Case Report

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ABO-incompatible granulocyte transfusion: Is ABO subgroup a barrier?

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Abstract:

Granulocyte transfusion (GTx) is an efficient and compelling treatment option for patients with neutropenia following hematopoietic stem cell transplant. The donor pool for granulocyte harvest is limited to close friends and family members and the donors accepted are often of the same ABO Rh type. We report a case of ABO-incompatible prophylactic GTx, in a case of acute myeloblastic leukemia. Postcollection processing of the granulocyte product was done to reduce the red blood cell volume to <5 ml, making it safe for transfusion. The transfusion was successful in stabilizing the total leukocyte counts in the patient. The patient was monitored, and there were no adverse reactions posttransfusion.

Keywords:

ABO incompatible, granulocyte transfusion, prophylactic granulocyte transfusion

Introduction

Granulocyte transfusion (GTx) is an efficient treatment option for patients with neutropenia following hematopoietic stem cell transplant (HSCT). It acts as a "bridge" that permits sufficient time for the recipient to develop their own immune response.[1]

The process of granulocyte donation poses challenges because of stimulation with mobilizing agents and the time consumed in donation. To add up, finding an ABO compatible donor is another challenge given the urgency. Removal of red blood cells (RBC) before transfusion overcomes this obstacle and allows safe transfusion in ABO incompatibility.

Case Report

A 10-year-old girl with relapsed acute myeloblastic leukemia (AML) and t (8;21); received induction therapy consisting of daunorubicin, cytarabine, and etoposide antibody-dependent enhancement followed by venetoclax and azacitidine. A diagnosis of relapsed AML in molecular remission was ascertained after bone-marrow examination and minimal residual disease (MRD) testing. Later, she had febrile neutropenia with Gram-negative sepsis for which antibiotics were started but did not respond.

The patient was planned for haplo-identical HSCT following MRD negativity.[2] Mother was given 5 doses of granulocyte colony-stimulating factor (G-CSF) (10ug/kg/day) and plerixafor (0.24 mg/kg) to mobilize stem cells. Transplant was successfully done with 10 × 10^6 cells/kg. On day 2, the patient developed fever of noninfectious etiology, commonly seen after HSCT.

The patient was planned for prophylactic GTx on account of the antecedent Gram-negative sepsis during pretransplant chemotherapy.[3] The mother was chosen for the GTx. She was of blood Group A positive

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and the patient's group was sub-group of A with anti-A1 antibody leading to a situation of an ABO-incompatible transfusion.

The patient's Anti-A antibody titer was performed by column-agglutination technique (DiaMed, Biorad, Switzerland) and was found to be 1. Immediate and AHG spin cross match was compatible. Two cycles of granulocyte collection were meticulously planned including postcollection processing of the product to avoid hemolytic transfusion reaction.

Informed consent was obtained. The donor was given G-CSF-10ug/kg and dexamethasone (20 mg) 12 h prior to collection. Donor's blood sample was checked for complete blood count (CBC), transfusion transmitted infections including human immunodeficiency virus I and II, hepatitis B and C virus, Malaria, Syphilis and found negative for these.

Granulocytes were collected using Spectra Optia using the mononuclear cell collection protocol. Owing to thin peripheral veins, internal jugular vein was used as the venous access. The anticoagulant used was 38 ml of trisodium citrate in 500 ml of 6% hydroxy ethyl starch (HES). A CBC was sent mid-procedure to help in approximation of the final volume of the product. A larger volume was targeted anticipating loss of granulocytes during postcollection processing.

A volume of 4787 mL of blood was processed over 131 min to obtain 303 mL of granulocytes. No adverse event was noted. The product CBC was done [Table 1]. The yield was 17.7×10^8/kg, patient's weight being 27.5 kg.

The product was processed immediately at 1080 rpm for 7 min. The product bag was then placed on the plasma extractor and the layer of leukocytes (268 mL) was separated from the RBCs into a satellite bag. The yield was 8.59×10^8/kg with Hematocrit of 0% [Table 1]. Product was irradiated to prevent graft-versus-host disease. GTx was done successfully on posttransplant day 6 at a Total Leukocyte (TLC) count of 0.06×10^3/uL. The transfusion process was monitored and was uneventful. Posttransfusion TLC was 1.06×10^3/l. The Absolute neutrophil count increased by almost 18 times.

The second granulocyte collection was performed similarly after 4 days. A volume of 5,446 mL of blood was processed over 146 min to obtain 400 mL of product. No adverse effects were observed in the donor. The yield was 14.9×10^8/kg [Table 1]. The product was processed and the yield after processing was 8.5×10^8/kg in 372 mL.

