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CASE REPORT

Cellular War: The Dominance Struggle of Polycythemia Vera and Chronic Lymphocytic Leukemia Clones Within a Patient

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SUMMARY

Background: **Polycythemia vera (PV) and chronic lymphocytic leukemia (CLL) are distinct hematological malignancies. While their coexistence is rare, it poses unique diagnostic and therapeutic challenges.**
Methods: **A 50-year-old male patient presented with elevated hemoglobin levels and a marked lymphocytosis. Diagnostic investigations revealed the presence of both PV and CLL. The patient received treatment for PV followed by CLL.**
Results: **Initial treatment with hydroxyurea for PV led to progression of CLL. Subsequent treatment with rituximab and venetoclax effectively managed CLL, although the JAK2V617F mutation re-emerged.**
Conclusions: **This case highlights the potential for independent origins of myeloid and lymphoid neoplasms. Further research is needed to understand the interplay between these two malignancies and optimize their management.**
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KEYWORDS

polycythemia vera, chronic lymphocytic leukemia, JAK2V617F mutation, stem cells

INTRODUCTION

According to the World Health Organization's 2016 classification, polycythemia vera (PV) is one of the Philadelphia chromosome-negative myeloproliferative neoplasms (MPNs), characterized by the overproduction of red blood cells [1]. Chronic lymphocytic leukemia (CLL), the most prevalent lymphoproliferative disorder, is characterized by the accumulation of morphologically mature but functionally defective B lymphocytes [2]. This case report describes a male patient with the rare presentation of coexisting PV and CLL. Subsequent to hydroxyurea therapy for PV, the patient's CLL progressed, highlighting the challenges of managing patients with multiple hematological malignancies.

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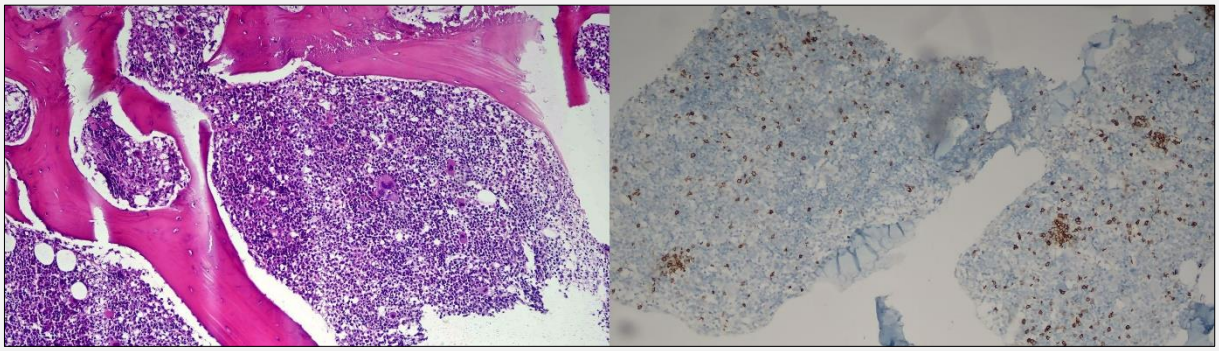

Figure 1. Bone marrow biopsy in December 2021 (hematoxylin-eosin and CD20 staining; original magnification × 10).

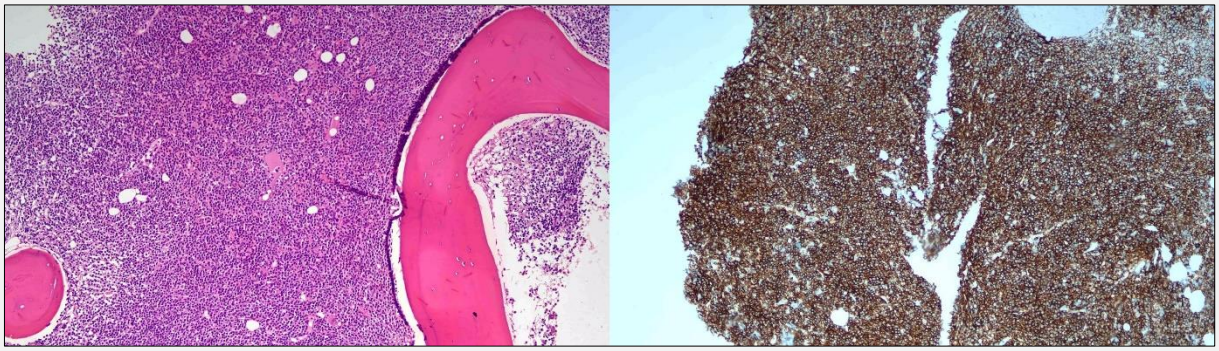

Figure 2. Bone marrow biopsy in December 2023 (hematoxylin-eosin and CD20 staining; original magnification × 10).

