CLL-620

Marrow-Dominant Aggressive Progression of *TP53*-Altered CLL/SLL After Reactive Myelofibrosis: A Diagnostic and Therapeutic Challenge

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CONTEXT

TP53-altered CLL/SLL is associated with high-risk biology, early treatment failure, and increased risk of aggressive progression. Diagnostic complexity increases when marrow failure, secondary myelofibrosis, splenomegaly, and blastoid morphology occur without overt peripheral lymphadenopathy, particularly in settings where access to targeted agents is limited.

OBJECTIVE

To describe a diagnostically challenging case of *TP53*-positive, unmutated IGHV CLL/SLL with autoimmune hemolytic anemia, secondary reactive myelofibrosis, and subsequent marrow-dominant aggressive progression raising concern for Richter transformation vs blastoid progression of CLL/SLL.

DESIGN

Single-patient clinical case observation with longitudinal follow-up from February 2023 to December 2025..

SETTING

Hematology referral care in a resource constrained therapeutic setting.

CONCLUSIONS

This case highlights marrow-dominant aggressive progression of high-risk CLL/SLL after reactive myelofibrosis, creating a clinically relevant diagnostic dilemma between blastoid CLL/SLL progression and Richter transformation. It underscores the need for integrated morphologic, immunophenotypic, molecular, and clinical assessment, especially where limited access to targeted therapy influences disease trajectory and treatment selection.t.

PATIENT

A 36-year-old woman was diagnosed in February 2023 with stage 1 CLL/SLL after evaluation for generalized lymphadenopathy and was initially managed with active surveillance. In September 2023, she developed autoimmune hemolytic anemia and disease progression. Molecular testing showed *TP53* positivity and unmutated IGHV.

INTERVENTIONS

Because novel agents were unavailable, the patient received obinutuzumab-CHOP for 6 cycles. Treatment was complicated only by transient grade 4 neutropenia, recovering within 3–5 days with filgrastim. After severe COVID-19 pneumonia in April 2024, persistent pancytopenia prompted marrow evaluation showing grade 3 myelofibrosis, approximately 2% residual lymphoma, and *JAK2* V617F negativity, supporting secondary reactive myelofibrosis. Ruxolitinib was started with initial count normalization. In late 2025, progressive splenomegaly and grade 4 pancytopenia developed; spleen size increased from 16 cm in October to 22 cm in December. Repeat marrow biopsy showed 69% lymphoma infiltration with blastoid morphology and mature B-cell immunophenotype. The patient received 1 cycle of obinutuzumab plus DHAP.

RESULTS

Following salvage therapy, leukocyte counts normalized, and hemoglobin stabilized around 9 g/dL. Severe thrombocytopenia persisted, with platelets approximately 12000/mm^3 after a nadir of 8000/mm^3, consistent with ongoing marrow failure and hypersplenism. Ascites developed; liver fibroelastography was normal, and paracentesis was deferred because of hemorrhagic risk.

KEYWORDS

CLL, SLL, *TP53* alteration, Richter transformation, myelofibrosis, resource-limited setting

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