Chronic Myelogenous Leukemia Ensuing in a Patient with Chronic Lymphocytic Leukemia

YASHVIN ONKARAPPA MANGALA, MD; JOHN PATRESAN, MD; DRAGOS LUCA, MD; GERALD ALEXANDER COLVIN, DO

CASE PRESENTATION

A 71-year-old Caucasian male was diagnosed with Rai stage 0 chronic lymphocytic leukemia in May 2019, with laboratory studies showing a leukocytosis of 34.4 x 109/L with 71% lymphocytes, a hemoglobin of 14.3 g/dL, and a platelet count of 268 x 109/L. Peripheral blood flow cytometry demonstrated lambda light chain restricted monoclonal B cells positive for CD5, CD19, dim CD20, and CD23, consistent with CLL. A bone marrow biopsy and aspiration confirmed a hypercellular marrow consistent with CLL; 30% of the marrow was occupied by small mature lymphocytes. Standard cytogenetics was normal, with loss of the Y chromosome, which is common in many older male patient

Figure 1. 200x magnification peripheral blood smear image of marked leukocytosis which includes a conglomerate of myeloid and lymphoid lineage cells.

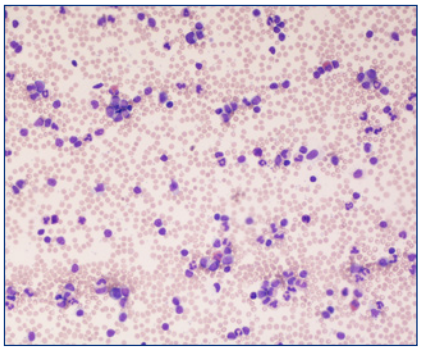
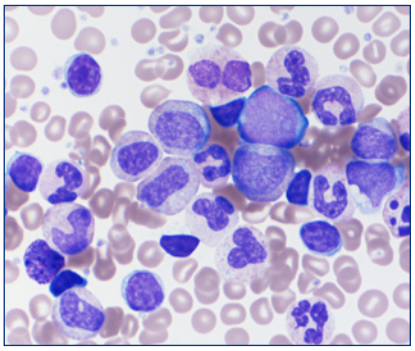


Figure 2. Peripheral blood smear at 1000x with oil immersion depicting full maturation spectrum of myeloid lineage including blasts, scattered lymphocytes and basophil.



He was followed in clinic without therapy. Four years later, his laboratory studies revealed a white blood cell count increasing from 72 x 10^9/L to 247.1 x 10^9/L with 54% lymphocytes, 20% neutrophils, 7% bands, 4% monocytes, 4% eosinophils, 2% basophils, 3% metamyelocytes, 6% myelocytes. There was also progressive anemia from a baseline hemoglobin 15.3 gm/dl to 11.1 g/dL, and a rise in the platelet count from 417 x 10^9/L to 1,480 x 10^9/L; this was believed to be reactive after a recent COVID-19 infection and pneumonia. Because of the delay in insurance approval of oral medication, one month later, he was given one dose of rituximab 375 mg/m^2 for progressive CLL with constitutional symptoms. He was subsequently started on treatment with a bruton's tyrosine kinase (BTK) inhibitor, ibrutinib. Four weeks after initiation of Ibrutinib, laboratory studies noted a white cell count of 635.3 x 10^9/L, hemoglobin 9.8 g/dL, and platelet count 2171 x 10^9/L. The differential found 13% neutrophils, 22% myelocytes, 6% metamyelocytes, 5% promyelocytes, 29% band forms, 20% lymphocytes, and 2% blasts. The peripheral blood smear displayed marked leukocytosis with predominant lymphocytosis consistent with known CLL, as well as a marked persistent left shift in the myeloid series with impressive thrombocytosis concerning for a superimposed myeloproliferative disorder (**Figures 1,2**).

