Letter to the Editor
Diagnostic Hematology

Ann Lab Med 2014;34:469-470
http://dx.doi.org/10.3343/alm.2014.34.6.469
ISSN 2234-3806 • eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

A Rare Case of Polycythemia Vera Following Acute Undifferentiated Leukemia Remission

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Polycythemia vera (PV) is a myeloproliferative neoplasm (MPN) characterized by the abnormal proliferation of red blood cells, and it is associated with leukocytosis and thrombocytosis [1]. A *Janus kinase 2* (*JAK2*) V617F mutation is found in 95% of PV patients and influences its pathogenesis and diagnosis [1-4]. Generally, AML development is a late event in PV patients [1, 5], and leukemic transformation occurs in 5-15% of patients [4]. We report a case of PV after complete remission (CR) of acute undifferentiated leukemia.

A 74-yr-old woman developed PV 3 yr after treatment for acute undifferentiated leukemia. At the time of AML diagnosis in 2010, complete blood count (CBC) indicated anemia and moderate thrombocytopenia with white blood cell (WBC) count, Hb level, and platelet (PLT) count of 6.29×10^9/L,10.4 g/dL, and 71×10^9/L, respectively. Mild hepatomegaly was noted on physical examination. Bone marrow (BM) biopsy showed hypercellular BM with 60.6% blasts, decreased myeloid and erythroid precursors, increased megakaryocytes, and mild marrow fibrosis (grade II/IV). Immunophenotype results were positive for cluster of differentiation 7 (CD7), HLA-DR, and CD117 (weak positive), and negative for CD2, CD3, cytoplasmic CD3 (cCD3), CD5, CD10, CD13, CD14, CD19, CD20, CD22, cCD22, CD23, CD33, CD34, CD41a, CD56, CD79a, CD61, CD64, terminal deoxynucleotidyl transferase (TdT), and cytoplasmic myeloperoxidase (cMPO). The patient was diagnosed as having acute undifferentiated leukemia, and the chromosomal abnormality der(15) t(1;15)(q11;q26.3) was detected in cytogenetic analysis. Induction therapy with idarubicin and cytarabine led to CR. Post-remission, the patient received a first consolidation therapy with cytarabine and mitoxantrone and a second consolidation therapy with cytarabine and idarubicin.

Mid-2013, approximately 3 yr after the diagnosis of acute undifferentiated leukemia, she noticed a bluish discoloration on her right finger, and her CBC revealed leukocytosis and erythrocytosis with WBC count, Hb level, Hct level, and PLT count of 11.8×10^9/L, 19 g/dL, 57.6%, and 283×10^9/L, respectively. Tests for PV revealed low erythropoietin level (3.5 U/L) and mild hepatosplenomegaly. A repeat BM biopsy showed hypercellular BM with 1.9% blasts, normal myeloid and erythroid precursors, and pleomorphic megakaryocytes, but no BM fibrosis. Results for amplification refractory mutation screening (ARMS)-PCR analysis of BM aspirates were positive for the *JAK2* V617F mutation. Reverse transcriptase (RT)-PCR results were negative for *BCR-ABL1* in whole blood samples. Cytogenetic evaluation of BM aspirates showed no abnormalities. Collectively, these findings, in accordance with the WHO criteria, led us to a diagnosis of PV.

We retrospectively re-examined her BM specimen using allele-specific real-time quantitative PCR. Interestingly, the *JAK2* V617F mutation was present in 34.4% of extracted DNA when her leukemia was first diagnosed. After CR, the level reduced to

Received: February 3, 2014
Revision received: April 30, 2014
Accepted: August 27, 2014

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14.8%, but gradually increased up to 39.5% during the hematological follow-up. Finally, at the time of PV diagnosis, the *JAK2* V617F mutation was present in 69.4% of extracted DNA, and phlebotomy and aspirin treatment were started. Normal Hb level (15.5 g/dL) and mildly elevated Hct level (47.6%), WBC count (11.5×10^9/L), and PLT count (477×10^9/L) were noted in the peripheral blood after 1 month of treatment. At present, the patient is being followed up regularly.

The *JAK2* V617F mutation is commonly observed in PV patients [3, 6]. However, in *de novo* AML patients, the *JAK2* V617F mutation is only found in 2.3% of patients with the AML-M2 subtype with t(8;21) or the AML-M4 subtype with a normal karyotype [7]. To the best of our knowledge, few cases have been reported where PV developed after AML treatment [2, 8-10]. In our case, the patient was initially diagnosed as having acute undifferentiated leukemia characterized by the *JAK2* V617F mutation, and we hypothesize that the *JAK2* V617F clone may have expanded following chemotherapy. In support of this hypothesis, Portell *et al*. [9] suggested that standard AML induction chemotherapy offers a suitable environment for *JAK2*-mutant clones to expand, either through direct transition of the BM stroma or removal of the AML clone. We carried out allele-specific real-time quantitative PCR and found that the allelic burden had increased by the time of PV diagnosis compared with that at the time of AML diagnosis. On the basis of these findings, we presume that as a result of AML treatment, the *JAK2* V617F sub-clone expanded after disappearance of chromosomally abnormal clones. The present case is noteworthy because it is the first of its kind in Korea to characterize the development of PV arising from acute undifferentiated leukemia with a *JAK2* V617F mutation.

Authors' Disclosure of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

Acknowledgements

This research was supported by Nano · Material Technology Development Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning (grant number 2012M3A7B4035289).

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