maintained. **Discussion:** This case is unique in that: • **Sequential triple malignancy**: PV, CLL, and EGFR-mutant NSCLC rarely occur together. • **Therapeutic synergy**: Dual-targeted therapy produced durable responses in both solid and hematological malignancies. • **JAK2 loss**: Post-treatment JAK2 negativity suggests clonal competition or epigenetic remission; parallels have been observed with interferon-alpha in MPN[5]. • **Clinical implications**: Supports feasibility of combinatorial targeted therapy in elderly with multiple malignancies. Clonal hematopoiesis of indeterminate potential (CHIP) and aging likely predisposed this patient to multiple neoplasms [^6]. The "clonal competition hypothesis" posits that dominant clones (e.g., NSCLC with EGFR mutation) may suppress other clones (JAK2+) via shared niche or resource limitation. Limitations include single-patient observation; further genomic investigation (e.g., NGS) could clarify clonal evolution mechanisms. We recommend longitudinal monitoring of allele burden and expanded studies on multi-targeted therapy interactions. **Conclusion:** Conclusion Elderly patients with multiple sequential malignancies can benefit from tailored, low-toxicity targeted therapies. The unexpected disappearance of JAK2 mutation invites further investigation into clonal dynamics and epigenetic remission phenomena. This case enriches our understanding of cancer ecology in aging patients.

https://doi.org/10.1016/j.htct.2025.106114

OP 5

Autoimmune Hemolytic Anemia as the Presenting Feature of Chronic Lymphocytic Leukemia: Two Contrasting Cases Across Different Age Groups

Naciye Nur Tozluklu *, Birol Güvenç

Çukurova University, Dept.of Hematology, Balcali_Adana, Turkiye

Introduction: Chronic lymphocytic leukemia represents the most common adult leukemia in Western countries, with autoimmune hemolytic anemia occurring as a complication in 5-10% of cases. AIHA as the presenting feature of CLL is uncommon, particularly in young adults where CLL incidence is extremely rare. The immunophenotypic heterogeneity of CLL, including atypical variants, may influence both clinical presentation and treatment response. **Case Reports:** Case 1: An 84-year-old female presented with progressive fatigue, weakness, and dyspnea. Laboratory evaluation revealed severe anemia (Hb: 9.3 g/dL), marked leukocytosis ($42.36 \times 10^3/\mu$L), and thrombocytopenia. Direct antiglobulin test was strongly positive (3+), confirming warm-type AIHA. Flow cytometry demonstrated classic CLL immunophenotype: CD19+ (93%), CD5+ (95%), CD23+ (84%), CD20+ (52%), with absent CD38 expression suggesting favorable-risk disease. Bone marrow biopsy confirmed CLL/SLL with 50% infiltration. Treatment with prednisolone rapidly resolved hemolysis, followed by ibrutinib therapy for CLL. The patient achieved sustained remission over 12 months with corticosteroid discontinuation after 3 months. Case 2: A 25-year-old male presented with dyspnea, palpitations, and fatigue. Initial workup revealed severe anemia (Hb: 7.8 g/dL), reticulocytosis (6.8%), and elevated LDH with spherocytes on peripheral smear. Direct antiglobulin test was strongly positive (4+). Investigation revealed lymphocytosis (14,200/mm^3, 68% lymphocytes) with atypical CLL immunophenotype: CD5+/CD19+/FMC7+/CD23-, distinguishing it from typical CLL while excluding mantle cell lymphoma through negative cyclin D1. TP53 abnormalities were absent. Initial prednisolone therapy provided insufficient response, prompting rituximab monotherapy (375 mg/m$^2 \times 4$ cycles). The patient achieved complete hematologic response with hemoglobin normalization (11.6 g/dL), reticulocyte count resolution, and lymphocytosis improvement. **Discussion:** These cases illustrate important clinical principles in CLL-associated AIHA management. The elderly patient presented with classic CLL immunophenotype and favorable prognostic markers (CD38-negative), supporting the choice of BTK inhibitor therapy appropriate for her age and comorbidities. The young adult case demonstrated atypical CLL immunophenotype (FMC7+/CD23-), representing a variant phenotype that required careful differentiation from mantle cell lymphoma. The treatment approaches differed significantly based on age and disease characteristics. The elderly patient benefited from targeted therapy (ibrutinib) combined with corticosteroids, while the young patient achieved excellent response with rituximab monotherapy after steroid failure. This highlights the importance of individualized treatment selection based on patient factors and disease biology. Both cases emphasize the critical role of comprehensive flow cytometric analysis in patients presenting with unexplained AIHA, regardless of age. Early recognition of underlying CLL enables appropriate targeted therapy and optimal outcomes. The contrasting immunophenotypes demonstrate the heterogeneity of CLL, with both classic (CD5+/CD23+) and atypical (CD5+/CD23-/FMC7+) variants capable of presenting with AIHA as the initial manifestation. **Conclusion:** AIHA may serve as the presenting feature of CLL across diverse age groups with varying immunophenotypic profiles. These cases underscore the importance of systematic flow cytometric evaluation in all AIHA patients and demonstrate that age-appropriate targeted therapies can achieve excellent clinical outcomes in both classic and atypical CLL variants.

https://doi.org/10.1016/j.htct.2025.106115

OP 6

HHV-8 Positive Kaposi Sarcoma in a Myelofibrosis Patient Treated with Ruxolitinib: A Rare but Clinically Relevant Association