Based on these findings, a bone marrow biopsy was performed and showed a hypercellular marrow (100%) with prominent myeloid hyperplasia, granulocytic left shift, megakaryocytic hyperplasia, moderate eosinophilia (15%), basophilia (12%), lymphocytosis (35%), and blasts (2%), consistent with a likely superimposed diagnosis of chronic myeloid leukemia- chronic phase (CML-CP), along with the preexisting CLL diagnosis. Fluorescence in situ hybridization (FISH) analysis showed BCR-ABL1 major transcript p210 with International Scale (IS) 58.39% (**Figure 3**), confirming CML. The trend in total WBC and absolute lymphocyte count over years after initial diagnosis of CLL with a decline in counts after the superimposed diagnosis of CML is shown in **Figure 4**.

After the diagnosis of CML was made, treatment with Ibrutinib was discontinued and the patient was started on CML directed therapy with a tyrosine kinase inhibitor, Imatinib. After six months he achieved a complete hematologic response, but has not yet achieved a major molecular response (MMR), defined as BCR::ABL1 IS <= 0.1%, with a BCR::ABL1% IS of 2.18%.

The existence of CML and CLL in the same patient is an extremely rare occurrence. An initial rise in leukocyte count is seen in patients receiving ibrutinib for CLL, as a class effect of BTK inhibitors. However, the presence of thrombocytosis along with worsening leukocytosis in a CLL patient should prompt consideration of additional workup for myeloproliferative disorder.

Figure 3. BCR-ABL1 transcript seen as yellow signal on fluorescent in-situ hybridization (FISH) analysis

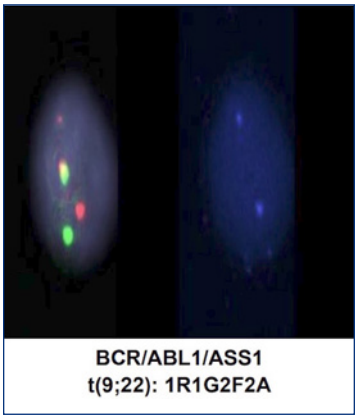
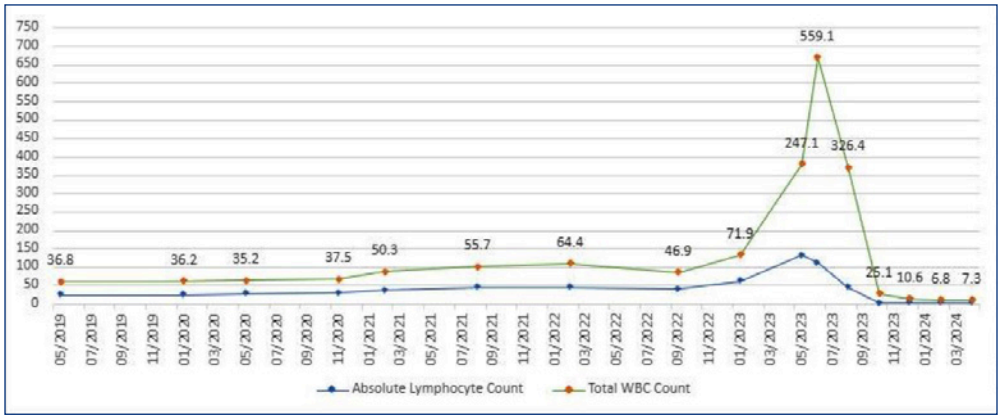


Figure 4. Trend of Total WBC (x109/L) and Total Lymphocyte Count (x109/L)



Authors

Yashvin Onkarappa Mangala, MD, Division of Hematology/Medical Oncology, Roger Williams Medical Center, Providence, RI.

John Patresan, MD, Division of Hematology/Medical Oncology, Roger Williams Medical Center, Providence, RI.

Dragos Luca, MD, Department of Pathology, Rhode Island Hospital, Brown University, Providence, RI.

Gerald Alexander Colvin, DO, Division of Hematology/Medical Oncology, Roger Williams Medical Center, Providence, RI.

Correspondence

John Patresan, MD
Clinical Fellow
Division of Hematology/Medical Oncology
Roger Williams Medical Center/Boston University
Providence, RI 02908
401-456-5790
john.patresan@chartercare.org