POLISH ARCHIVES OF
Internal Medicine
POLSKIE ARCHIWUM MEDYCYNY WEWNĘTRZNEJ

ONLINE FIRST

This is a provisional PDF only. Copyedited and fully formated version will be made available soon.

Post polycythemia vera myelofibrosis with myelodysplastic-like progression in a patient with chronic lymphocytic leukemia

Authors: Grzegorz Jodlowski, Artur Borkowski, Zuzanna Dybko, Ugo Giordano, Krzysztof Zduniak, Jarosław Dybko

Article type: Clinical image

Received: February 24, 2024.

Revision accepted: April 19, 2024.

Published online: April 24, 2024.

ISSN: 1897-9483

Pol Arch Intern Med.

doi:10.20452/pamw.16735

Post polycythemia vera myelofibrosis with myelodysplastic-like progression in a patient with chronic lymphocytic leukemia

Grzegorz Jodlowski[1], Artur Borkowski[2], Zuzanna Dybko[3], Ugo Giordano[4], Krzysztof Zduniak[5,] Jarosław Dybko[6,5]

1 Endocrinology Department, Queens Medical Centre, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom

2 Clinical Endocrinology Department, 4th Military Clinical Hospital with Polyclinic, Wrocław, Poland

3 Faculty of Medicine, Wroclaw Medical University, Wrocław, Poland

4 Department and Clinic of Endocrinology, Diabetes and Isotope Therapy, Wroclaw Medical University, Wrocław, Poland

5 Lower Silesia Centre of Oncology, Pulmonology and Hematology, Wrocław, Poland

6 Department of Oncology and Hematology, Faculty of Medicine, Wroclaw University of Science and Technology, Wrocław, Poland

Correspondence to: Grzegorz Jodlowski, MD, Endocrinology Department, Queens Medical Centre, Nottingham University Hospitals NHS Trust, NG72UH Nottingham, United Kingdom, phone: +44 0115 9194 47, email: grzejodlowski@gmail.com

Chronic lymphocytic leukemia (CLL) is the most frequent lymphoproliferative disease in the modern world, caused by a relentless accumulation of $CD5^+$ B lymphocytes in the blood, bone marrow, and secondary lymphoid organs [1]. Polycythemia Vera (PV) is a Philadelphia chromosome negative myeloproliferative neoplasm (MPN) [2]. The co-existence of these two

conditions is a rare occurrence, with few cases reported in the literature [3]. In this case report we describe a case of indolent CLL complicated by PV and then post-PV myelofibrosis.

An 82-year-old gentleman with indolent CLL, who had not required treatment since his diagnosis five years previously, presented to hospital with fatigue, hyperhidrosis and weight loss of 20kg over a 2-year period. Physical examination detected no abnormalities. His blood results showed a hematocrit of (60.1 %, reference range, 40–54%) and elevated Lactate dehydrogenase, beta2microglobulin, C-reactive protein and uric acid. He had undergone a venesection without complications. Other tests revealed 76% pathological Lymphocytes B: CD19+, CD5+, CD79b (-), CD23+, CD200+, CD20+, CD43+, Kappa Free Light Chain +. Mutation V617F in JAK2 gene was positive, and Chromosome 13 and gene TP53 (17p13) deletion was recorded. In addition, a substitution in the CEBPA gene was detected. No other abnormalities were found on the karyotype. Erythropoietin was also low (2.53 mU/ml, reference range, 4–26 mU/ml). A computed tomography (CT) was performed scan showed hepatosplenomegaly but no enlarged lymph nodes. An assumption of CLL accompanied by PV was made, and trephine biopsy and cytogenetic tests were taken. The patient was discharged with aspirin, allopurinol and folic acid. Subsequently, he was re-admitted the following month with elevated red blood cells and hematocrit, therefore venesection was again undertaken. Three months later, he came to the hospital again and had a Positron Emission Tomography (PET) scan that showed an active metabolic process in the bone marrow, possibly related to the primary disease. Deranged metabolism in the liver and spleen was also noted. The trephine biopsy showed coexistence of two pathologies, CLL and post PV myelofibrosis (MF) with myelodysplastic (MDS-like) progression (Figure 1A-D). Treatment with Ruxolitinib was commenced. Subsequently, during another routine appointment he was found to be anemic, requiring admission and blood transfusion, and so further doses of Ruxolitibib were reduced by 50%. Three months later, he was re-admitted

with neutrophilia (23 g/l, reference range, 2.5–7 g/l) and worsening general status. An assumption of acceleration was made.

He had another trephine biopsy. A month later he was readmitted with profound anemia, in poor general condition, with shortness of breath on exertion, and an enlarged abdomen. Ultrasound showed hepatosplenomegaly. He required blood transfusion, broad spectrum antibiotics, steroids and darbepoetin and was deemed unsuitable to be treated with fedratynib. As the patient's condition improved, he was discharged home to continue his previous treatment regime with surveillance.

The mechanism and pathology underlying the co-existence of CLL and PV are not fully understood [3]. As suggested in a retrospective analysis, patients with concomitant CLL and PV usually have an indolent lymphoproliferative disease, and in most cases, they have not previously received chemotherapy. This may suggest that the rather than being caused by the leukemogenic effect of chemotherapy, it may be connected to immunodeficiency inherent to CLL [3]. Despite this, there is ample evidence to prove that the TP53 deletion is a negative predictive marker in CLL [4], and this has also been described as a risk factor for acceleration in PV [2]. It was acknowledged in the literature that the 13q deletion plays a significant role in CLL and PV development [5]. These rare occurrences require further studies to assess the molecular pathology and epidemiology.

