Case report: Pseudo-Richter Transformation in a patient with chronic lymphocytic leukemia after cessation of therapy with Venetoclax/Ibrutinib

SOHC
SWISS ONCOLOGY & HEMATOLOGY CONGRESS

Clinical hemato-oncology

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Introduction:
- Pseudo-Richter transformation (Pseudo-RT) in chronic lymphocytic leukemia (CLL) describes a phenomenon where patients exhibit rapid disease progression and systemic symptoms suggestive of Richter transformation
- Symptoms may include: lymphadenopathy, fever, and elevated lactate dehydrogenase (LDH)
- Unlike classical Richter transformation Pseudo-Richter transformation may reflect accelerated CLL progression or transformation into a more proliferative phase without clonal evolution.
- Pseudo-RT occurs typically after interruption or cessation of therapy with a Bruton Tyrosine kinase inhibitor (BTKi).

Case Report:
- A 69-year-old man with symptomatic CLL due to severe anemia (Hb 64 g/l), thrombocytopenia (40 G/l) as well as adenopathy and splenomegaly was treated with ibrutinib (cycles 1–15) and venetoclax (cycles 4–15) according to the GLOW trial[1] and showed complete clinical and hematological response at end of treatment.
- One week after cessation the patient developed fever, abdominal pain, and recurrent lymphadenopathy. Blood count showed leucocytosis (42 G/l).
- Imaging revealed partial regression and new progression of lymph nodes (Image 1), splenic infarction, and an eventual splenic rupture requiring emergency splenectomy due to hemorrhagic shock.
- Histology (Image 2) showed sheets of large cells and paraimmunoblasts in lymph node, bone marrow and spleen biopsy with high proliferation index (~50%), suspicious of Richter Transformation (RT)
- Molecular testing ruled out a high grade B-cell lymphoma with double hit and PET-CT did not support it as well.
- Suspecting pseudo-RT ibrutinib was reintroduced 14 days after cessation, leading to rapid normalization of leukocyte counts and clinical improvement.

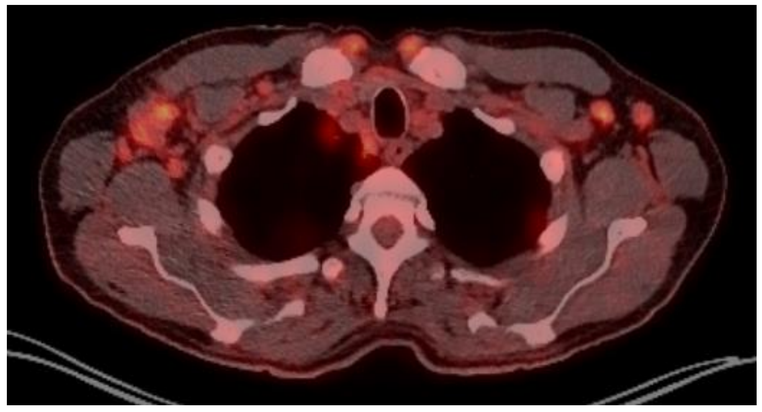

Image 1: FDG-PET-CT showing moderate metabolic activity (SUVmax: 3.2)

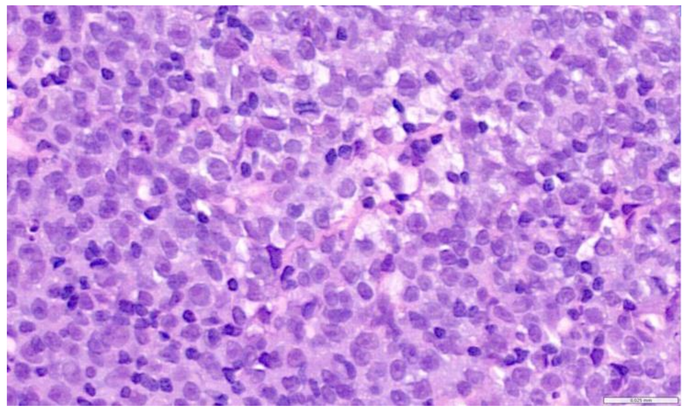

Image 2: H&E stain of the lymph node biopsy of the right axilla showing sheets of large cells and immunoblasts

Conclusion:
- Prior reports of pseudo-RT involved patients after BTKi Monotherapy[2,3]
- Rapid onset of transformation-like symptoms following recent BTKi interruption should raise suspicion for pseudo-RT though true RT needs to be ruled out.
- Pseudo-RT is diagnosed in clinical context. Interdisciplinary collaboration is essential for appropriate management.
- Pseudo-RT might become more common with increase of BTKi use in CLL
- Further research is needed to develop rapid diagnostic tools to distinguish pseudo-RT from true RT.

References: **(1)** Kater AP et al. Fixed-Duration Ibrutinib-Venetoclax in Patients with Chronic Lymphocytic Leukemia and Comorbidities, NEJM Evid. 2022 Jul;1(7):EVIDoa2200006. doi: 10.1056/EVIDoa2200006. **(2)** Slonim LB et al, Pseudo-Richter transformation of chronic lymphocytic leukaemia/small lymphocytic lymphoma following ibrutinib interruption: a diagnostic pitfall, Br J Haematol. 2020 Oct;191(1):e22-e25. doi: 10.1111/bjh.16948. Epub 2020 Jul 17. **(3)** Shi et al. Pseudo-Richter Transformation of Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma After Temporary Acalabrutinib Interruption, Mayo Clin Proc. 2024 Jun;99(6):867-868. doi: 10.1016/j.mayocp.2024.01.015.

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