A case that has it all: Chronic and acute, lymphoid and myeloid

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Clinical History

- 71-year-old female with a 5-year history of chronic lymphocytic leukemia (CLL)
- Past medical history of atrial fibrillation with nonischemic cardiomyopathy now presenting with worsening fatigue

Peripheral Blood

• CBC

- Normocytic anemia
 - Hgb 8.3 g/dL (Reference range 11.6-15.2 g/dL)
 - MCV 98 fL (81-98 fL)
- Leukopenia
 - WBC 3,170/cmm (4,000-12,400/cmm)
 - ANC 1,330/cmm (2,200-8,850/cmm)
- Thrombocytopenia
 - PLT 60,000/cmm (141,000-377,000/cmm)
- Pancytopenia prompted bone marrow biopsy

Recommended Analysis Strategy

- Given the clinical history of CLL:
 - Screening Panel:
 - Kappa, Lambda, CD5, CD56, CD20, CD38, CD19, CD10, CD45, CD11c
 - CD8, CD33, CD4, CD56, CD34, CD3, CD16, HLA-DR, CD45, CD117
 - Add-on CD5LPD tube: Kappa, Lambda, CD20, CD19, CD23, CD200, CD49d, FMC7, CD45, CD5
- Additional findings during evaluation prompted:
 - AML1 tube: CD2, CD33, CD34, CD56, CD13, CD64, CD14, HLA-DR, CD45, CD117
 - A LOT tube: nTdT, cMPO, cCD79a, CD19, CD34, CD3, cCD3, CD45, CD7

Pertinent Findings on Flow Cytometry

• Consistent with prior findings of CLL, a CD5+, CD19+, CD200+, CD23 dim, FMC7-, kappa-restricted B-lymphocyte population was present.



Pertinent Findings on Flow Cytometry

 However, the presence of a notable population of CD34+, dimCD45+ cells prompted further investigation.



Pertinent Findings on Flow Cytometry

• This CD34+ population was positive for CD117, cMPO, HLA-DR, dimCD11c, dimCD56, and CD33 expression, accounting for 20% of total events.



Diagnostic Considerations

- Based on flow cytometry results, this case has a classic immunophenotype of CLL and is similar to that seen previously in this patient.
- The presence of a coincident CD34+ blast population requires morphologic enumeration for diagnosis, as flow is not a quantitative method of evaluation.

Bone Marrow Biopsy



Bone Marrow Biopsy



(A) CD3 highlights scattered T-lymphocytes



(B) Pax-5 highlights clusters of B-lymphocytes



(C) CD20 highlights clusters of B-lymphocytes

Bone Marrow Biopsy



(A) CD34 highlights blast population



(A) CD117 confirms the myeloid origin of blasts

Diagnosis

- Bone marrow aspirate had 44% blasts on manual differential.
- Therefore, this case represents a case of chronic lymphocytic leukemia with a concomitant acute myeloid leukemia.

Follow-Up

• Molecular analysis

– Pathogenic variants in TP53 and RUNX1

- Cytogenetics
 - Complex karyotype with multiple structural and numerical abnormalities

Case Discussion and take away points

- This is an interesting case of a concomitant chronic lymphoid malignancy and an acute myeloid malignancy in the same flow sample.
- This case represents the detection of acute myeloid leukemia in a patient receiving chemotherapeutics for their chronic lymphocytic leukemia.
- This is the more common form of co-existence of the two hematological entities and is more likely to be seen in patients with progression of disease despite therapy resulting in escalation of therapy.
- Within the literature, one hypothesis suggests the possibility of therapies allowing the clinical emergence of an already existing clone for AML in a patient with two simultaneously occurring but separate diseases.
- Another hypothesis suggests the development of AML as a consequence of cytotoxic therapy.
- Co-existence of acute promyelocytic leukemia with chronic lymphocytic leukemia has also been reported but represents a much rarer occurrence.

References

- Lee HY, Park CJ, You E, Cho YU, Jang S, Seo EJ. A Case of Acute Myeloid Leukemia Concurrent With Untreated Chronic Lymphocytic Leukemia. Ann Lab Med. 2017;37(4):336-338. doi:10.3343/alm.2017.37.4.336
- Boddu P, Schlette E, Thakral B, et al. Acute promyelocytic leukemia in a patient with chronic lymphocytic leukemia—A case report. Hematol Oncol Stem Cell Ther. 2019;12(3):161-165. doi:10.1016/j.hemonc.2017.07.004
- Al Mussaed E, Osman H, Elyamany G. Simultaneous existence of acute myeloid leukemia and chronic lymphocytic leukemia: a case report. BMC Cancer. 2016;16(1):739. doi:10.1186/s12885-016-2780-5
- WHO Classification of Tumours Editorial Board. Haematolymphoid tumours [Internet; beta version ahead of print]. Lyon (France): International Agency for Research on Cancer; 2022 [cited YYYY Mmm D]. (WHO classification of tumours series, 5th ed.; vol. 11). Available from: <u>https://tumourclassification.iarc.who.int/chapters/63</u>.



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