Article information

Funding This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest None declared.

How to cite Jodlowski G, Borkowski A, Dybko Z, et al. Post polycythemia vera myelofibrosis with myelodysplastic-like progression in a patient with chronic lymphocytic leukemia. Pol Arch Intern Med. 2024; XX: 16735. doi:10.20452/pamw.16735.

References

1 Ghia P, Ferreri AM, Caligaris-Cappio F. Chronic lymphocytic leukemia. Crit Rev Oncol Hematol. 2007; 64: 234-246.

2 Farnoud N, Famulare C, Papaemmanuil E, et al. Landscape of TP53 Mutations in MPN. Blood. 2019; 134, Supplement 1: 1681.

3 Laurenti L, Tarnani M, Nichele I, et al. The coexistence of chronic lymphocytic leukemia and myeloproliperative neoplasms: a retrospective multicentric GIMEMA experience. Am J Hematol. 2011; 86: 1007-1012.

4 Soussi T, Baliakas P. Landscape of TP53 alterations in chronic lymphocytic leukemia via data mining mutation databases. Front Oncol. 2022; 12: 808886.

5 Yi S, Li H, Li Z, et al. The prognostic significance of 13q deletions of different sizes in patients with B-cell chronic lymphoproliferative disorders: a retrospective study. Int J Hematol. 2017; 106: 418-425.

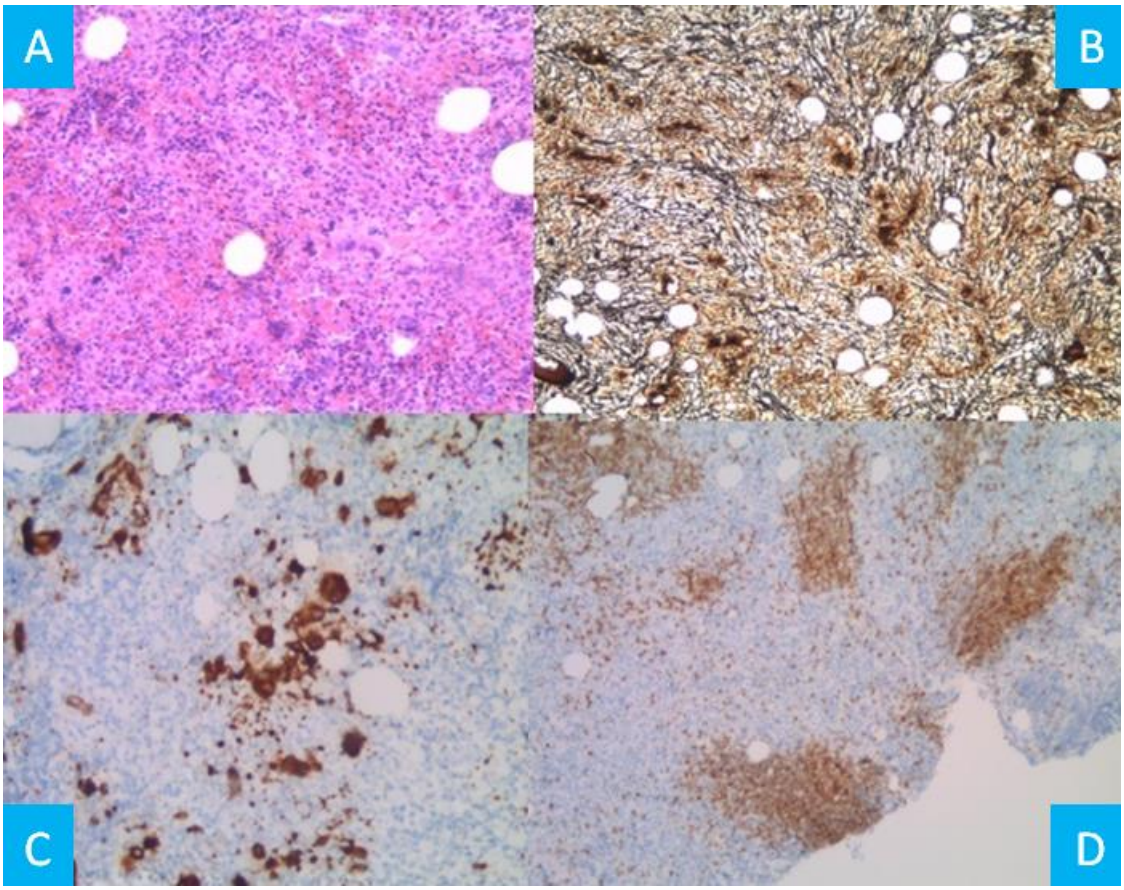

Figure 1 A – Hypercellular bone marrow with trilineage prolliferation and megakaryocytic atypia (Hematoxylin and eosin, mag. 200x); B – grade 3 bone marrow fibrosis (reticulin staining); C – megakaryocytic clustering (CD61 Immunohistochemistry stain, mag. 200x); D – multifocal chronic lymphocytic leukemia infiltration (CD20 Immunohistochemistry stain, mag. 100x)

Short title: Post PV Myelofibrosis with MDS-like progression in a patient with CLL