CASE

A 50-year-old male patient presented with persistently elevated hemoglobin levels despite a six-year history of regular blood donations. He was referred to our hematology clinic for evaluation. Hematological investigations revealed hemoglobin (Hb) of 15.5 g/dL, hematocrit (Hct) of 55.1%, white blood cell (WBC) count of 29.9 x 10^9/L, with a marked lymphocytosis of 18.3 x 10^9/L, and platelet (PLT) count of 203 x 10^9/L. Peripheral blood smear demonstrated an increase in mature lymphocytes. The patient was found to harbor a JAK2-V617F mutation (11.3%) with no detectable bcr-abl fusion gene. Abdominal ultrasonography revealed splenomegaly (length, 160 mm). Bone marrow (BM) examination showed hypercellularity (80%) with erythroid hyperplasia, mild granulocytic hyperplasia, increased megakaryocytes, and grade 1 reticulin fibrosis, consistent with panmyelosis. Erythropoietin levels were within the normal range (8.3 mIU/mL). Based on these findings, the patient was diagnosed with polycythemia vera according to WHO criteria. Flow cytometry confirmed the diagnosis of chronic lymphocytic leukemia (CLL) in 79% of CD5+/CD19+ cells, characterized by a CD10-/CD38-/CD23+ phenotype. The patient was diagnosed with coexisting B-cell CLL. A “watch and wait” approach was adopted for CLL management. Initial treatment for PV included hydroxyurea 500 mg/day and aspirin 100 mg/day. After six months, Hb was 16 g/dL, Hct was 51.6%, WBC count was 35.6 x 10^9/L, and PLT count was 307 x 10^9/L. Splenomegaly had decreased to 145 mm. Hydroxyurea was increased to 1,000 mg/day.

One year later, the patient presented with Hb of 13.3 g/dL, Hct of 43.1%, WBC count of 38.5 x 10^9/L, and a

marked lymphocytosis of 31.6 x 10^9/L, with thrombocytopenia (58 x 10^9/L). Hydroxyurea was discontinued. Whole-body computed tomography scan revealed extensive lymphadenopathy involving the cervical, mediastinal, and intra-abdominal regions, with a maximum lymph node size of 5 cm. Hepatomegaly (20 cm) and splenomegaly (23.5 cm) were also noted. Although JAK2V617F mutation was initially detected, subsequent real-time PCR analysis was negative. A BM biopsy demonstrated hypercellularity (90%) with diffuse infiltration by CD5+/CD23+/CD79a+/CD20+ lymphoid cells. Cytogenetic analysis revealed a karyotype of 45,XY,-10/46,XY. Fluorescent in situ hybridization did not detect trisomy 12 or deletions in 11q22.3, 13q14, or 17p13. Based on the WHO and International Workshop on CLL criteria, the patient was classified as CLL Rai stage 4, Binet stage C. The treatment was initiated with rituximab and venetoclax. After six cycles, Hb was 13.4 g/dL, Hct was 46.1%, WBC count was 5.5 x 10^9/L, with lymphocytosis of 1.3 x 10^9/L and PLT of 137 x 10^9/L. Despite effective treatment of CLL, the JAK2V617F mutation re-emerged (2.2%). The patient is currently receiving venetoclax monotherapy with the goal of completing treatment within two years.

DISCUSSION

A well-established association exists between MPNs and an increased risk of secondary lymphoproliferative disorders [3]. The Italian GIMEMA group has reported the rare occurrence of concomitant MPN and CLL diagnoses, with MPN treatment demonstrating no impact on CLL patient prognosis [4]. The underlying mechanism driving the coexistence of MPN and CLL remains elusive, with possibilities including shared genetic underpinnings, a common microenvironment, or distinct hematopoietic stem cell (HSC) origins [5]. Notably, cases of concurrent JAK2V617F-positive PV and CLL have been attributed to separate HSC clones [6].

In summary, our case of simultaneous JAK2V617F-positive PV and CLL supports the hypothesis that myeloid and lymphoid neoplasms can arise from independent HSC origins, underscoring the presence of two competing hematological diseases. The extent to which the JAK2V671F-positive clone influences the expansion of the CLL clone remains to be elucidated.

Patient Consent:

Written informed consent was obtained from the patient for publication.

Declaration of Interest:

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

No conflict of interest was declared by the authors.

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