Received: 5 November 2022 | Revised: 20 February 2023 | Accepted: 4 March 2023

DOI: 10.1002/jcla.24869

CASE REPORT

WILEY

Leukemic phase follicular lymphoma in a young adult

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Abstract

Background: Leukemic presentation of follicular lymphoma (FL) is uncommon, with most cases reported in older adults.

Design: This report describes an unusual case of a young adult diagnosed with leukemic phase of FL. We reviewed the existing literature on this rare presentation of the disease and its potential impact on patient outcomes.

Results: Leukemic phase of FL in young adults can be mistaken for other high-grade hematologic malignancies. Morphology assessment and ancillary testing, such as flow cytometry and FISH analysis, can assist in achieving an accurate diagnosis of the leukemic phase of FL. Notably, our young patient responded well to therapy, which is different from what is typically observed in older patients who have a poorer prognosis. Further cases are needed to investigate the prognostic impact of the leukemic phase of FL in younger patients.

KEYWORDS
BCL2 rearrangement, follicular lymphoma, leukemic phase, lymphocytosis

1 | INTRODUCTION

Follicular lymphoma (FL) is the second most common type of non-Hodgkin lymphoma (NHL) in Western countries, accounting for 35% of cases.[1] It typically affects elderly patients with a median age of diagnosis at 65 years.[1,2] The presentation of the disease can vary, from no symptoms to mild or severe symptoms such as lymphadenopathy, fever, excessive night sweats, and unintentional weight loss.[2–4] Bone marrow involvement is present in 70% of cases. The (14;18) translocation, which leads to overexpression of the BCL-2 protein, is present in around 85% of patients with FL.[5]

Leukemic presentation of FL is rare, with most cases reported in patients over 60 years old.[3,6] In recent years, the use of rituximab treatment has improved the overall survival rate for patients with follicular lymphoma to around 80%.[7] However, studies have shown that leukemic presentation of follicular lymphoma and high-risk follicular Lymphoma International Prognostic Index (FLIPI) have been associated with shorter progression-free survival (PFS).[8] In this case report, we present a young adult patient with an uncommon presentation of follicular lymphoma in a leukemic phase.

2 | CASE PRESENTATION

A 34-year-old man with a history of asthma presented to the emergency department complaining of fever, drenching night sweats, a 20-pound weight loss, and fatigue over the past two months. Laboratory test results showed anemia, thrombocytopenia, and marked leukocytosis with lymphocytosis. The peripheral blood smear revealed numerous atypical lymphoid cells, predominantly small to intermediate in size, with bilobed to multilobed nuclei and clumped chromatin. Some cells had butterfly-shaped nuclei, and most had clover-like nuclei. (Figure 1A–F) No left-shift granulocytes or blasts were identified. Flow cytometry revealed an aberrant

B-cell population that was positive for CD10, CD19, CD20, CD45, and CD52 and negative for CD2, CD3, CD4, CD5, CD7, CD8, CD34, and TDT. (Figure 1G) Fluorescence in situ hybridization (FISH) analysis using FISH probes for high-grade/large B-cell lymphoma and t(8;14) demonstrated the abnormalities involving the BCL2 probe set (1R1G1F, 88.0%, normal <5.7%) indicative of *BCL2* rearrangement, and the t(8;14) probe set (2R3G2A, 85.0%, normal <5.0%) suggestive of duplication of IGH/chromosome 14 or an IGH rearrangement to a locus other than *MYC*. *BCL6* rearrangement and *MYC* rearrangement/amplification were not detected. The overall findings were consistent with follicular lymphoma (FL) in the leukemic phase.

On follow-up examination, the patient was found to have palpable bilateral cervical lymph nodes and splenomegaly. A bone marrow biopsy showed a hypercellular marrow with decreased maturing hematopoiesis and a marked lymphoid infiltrate, consistent with a diagnosis of follicular lymphoma. The patient was classified as high risk for FL based on the FLIPI score of 4 and was started on cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (CHOP) chemotherapy. Due to COVID-19 infection and treatment with Remdesivir, Rituxan was not administered. Despite this, the patient has responded well to therapy.

3 | DISCUSSION

Literature review shows that reported cases of leukemic phase FL primarily occur in older patients.[3,4] However, in our case, the patient was diagnosed with leukemic phase FL at the age of 34. Leukemic phase follicular lymphoma is characterized by unusual lymphoid cells with “notched” or “buttock” shaped nuclei. Our patient's peripheral blood smear showed abnormal lymphoid cells with nuclei that were “clover-like” in shape, which is a previously undescribed cytomorphological feature of leukemic phase follicular lymphoma.

Initially, the unusual appearance of the lymphoid cells and the patient's young age made it difficult to diagnose. Further testing with FISH analysis allowed us to confirm the diagnosis and rule out