Second dose of GTx was given on day 10, at a TLC of $0.02 \times 10^3/\mu L$. Transfusion was uneventful. Posttransfusion TLC was $1.51 \times 10^3/\mu L$. The patient showed a positive response and the TLC counts became stable thereafter, requiring no further transfusions.

Discussion

There are essentially two ways of preparing granulocytes. First technique, involves deriving it from whole blood and the second one by apheresis. Apheresis provides advantages over the other, allowing greater volume of collection from a single donor over few hours as opposed to using almost 20 whole blood donations for preparing a significant amount i.e., 2×10^{10} granulocytes.[4] It utilizes HES which allows for better yield with lesser RBC and platelet contamination.[5]

The patient was on immunosuppressant as a part of the HSCT and the patient's anti-A titer was 1. These two factors were advantageous for ABO-incompatible GTx. Collection of granulocytes was done ensuring least contamination with RBCs using HES and reduce its volume to <5 mL, the recommended level for avoiding transfusion reactions in cases of incompatibility.[1,6] The patient had no clinical or laboratory evidence of hemolysis after transfusion. She showed an increment of $1.0 \times 10^3/\mu L$, making her TLC count reach $1.06 \times 10^3/\mu L$ from $0.06 \times 10^3/\mu L$, after the first transfusion. After the second one, the increment was larger, shooting her TLC to $1.51 \times 10^3/\mu L$ from $0.02 \times 10^3/\mu L$, an increase of almost 75.5 times the initial value.

Usually, ABO-compatible donors are selected for GTx. Such transfusions in the past, have shown detectable

Table 1: Complete blood count of first and second granulocyte product before and after processing

	First granulocyte product		Second granulocyte product	
	CBC of product before processing	CBC of product after volume reduction	CBC of product before processing	CBC of product after volume reduction
TLC ($\times 10^3$/uL)	172	102.35	109.44	70.55
Gran count ($\times 10^3$/uL)	161.11	88.19	102.50	63.58
RBC	0.90×10^6/uL	0.01×10^6 cells/uL	0.83×10^6 cells/uL	0.61×10^6 cells/uL
Hb	1.8 g/dl	1.1	1.9 g/dl	1.1 g/dl
HCT (%)	6.9	0.0	6.3	5.1
PLT	116×10^3/uL	4×10^3/uL	156×10^3 cells/ul	182×10^3 cells/ul

CBC=Complete blood count, RBC=Red blood cells, Hb: Hemoglobin, HCT=Hematocrit, PLT=Platelet count, TLC=Total leukocyte count

increments in neutrophil counts and have been successful in bringing down fever in almost 62% patients in a study by Cherif *et al*.[7] However, there is strong evidence that ABH antigens are not a part of granulocyte and products with <5 mL of RBC can be safely transfused without deleterious reactions.[8] The American Association of Blood Banks standards state that "RBCs in granulocytes shall be ABO compatible with the recipient's plasma" and that "granulocytes must be cross-matched unless the component is prepared by a method expected to result in a component containing <5 mL of RBC.[1,6] In such a situation, a variety of methods including sedimentation, semi-automated differential centrifugation, and density gradient separation have been reported to be safe and effective for depletion of incompatible RBCs.[9]

Bryant *et al*., used the sedimentation technique and achieved significant depletion of RBC upto 92 ± 4%. They had a granulocyte recovery of 80 ± 15% postprocessing. However, this technique is time consuming and unsuitable for urgent requirements. We used the centrifugation technique to save time. The granulocyte recovery was about 57% but this did not compromise the quality of the product as a higher volume was targeted in anticipation of this loss. The final dose was above the minimum required dose of 8×10^8/kg body weight.[10]

Wuest *et al*., also used gravity sedimentation technique with hetastarch to remove ABO-incompatible RBCs. After processing, component contained 82 ± 13% of the white cells and 5 ± 3 mL of RBCs. The transfusion was carried out with no reactions.[1]

Infections continue to cause significant morbidity and mortality in patients with neutropenia who have undergone intensive chemotherapy and HSCT. In such cases, GTx comes to rescue meanwhile patient develops immunity preemptive GTx are successful in preventing postHSCT complications.[4,11] The short shelf life creates an urgency because of the need to recruit a donor every time a transfusion is planned. ABO-incompatible donors can thereby be safely accepted by using the above mentioned techniques.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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