EDTA-induced pseudothrombocytopenia in hematopoietic stem cell donor

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Abstract

We herein report a case of peripheral blood stem cell transplantation (PBSCT) from EDTA-induced pseudothrombocytopenia (PTCP). The apheresis product was inspected for 24 hours and there was no platelet clumping or thrombocytopenia. In the first 10 months after PBSCT, there has been no transfer symptom of PTCP.

Title page

Case Report

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Running title: PBSCT from EDTA-PTCP donor

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patient consent statement: Informed consent was obtained from this patient.

Abstract (47 words)

We herein report a case of peripheral blood stem cell transplantation (PBSCT) from EDTA-induced pseudothrombocytopenia (PTCP). The apheresis product was inspected for 24 hours and there was no platelet clumping or thrombocytopenia. In the first 10 months after PBSCT, there has been no transfer symptom of PTCP.

Keywords: hematopoietic stem cell transplantation, peripheral blood stem cell harvest, EDTA, pseudothrombocytopenia

Main text

1. Introduction

Pseudothrombocytopenia (PTCP) is an in vitro reaction in which blood anticoagulation, mainly using ethylenediaminetetraacetic acid (EDTA), is associated with in vitro agglutination of platelets, resulting in a spuriously low platelet count. This phenomenon arises from a platelet autoantibody targeting a concealed epitope on the platelet membrane glycoprotein (GP) IIb/IIIa; this epitope becomes exposed by EDTA-induced dissociation of GP IIb/III [1, 2]. Microscopic examination can identify platelet clumping, and repeat tests using heparin or citrate as an anticoagulant can confirm the diagnosis. This in vitro artifact usually persists over the course of long-term follow-up. Three studies evaluated the prevalence of PTCP in blood and platelet apheresis donors, with frequencies ranging from 0.01% to 0.2% [3, 4, 5]. In allogeneic hematopoietic stem cell transplantation (HSCT), autoimmunity and allergy can be transferred from donors to recipients, and this includes autoimmune diseases [6, 7]. B cells do not become fully reconstituted until at least 1–2 years after HSCT, mainly because of graft-versus-host disease (GVHD) prophylaxis and treatment using immunosuppressive drugs. However, mature B cells are transferred from donors to recipients. Therefore, it is possible to transfer PTCP during HSCT, but there is minimal information on this phenomenon so far. Herein, we present the clinical course a case of peripheral blood stem cell transplantation (PBSCT) patient from EDTA-induced PTCP donor.

2. Case presentation

The patient was a 39-year-old Japanese man who was admitted to a local hospital with a chief complaint of swelling of the gingiva and cervical lymph nodes. The patient underwent excisional biopsy of a cervical lymph node and was diagnosed with extranodal NK/T-cell lymphoma nasal type (ENKTL). He was initially treated with radiotherapy and dexamethasone, etoposide, ifosfamide, and carboplatin (RT-DeVIC), and achieved complete response (CR). One and a half years after treatment, he was admitted to a local hospital due to fever. Peripheral blood evaluation revealed pancytopenia and liver dysfunction. Bone marrow biopsy revealed ENKTL relapse. He began the DeVIC regimen and was admitted to our hospital with the plan of performing allogenic HSCT using peripheral blood from an HLA-identical sibling donor. The donor was accepted after no abnormalities were found during medical examination. Of note, the donor's platelet count was 157×10^9 /L. The day after the donor started filgrastim, her platelet count decreased to 62×10^9 /L and aggregation was observed on a peripheral blood smear. The platelet count was re-evaluated immediately after drawing blood using anticoagulation with EDTA and citrate acid (CA), and was found to be 209×10^9 /L with EDTA and 202×10^9 /L with CA. The thrombocytopenia was considered to represent EDTA-induced PTCP, in which the platelet count decreases with time after the blood is drawn. After that, until the peripheral blood stem cell harvest (PBSCH), there was no decrease in platelet count when it was measured immediately after blood sampling. PBSCH was performed on the fourth day of treatment with high-volume granulocyte

colony-stimulating factor (G-CSF), using combined anticoagulation with heparin and acid-citrate-dextrose solution A for the continuous mononuclear cell protocol on the Spectra Optia. A total of 2.3×10^6 CD34+ cells/kg were collected and cryopreserved. The apheresis product was inspected for 24 hours and there was no platelet clumping or thrombocytopenia with either EDTA or CA evaluation (Table 1). HSCT was performed with a reduced-intensity conditioning regimen (fludarabine 30 mg/m^2 and melphalan 140 mg/m^2, and GVHD prevention with tacrolimus and methotrexate), and the patient's disease condition was CR after 3 courses of the DeVIC regimen. Granulocyte engraftment occurred on day 14, and platelets engrafted on day 21. Acute GVHD began on day 19, and developed into grade II and gut stage 1. The patient responded to treatment with hydrocortisone and beclomethasone dipropionate, and achieved CR. Because of chronic GVHD with mouth, skin and liver, low dose tacrolimus is ongoing 10 months after PBSCT. Platelets remained within normal limits without clumping or disease relapse.

3. Discussion

PTCP may begin after HSCT when the B-cell repertoire develops, but in our case PTCP was not transferred from the stem cell donor to the recipient, and the apheresis product did not show platelets clumping or thrombocytopenia. Only one previous case report has described the risk of transmission of PTCP from donor to recipient in the context of HSCT [8]. As in our case, PTCP did not occur in the recipient, but it did not describe an analysis of the apheresis product. Another article on plateletpheresis donors found no transfer of PTCP to recipients, but it similarly did not describe an analysis of the apheresis product [9]. To the best of our knowledge, this is the first report of inspecting apheresis product in PTCP donor and no platelet clumping or thrombocytopenia in apheresis product.

4. Conclusion

Although there are limited reports, including our own, there has been no transfer of PTCP from stem cell donor to recipient and PTCP should not be regarded as an exclusion criterion for stem cell donation. A larger study should be performed to determine the likelihood of transferring PTCP to patients undergoing HSCT.

Author contributions

M.T. and M.K. contributed to the conceptualization, investigation, and writing of the original draft. S.N., N.T., S.T., Y.A., C.I., K.O., S.U., M.W., J.A., A.I., T.T., Y.I., and S.W.K. contributed to the investigation and to manuscript review and editing. N.M., H.M., and T.F. contributed to manuscript review and editing and to supervision.

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Table legend

Table 1. Results of longitudinal inspection of the stem cell harvest from a donor with EDTA-induced pseudothrombocytopenia

EDTA:ethylenediaminetetraacetic acid, CA:citric acid