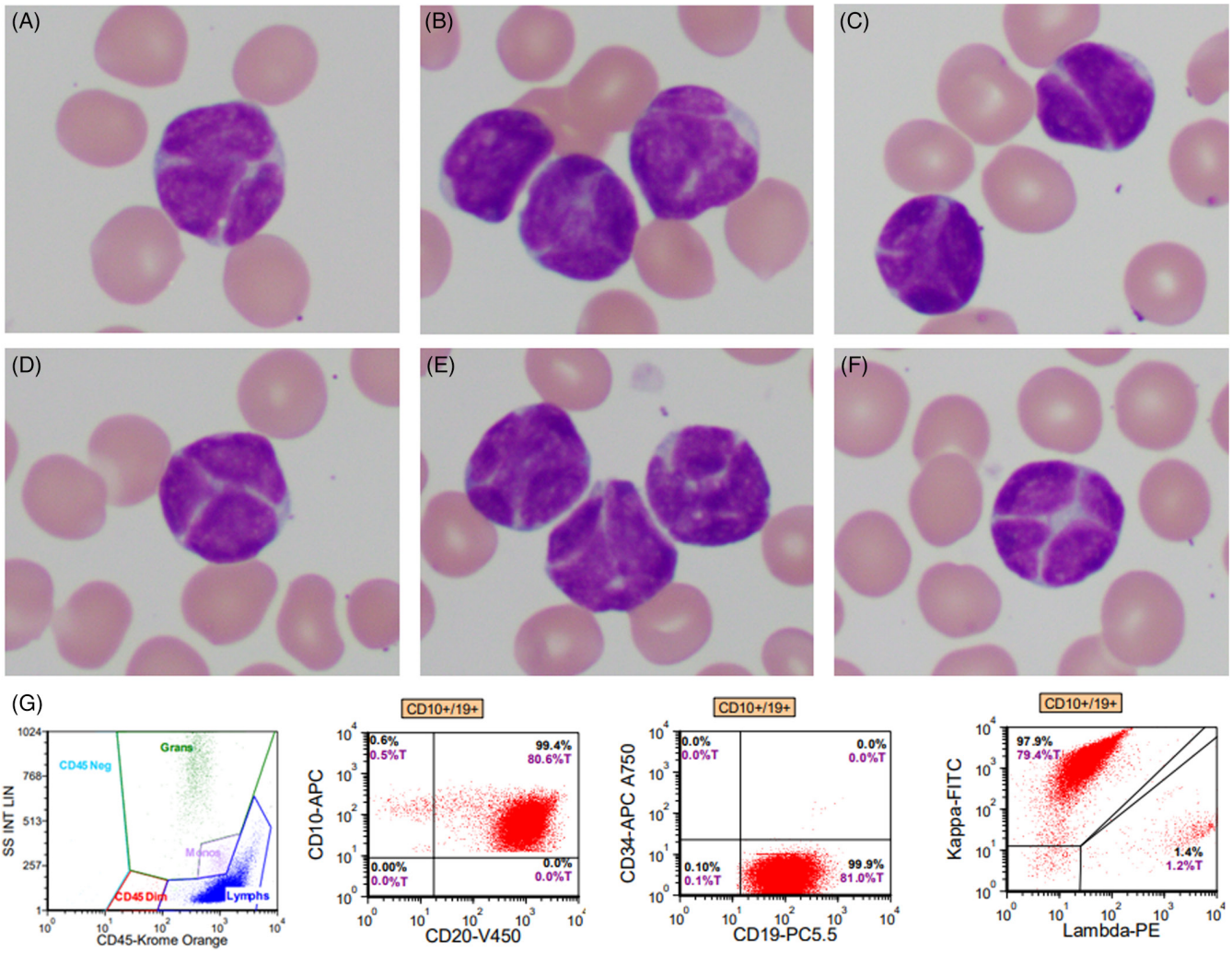

FIGURE 1 Panels A–F: Peripheral blood smear showed numerous small atypical lymphoid cells with cleaved or lobulated nuclei, clumped chromatin without nucleoli, and scant agranular cytoplasm. Panel G: Flow cytometry analysis on peripheral blood specimen revealed an aberrant B-cell population (81%) positive for CD10 (98%), CD19, CD20, CD45, and monotypic surface Kappa immunoglobulin light chain expression.[4]

other possibilities, such as mantle cell lymphoma (MCL) in a leukemic phase, chronic lymphocytic leukemia (CLL), and high-grade B-cell lymphomas.[9,10] Flow cytometry revealed that these lymphoid cells had an immunophenotype characteristic of follicular lymphoma. It is worth noting that lack of CD10 expression cannot exclude the possibility of leukemic phase FL, as reported by Maeshima et al.[11,12]

Studies have shown that high-risk FLIPI and leukemic phase are associated with shorter progression-free survival (PFS) in patients with follicular lymphoma.[8] Furthermore, patients with FL in leukemic phase may show suboptimal response to rituximab-containing regimens.[13] Our younger patient had a high-risk FLIPI score and presented with an aggressive form of follicular lymphoma but responded well to CHOP therapy. This outcome is different from what is typically observed in older patients, which raises the possibility that the prognostic impact of the leukemic phase of FL may differ between younger and older patients. Further investigation is warranted to explore this possibility. In addition, this case highlights the need to study the incidence of histologic transformation in patients with the leukemic phase of FL, particularly in younger patients.

In conclusion, when evaluating a young adult patient with leukocytosis and lymphocytosis, the possibility of follicular lymphoma in a leukemic phase should be considered. An accurate diagnosis can be made by evaluating the morphology of the lymphoid cells and utilizing ancillary testing such as flow cytometry and FISH analysis on peripheral blood specimens. In addition, our patient's positive response to chemotherapy might indicate the need for an individualized treatment approach for young patients with leukemic phase of follicular lymphoma.

AUTHOR CONTRIBUTIONS

Daniel Rivera wrote the article. Zhihong Hu diagnosed this case and provided critical review and revisions to the article. Wei Wang and Zubaidah Al-Jumaili participated in the diagnosis of the patient. All authors reviewed and approved the final version of the article.

ACKNOWLEDGMENT

This case was written under the mentorship of Zhihong Hu, M.D, Ph.D.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to report.

DATA AVAILABILITY STATEMENT

Not applicable.

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How to cite this article: Rivera D, Wang W, Al-Jumaili Z, Hu Z. Leukemic phase follicular lymphoma in a young adult. *J Clin Lab Anal*. 2023;37:e24869. doi:10.1002/jcla.24869