A Visit to the ER for Cellulitis Leading to the Discovery of Leukemia

U. Hasan DO, J. Hewlett MD, C. Joyce MD
Yale New Haven Health. Greenwich Hospital. Internal Medicine Residency Program.

Introduction

Simultaneous chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML) is a rarely reported entity. Usually, AML develops in patients with CLL while receiving chemotherapy agents for CLL.

Clinical Presentation

- 75 year-old male patient with a five-month history of low-grade B-cell CLL which was undergoing surveillance who presented after failure of outpatient cells treatment.
- Incidentally, labs were remarkable for a mild anemia, normal white blood cell count and new onset thrombocytopenia with a platelet count of 23,000.
- Initial blood smear revealed relative lymphocytosis with some abnormal forms suggestive of involvement by the patient’s known low grade B-cell lymphoproliferative disorder.
- The patient was initially treated for cells with daptomycin but due to two episodes of worsening fever and skin flushing concerning for allergic reaction, the patient was switched to azithromycin.
- On the third night of admission, the patient was febrile and had a change to his baseline mental status associated with visual hallucinations and neck stiffness. His antibiotic regimen was adjusted to piperacillin-tazobactam with doxycycline and acyclovir.
- Lumbar puncture was deferred due to thrombocytopenia. MRI of brain and spine was obtained but were unremarkable.
- Flow cytometry revealed persistent involvement of peripheral blood by the patient’s known monoclonal B cell lymphoproliferative disease, with current monoclonal B-cell counts meeting WHO criteria for CLL.
- A bone marrow (BM) biopsy was performed and the patient was started on high-dose steroids and rituximab for CLL treatment pending the results. The BM biopsy revealed a mildly hypocellular marrow with approximately 30% CD34-positive blasts consistent with involvement by AML. He was started on decitabine and venetoclax and transferred to a tertiary center for further management.

Diagnostics

FLOW CYTOMETRY (Blood)

Involvement of marrow by the patient’s known monoclonal B cell lymphoproliferative disease with immunophenotypic features in marrow (as well as recently reported in blood) most consistent with CLL. About 32-33% of total marrow cellularity consists of dim kappa-restricted CD19+ CD20dim+ CD5+ CD10- CD23dim mononuclear B cells.

Otherwise, there is no significant increase in CD34+ CD13+ blasts, at about 2-3% of total cellularity and T-cells detected possess a normal, mature immunophenotype. Recommend correlation with core histology to confirm and for further evaluation.

BONE MARROW BIOPSY

Variously cellular, overall mildly hypocellular marrow for age (40% cellular).

Approximately 50% of the cellularity is comprised of an intratumoral infiltrate of polymorphic cells including large atypical monosomes and monocytes with round to oval nuclei, vesicular chromatin, small nucleoli and moderate cytokinesis, occurring singly and in large aggregates. Megakaryocytes are markedly decreased and include dysplastic forms. Erythroid elements are markedly decreased and exhibit maturation. Maturing myeloid elements are markedly decreased. Granulocytes are not seen.

Reticulin stain reveals that reticulin is mildly increased within the nodular aggregates of megakaryocytes. Trabeclar bone is unremarkable. The clot section shows peripheral blood clot only with no spicules.

IMMUNOSTAINS

CD34 highlights approximately 50% of the cellularity as megakaryocytes. MPO highlights numerous myeloid forms. CD25, Paes and CD34/abs stain rare scattered 8 cells. CD3 highlights scattered T-cells.

BONE MARROW ASPIRATE

The aspirate smear is markedly hypocellular and aspirable. Scattered small lymphocytes are seen. A representative cell count could not be performed due to marked hypocellularity. Prussian blue iron stain reveals trace storage iron, no increase in ring sideroblasts is seen.

FLOW CYTOMETRY

By report, flow cytometric analysis reveals about 32-33% of total marrow cellularity consists of dim kappa-restricted, B-cells positive for CD19, CD20, and dim to negative for CD20, and negative for CD34. Otherwise, there is no significant increase in CD34 and CD13, blasts at about 2-3% of total cellularity and T-cells detected possess a normal, mature immunophenotype.

Discussion

CLL has been commonly associated with other secondary solid organ tumors, especially lung and skin cancers. There have been reports of AML and CLL association, but this usually occurs after chemotherapeutic treatment for CLL.

It is extremely rare to present with CLL and AML independently, as these entities more commonly appear as unrelated malignancies. In this case, the flow cytometry met the criteria for CLL, yet the bone marrow biopsy met the criteria for AML. Multiple theories have been postulated for the development of AML in patients with CLL. The first theory revolves around immunosuppression in these patients leading to development of AML. Others stipulate that the simultaneous occurrence of AML and CLL may be due to a common stem cell defect, leukemogenic factors, or other genetic defects.

Conclusions

The risk of other cancers in patients with CLL may warrant research into increased surveillance in these patients and higher clinical suspicion for secondary malignancies in these susceptible individuals.

References

1. MKSAP 18