Case Report

Janus kinase 2 V617F mutation in an unrelated peripheral blood stem cell donor

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ABSTRACT

Polycythemia vera (PV) is relatively uncommon in early adulthood, and evidence about the prevalence of the Janus kinase 2 (JAK2) V617F mutation in the general population is limited. Here, we report a previously healthy volunteer peripheral blood stem cell (PBSC) donor who developed symptomatic PV with the JAK2 V617F mutation 2 years after PBSC mobilization and harvest. The characteristic mutation was identified retrospectively in the blood sample of the donor at the confirmation typing stage, which was before granulocyte-stimulating factor injection. This report presents a safety issue for both donor and recipient of hematopoietic stem cell transplantation. Clinicians should be aware of this during health workup and postdonation follow-up of unrelated PBSC donors. Any abnormal and/or equivocal laboratory data, especially during the donor workup stage, should not be overlooked.

KEYWORDS: Granulocyte colony-stimulating factor, Janus kinase 2 V617F mutation, Peripheral blood stem cell harvest, Polycythemia vera, Unrelated donor

INTRODUCTION

Granulocyte colony-stimulating factor (G-CSF)-mobilized peripheral blood stem cells (PBSC) have become the major stem cell source for allogeneic hematopoietic stem cell (HSC) transplantation over the past decade. Although most donors experience the discomfort of varying severity during mobilization and/or leukapheresis, PBSC collection in unrelated donors is generally safe \cite{1,2}. G-CSF injection may cause a dramatic rise in the leukocyte count, along with a modest decrease in the hemoglobin level and platelet count. The blood cell counts return to baseline levels by 1 month after cessation of G-CSF administration \cite{1,2}. No specific association has been found between transient variations in the blood cell counts and hematologic malignancies after G-CSF mobilization \cite{3}. No case of acute myelogenous leukemia or myelodysplasia was reported in a prospective study of 2408 unrelated PBSC donors in the National Marrow Donor Program \cite{1}. Myeloproliferative neoplasms (MPNs) have not been reported in PBSC donors who underwent G-CSF mobilization and stem cell harvest. We report a young woman who underwent PBSC harvest and was diagnosed with Janus kinase 2 (JAK2) V617F mutation polycythemia vera (PV) 2 years after donation.

CASE REPORT

A 33-year-old, nonsmoking woman volunteer donor was eligible for PBSC donation after a comprehensive workup for donor health assessment. She had no relevant medical history and did not complain of any clinical symptoms. Laboratory study results showed that no abnormalities except her hemoglobin, hematocrit levels, and platelet count were all in the borderline reference range for females (16 g/dL, 50.2%, and 488,000/μL, respectively). Due to clinical urgency in the recipient, PBSC collection proceeded in 1 month.

The donor underwent a standard PBSC harvest procedure in our institution. In brief, she received daily injections of G-CSF (Filgrastim; Kyowa Hakko Kirin Co., Gunma, Japan) for 5 days. Large volume leukapheresis by a continuous flow cell separator (COBE Spectra; Terumo BCT, CO, USA) through peripheral vascular accesses was performed on the 5\textsuperscript{th} day after injection of the 5\textsuperscript{th} dose of G-CSF. Due

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to insufficient product CD34+ cells in the first harvest, another leukapheresis was performed after the 6th dose of G-CSF on the following day. Before the first leukapheresis, moderate leukocytosis (29,390/μL) and mild thrombocytosis (511,000/μL) were identified. The hemoglobin and hematocrit levels were 14.5 g/dL and 46.8%, respectively. The donor tolerated the whole procedure of PBSC harvest well. Her leukocyte count peaked after the 6th dose of G-CSF, and the platelet counts were slightly decreased after leukapheresis. The hemoglobin and hematocrit levels were also decreased but were still relatively high for females [Figure 1]. The preharvest CD34+ cell was 40.96/μL and the final product CD34+ cell yield after two collections was $4.85 \times 10^8$/kg of the recipient’s body weight.

Slowly elevating hemoglobin and hematocrit levels without specific discomfort were noted during serial postdonation follow-ups [Figure 1]. The donor was referred to a hematologist for further evaluation 25 months after harvest. She complained of mild headaches, fatigue, and exertional dyspnea for a few months. Extremely high hemoglobin (20.5 g/dL) and hematocrit (62.4%) levels were found, and PV was diagnosed after the characteristic JAK2 V617F mutation was identified by polymerase chain reaction. She then underwent serial phlebotomy and follow-up for PV. Her blood sample at the stage of HLA confirmation typing was retrospectively examined and was positive for the JAK2 V617F mutation. From the limited information reported by the transplantation center, the recipient had not developed any symptoms of PV, but further detailed laboratory results were not available.

**DISCUSSION**

PV is a clonal hematologic disorder, characterized by unwar

The consequences of exogenous short-term G-CSF activation in persons with the JAK2 V617F mutation remain an interesting question. The leukocyte count and circulating CD34+ cell count of our donor were not extraordinarily high after G-CSF mobilization. Her hemoglobin and hematocrit levels were slightly decreased, whereas the elevated platelet count was an unusual finding compared with that in the literature [1,2].

This case represents a safety consideration for HSC harvest from donors with subclinical JAK2 V617F mutations. Individuals with the characteristic mutation should be permanently deferred from HSC donation, not only because these donors are at risk of evolution to symptomatic MPNs but also because of the possibility of transmission of the mutated JAK2

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**Figure 1:** Serial donor blood counts. (a) White blood cell counts. (b) Hemoglobin and hematocrit levels. (c) Platelet counts
gene to recipients. Any equivocal laboratory data during donor workup, mobilization/harvest, and postdonation follow-up should not be overlooked. JAK2 V617F mutation should be carefully clarified in all donors with high hemoglobin and/or hematocrit levels. Further investigation is needed to determine whether PBSC mobilization by G-CSF injection accelerates the natural course of PV.

**Declaration of patient consent**

The authors certify that the patient obtained an appropriate patient consent form. In the form, the patient gave her consent for her clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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