Berra Nur İşçi *, Birol Güvenç, İdil Yürekli

Çukurova University, Dept.of Hematology, Balcali_Adana, Turkiye

Introduction: Kaposi sarcoma (KS) is a rare vascular tumor strongly associated with human herpesvirus 8 (HHV-8) and typically seen in immunocompromised states such as HIV/AIDS or post-transplant settings. However, with the increasing use of immunomodulatory therapies in hematologic

malignancies, KS has also been reported in patients receiving Janus kinase (JAK) inhibitors. We present a case of HHV-8-positive cutaneous Kaposi sarcoma developing in a patient with primary myelofibrosis under ruxolitinib treatment. **Methods:** A 72-year-old female with a 2-year history of intermediate-2 risk primary myelofibrosis, positive for the JAK2 V617F mutation, was being followed in our hematology department. She had been on ruxolitinib (2×10 mg/day) for symptom control, which provided initial improvement in systemic complaints and splenomegaly. However, after 14 months of treatment, she developed painless violaceous plaques and nodules on her lower extremities, raising suspicion for Kaposi sarcoma. Dermatologic examination confirmed the presence of multiple dark purple nodules predominantly on the left lower leg. A punch biopsy was performed, and histopathological examination revealed spindle-cell proliferation consistent with Kaposi sarcoma. Immunohistochemical staining was strongly positive for HHV-8. **Results:** Laboratory evaluation revealed hemoglobin of 9.2 g/dL, white blood cell count of 13,000/mm^3, and platelet count of 120,000/mm^3. Peripheral smear showed typical findings of myelofibrosis, including teardrop-shaped erythrocytes. HIV, HBV, and HCV tests were all negative. Abdominal ultrasonography confirmed stable splenomegaly (19 cm). The ruxolitinib treatment was discontinued, and hydroxyurea was initiated as an alternative. Given that the Kaposi lesions were localized and the patient remained asymptomatic, systemic chemotherapy was not started. The patient is being followed with close dermatological and hematological monitoring. **Discussion:** This case highlights a rare but clinically significant complication of ruxolitinib therapy in a patient with primary myelofibrosis. JAK inhibition may lead to immune dysregulation, impaired antiviral T-cell responses, and viral reactivation—particularly HHV-8 in susceptible individuals. Although KS is commonly associated with HIV, this patient had no underlying immunodeficiency other than the JAK inhibitor–mediated suppression. The temporal relationship between ruxolitinib exposure and KS onset, combined with HHV-8 positivity and regression of symptoms after discontinuation of the drug, supports a probable causal association. Clinicians should remain vigilant for unusual infections or neoplasms in patients undergoing JAK inhibitor therapy.

https://doi.org/10.1016/j.htct.2025.106116

OP 7

Sequential Autoimmune Hematological Manifestations: From Isolated Lupus Anticoagulant to Post-COVID-19 Autoimmune Hemolytic Anemia

Berrak Çağla Şenol*, Birol Güvenç

Çukurova University, Dept.of Hematology, Balcali_Adana, Turkiye

Introduction: Autoimmune hematological disorders can present with variable phenotypes over time, suggesting underlying B-cell dysregulation. We report a unique case of sequential, distinct autoimmune manifestations occurring five years apart in the same patient, highlighting the heterogeneous nature of autoimmune hematological conditions and their potential triggers. **Case Presentation:** A middle-aged woman with no history of systemic autoimmune disease presented in 2019 with incidentally discovered coagulopathy. Routine laboratory evaluation revealed an INR >3 without bleeding symptoms. Further workup showed prolonged PT with normal aPTT, normal liver function, and normal levels of factors VIII, IX, and XI. Lupus anticoagulant testing was positive, while anticardiolipin and β2-glycoprotein I antibodies were negative. The patient did not meet criteria for systemic lupus erythematosus or antiphospholipid syndrome. Without specific treatment, the coagulation abnormalities spontaneously resolved within three months. Five years later, in 2024, the patient developed fatigue, jaundice, and anemia two weeks after COVID-19 infection. Laboratory findings revealed: markedly decreased hemoglobin, elevated LDH, suppressed haptoglobin, and elevated indirect bilirubin. Direct antiglobulin test (DAT) was strongly positive for IgG. Interestingly, lupus anticoagulant and other antiphospholipid antibodies were negative at this presentation. Bone marrow aspiration showed normocellular marrow with erythroid hyperplasia, excluding malignancy or dysplasia. The diagnosis of COVID-19-associated autoimmune hemolytic anemia (AIHA) was established. Treatment with rituximab 375 mg/m^2 weekly for four doses was initiated. The patient demonstrated dramatic response within two weeks, with rapid normalization of hemoglobin, LDH, and bilirubin levels. The DAT became negative, and the patient remains in remission on regular follow-up. **Discussion:** This case illustrates the dynamic nature of autoimmune hematological disorders. The initial presentation of isolated lupus anticoagulant positivity with spontaneous resolution, followed years later by post-viral AIHA, suggests an underlying predisposition to B-cell mediated autoimmunity with variable clinical expression. COVID-19 has been increasingly recognized as a trigger for autoimmune phenomena, including AIHA. The temporal relationship between COVID-19 infection and AIHA development in our patient, combined with the excellent response to B-cell depletion therapy, supports this association. The contrasting immunological profiles between episodes—positive lupus anticoagulant initially versus positive DAT with negative antiphospholipid antibodies later—demonstrates that autoimmune manifestations can evolve independently over time. This heterogeneity poses diagnostic and therapeutic challenges but also provides insights into the complexity of autoimmune regulation. **Conclusion:** Sequential development of distinct autoimmune hematological disorders in a single patient underscores the importance of comprehensive evaluation and long-term monitoring. The dramatic response to rituximab in the second episode highlights the central role of B-cell dysregulation in these conditions. This case emphasizes the need for heightened awareness of post-viral autoimmune complications and the potential for evolving autoimmune phenotypes over time.

https://doi.org/10.1016/j.htct.2025.106117