

Chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL) are entirely different in terms of pathogenesis, presentation, diagnostic work-up, treatment, and prognosis: CML is a myeloproliferative condition, whereas CLL involves lymphoid population. Here we discuss a very rare case of co-occurrence of CML and CLL in the same patient.

Case presentation

A 60-year-old man with a recent diagnosis of CML presented to clinic for follow-up. He reported feeling well. His physical exam was unremarkable. The results of a complete blood count (CBC) test showed a white blood cell count of 10,600/ μ L with a lymphocyte count of 5,700/ μ L. His initial presentation 6 months earlier was with fatigue, when his WBC count was 93,000/ μ L, his hemoglobin level was 9.3g/dL, and his platelet count 140,000/ μ L. A peripheral blood smear and bone marrow biopsy at his initial presentation confirmed a diagnosis of CML. A computed tomography scan showed splenomegaly but no adenopathy. He achieved complete hematological response, and major cytogenetic and molecular responses with the tyrosine kinase inhibitor, imatinib. Repeat bone marrow biopsy at 6 and 12 months revealed no morphological evidence of CML but showed a monoclonal B-cell (lymphocyte) population that had not been evident on initial bone marrow biopsy. A repeat CT scan showed resolved splenomegaly but scattered adenopathy in chest and abdomen. At 18 months, he had a molecular relapse of CML that necessitated switching from imatinib to dasatinib.

Discussion

Co-occurrence of CML and CLL in the same

patient is extremely rare. An extensive search of online literature showed fewer than 19 case reports of similar co-occurrence. In 10 of those cases, CML developed after CLL and was attributed to an impaired immune system or chemotherapy received as part of CLL treatment. In 6 case reports, CML and CLL were diagnosed simultaneously,¹ though it is not known how many of those patients had undiagnosed asymptomatic CLL before their presentation with CML given the chronic nature of CLL.

There are only 3 case reports of CLL developing in patients with chronic phase of CML, with CLL occurring 20-74 months after diagnosis of CML. All 3 of those patients were in chronic phase of CML when CLL was diagnosed. One patient had received hydroxyurea, interferon alpha, and imatinib before being diagnosed with CLL. The second patient received hydroxyurea and chlorambucil. The third patient received imatinib alone, and CLL was diagnosed 74 months after the CML diagnosis.²

Our patient was diagnosed with CLL 6 months after he had been diagnosed with CML and started on imatinib. To our knowledge, the current case is likely the only case in which CLL developed when the patient was in hematological and molecular remission for CML and had been receiving treatment with a tyrosine kinase inhibitor alone for only 6 months. We realized that the CLL diagnosis was unusual, so we reviewed the results of the initial bone marrow biopsy. They did not show any immunophenotypic feature corresponding to the monoclonal B-cell lymphocytosis that was evident in the subsequent bone marrows. In particular, they were negative for CD5.

Imatinib is not known to cause lymphoproliferative disease. A recent retrospective analysis of 1,445 patients who received tyrosine kinase inhibitors at

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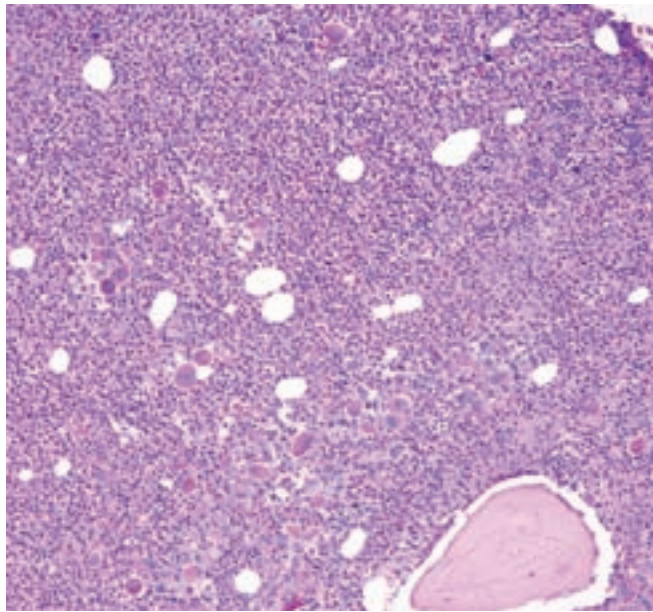


FIGURE 1 On initial diagnosis, a bone marrow biopsy showed a moderately hypercellular marrow with hyperplasia of myeloid cells and hyperplasia of megakaryocytes. The myeloid cells were in all stages of maturity, with 3.6% blasts and basophilia. These findings and the cytogenetics and molecular studies are diagnostic of chronic myeloid leukemia.

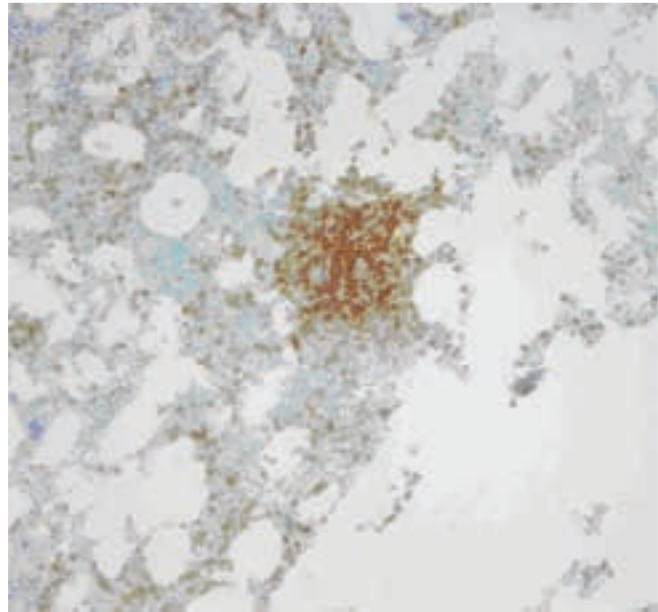


FIGURE 2 A subsequent bone marrow biopsy showed scattered lymphoid aggregates that expressed CD5, CD23, and CD20. The aggregates comprised about 15% of the core. There is no morphological evidence of residual chronic myeloid leukemia, but molecular studies showed residual disease. The picture is of a representative lymphoid aggregate with immunohistochemical stains.

MD Anderson Cancer Center in Houston, Texas, did not show any evidence of increased incidence of secondary malignancies with TKIs.³ Patients with CLL are at increased risk of secondary malignancies because their immune systems are impaired. However, this is not the case for patients with CML, whose natural history is to evolve into blast crisis, not to develop secondary malignancies. This raises the possibility that an abnormality in pluripotent stem cells could lead to leukemic proliferation of both myeloid and lymphoid cells. Further studies are needed to identify an etiology.

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