effective alternatives, particularly in patients where phlebotomy is less feasible. In both siblings, ferritin levels declined substantially with deferasirox monotherapy. Third, interruption of treatment, as seen in the elder sibling, allows ferritin to rise again, underlining the importance of sustained long-term management. **Conclusion:** We report two siblings with homozygous HFE-related hereditary hemochromatosis and significant hyperferritinemia. Both responded favorably to deferasirox therapy with substantial reductions in ferritin levels. These findings emphasize the value of family screening, genetic testing, and consistent treatment in the management of hereditary hemochromatosis.

https://doi.org/10.1016/j.htct.2025.106159

Adult Hematology Abstract Categories

Lymphoma

PP 26

From CD5-Negative Indolent B-Cell LPD to Therapy-Related CLL/SLL with Unmutated IGHV After Breast Cancer: Rationale for BTK-Inhibitor–Based First-Line Therapy

Birol Güvenç *

Çukurova University, Dept.of Hematology, Balcali_Adana,Turkiye

Introduction: Therapy-related chronic lymphocytic leukemia/small lymphocytic lymphoma (t-CLL/SLL) is uncommon compared with therapy-related AML/MDS. We report a breast-cancer survivor who evolved from a CD5-negative low-grade B-cell lymphoproliferative disorder (LPD) to classical CLL/SLL with **unmutated IGHV**, underscoring why targeted BTK inhibition may supersede chemo-immunotherapy in this setting. **Methods:** Single-patient case review of prospectively collected data. We extracted longitudinal clinical, imaging (PET-CT), bone-marrow histology, multiparameter flow cytometry, and cytogenetics (FISH, IGHV mutation testing). Treatment decisions were individualized by a multidisciplinary team. **Results:** A 1959-born woman had invasive ductal breast carcinoma (2009) treated with adriamycin–cyclophosphamide, weekly paclitaxel, and radiotherapy, achieving long-term remission. In 2018 bone marrow was normal; in 2019 splenectomy for progressive splenomegaly revealed florid follicular hyperplasia. Between 2020–2022, bone-marrow biopsies showed a **low-grade B-cell LPD** ($CD20^+$, **CD5–/CD23–/CD10–**), managed with **rituximab–bendamustine (8 cycles)**, yielding metabolic complete remission. In 2025 she re-presented with profound fatigue and anemia. Labs showed marked lymphocytosis (WBC 46×10^9/L), hemoglobin severely reduced, and PET-CT consistent with medullary disease. Bone marrow showed **40–50%** intertrabecular lymphoid infiltration. **Flow cytometry now demonstrated classical CLL/SLL** ($CD19^+$, $CD20^+$, **$CD5^+$, $CD23^+$**, κ-restriction). Molecular work-up: **IGHV unmutated**; FISH: **monoallelic del(13q)**; **del(17p)/del(11q) negative**. Given prior anthracycline exposure/radiation and the high-risk biology conferred by unmutated IGHV despite isolated 13q deletion, the tumor board selected **acalabrutinib plus rituximab** rather than re-exposure to chemo-immunotherapy. Transfusion support and infection prophylaxis accompanied therapy planning. **Discussion:** This case is notable for: (i) **Therapy-related CLL/SLL** emerging years after breast-cancer treatment—an under-recognized survivorship risk; (ii) **Phenotypic evolution** from an initially **CD5-negative** indolent B-cell LPD to **typical $CD5^+$/$CD23^+$ CLL/SLL**, highlighting clonal drift and the need for repeat immunophenotyping at relapse; (iii) **Risk adjudication** where **unmutated IGHV** outweighs the generally favorable isolated **13q deletion**, steering first-line choice away from bendamustine-rituximab toward **BTK-inhibitor–based therapy**; and (iv) pragmatic considerations in a previously anthracycline-exposed patient, favoring targeted agents for efficacy and tolerability. Educationally, the case adds to scarce real-world documentation of t-CLL, illustrates immunophenotypic switch over time, and provides a clear management rationale aligned with modern risk biology. **Conclusion:** In this therapy-related CLL/SLL with **unmutated IGHV** and prior breast-cancer treatment, **acalabrutinib + rituximab** was selected as the preferred front-line strategy over chemo-immunotherapy. The case emphasizes the importance of serial phenotyping and genomics to detect evolution and to personalize therapy in cancer survivorship.

https://doi.org/10.1016/j.htct.2025.106160

PP 27

ISOLATED SPLENIC RELAPSE IN CLASSICAL HODGKIN LYMPHOMA: A CHALLENGING CASE REQUIRING NOVEL THERAPEUTIC APPROACHES

Birol Güvenç *

Çukurova University, Dept.of Hematology, Balcali_Adana,Turkiye

Case Report: A 63-year-old male initially presented in 2024 with splenomegaly and was diagnosed with classical Hodgkin lymphoma following tru-cut biopsy. Immunohistochemistry confirmed CD30+, PAX5+, and MUM1+ Reed-Sternberg cells with negative CD3, CD20, and LCA expression. Initial staging revealed isolated splenic involvement without mediastinal or peripheral lymph node involvement. The patient received standard ABVD chemotherapy (adriamycin, bleomycin, vinblastine, dacarbazine) with concurrent rituximab therapy. Treatment resulted in partial response with persistent residual splenic lesions despite completing the planned regimen. In June 2025, surveillance PET-CT demonstrated disease progression with a 5-cm splenic mass showing intense metabolic activity (SUVmax: 17.2) without involvement of other anatomical sites. Bone marrow biopsy revealed 50% cellularity with normal hematopoiesis, reticulin score 0/4, negative CD30, and sparse PAX5 positivity, confirming absence of bone marrow involvement. Repeat splenic tru-cut biopsy confirmed relapsed classical Hodgkin lymphoma with characteristic immunophenotype: CD30+, PAX5+, MUM1+, GATA3+ with negative CD3, CD20, and LCA, consistent with the