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Case Report

Transfusion management in a pediatric patient with febrile neutropenia with red blood cell autoantibodies: a case report

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ABSTRACT

Febrile neutropenia is a common complication of chemotherapy especially in hematological malignancies associated with sepsis or severe infection. We report a case where a seven-year-old girl with T – cell acute lymphoblastic leukemia (ALL) developed febrile neutropenia (absolute neutrophil count - ANC <500/µl). Patient developed transient red blood cell (RBC) autoantibodies which interfered with compatibility testing and posed a challenge in donor selection for granulocyte transfusion. Direct antiglobulin test (DAT) and compatibility testing were done by column agglutination technique (CAT) using polyspecific anti-human globulin gel cards. Antibody screen was also done by CAT using 3-cell panel. Granulocyte concentrate was collected from eligible donors after taking an informed consent using a cell separator based on continuous flow principle. The patient's blood group was AB RhD positive, however, the auto-control was positive (2+), DAT was positive (1+) but the antibody screen was negative. Monospecific DAT revealed the characteristic of antibody to be IgG (2+). The donor for granulocyte harvesting was selected on the basis of adopting a least incompatible donor approach. During her hospital stay she was transfused with four granulocyte concentrates, and other blood components without any adverse events. The patient's blood culture was sterile on day 33 of hospital stay and subsequently she remained afebrile and finally discharged on day 41 in a hemodynamically stable state. The hemogram was- Hb:10.7g/dl, Total leucocyte count (TLC): 5610/µl, ANC: 4375/µl, PLT: 22000 /µl. This case draws a special attention to the importance of serological testing in selection of donor for granulocyte transfusion.

Keywords: Febrile neutropenia, Autoantibodies, Red cell transfusion, Granulocyte transfusion

INTRODUCTION

Patients with hematological malignancies on chemotherapy face the risk of febrile neutropenia (FN) which could be life threatening.[1,2] FN can be managed by intravenous broad-spectrum antibiotics. Repeated granulocyte transfusions (GTx) were recommended in severe sepsis especially in neutropenia patient with gram negative infection in a pioneer study.[3] In a large multicentric randomized controlled trial (RING trial) subjects with neutropenia {absolute neutrophil count (ANC) <500/µL) and having infection were enrolled and it was found that the success rates for granulocyte and control arms did not differ within any infection type, however, subjects who received an average dose per transfusion of $\geq 0.6 \times 10^9$ granulocytes/kg tended to have better outcomes.[4] We report a case where a patient with FN required GTx due to severe sepsis and selection of a compatible granulocyte donor was a challenge due to

presence of red blood cell (RBC) autoantibodies in the recipient.

CASE REPORT

A seven-year-old girl who was a known case of T-cell acute lymphoblastic leukemia (ALL) on consolidation phase therapy presented to the pediatric emergency of our institute with high-grade fever and vomiting. The relevant laboratory investigations during her hospital stay are given in table 1.

Blood grouping (ABO and RhD) was done by tube technique. Direct antiglobulin test (DAT), antibody screen (ABS) (3-cell panel) and compatibility testing were done by column agglutination technique (CAT) (LISS Coomb's card, Bio-Rad, Switzerland).[5] Granulocyte concentrate (GC) was collected from eligible donors after taking an informed consent using a cell separator (Cobe Spectra, Caridian BCT, Lakewood, CO, USA; Version 7.0, PMN program) by bilateral peripheral vascular access as per the departmental standard operating procedure.[6] Each donor received injection G-CSF (300 µg) and oral dexamethasone (8mg) 12 hours prior to donation.

On the basis of history, examination and laboratory parameters a diagnosis of T-cell ALL on consolidation phase with complicated FN was made, having components of multiple organ dysfunction syndrome and sepsis. As her hemoglobin (Hb) was 6.9 g/dl, a requisition was sent to our department for packed RBC (PRBC). The blood group was found to be AB RhD positive, however, the auto-control was positive (1+ on tube, 2+ by CAT) and DAT was also positive (1+), but the ABS was negative.

Table 1: Serial laboratory investigations of the patient.

Parameters	Day of hospital stay												
	1	3	5	7	9	18	22	31	33	35	37	39	41
Hb (g/dl)	6.9	9.8	7.9	7.8	10.8	13.3	12.8	13.0	13.2	13.3	12.1	11.1	10.7
Total leucocyte count (/µl)	110	40	20	10	320	250	670	2290	4380	7260	8900	7180	5610
Platelet count ($\times10^3$/µl)	2000	29000	3000	11000	23000	44000	14000	21000	26000	12000	23000	18000	22000

Table 2: Details of granulocyte concentrate (GC) collection from donors and its transfusion.

Parameters	GC 1 (Day 21)	GC 2 (Day 23)	GC 3 (Day 25)	GC 4 (Day 27)
Hemoglobin (g/dl)	13.6	15	14.6	14.3
Platelets ($x10^3$/µl)	300	217	201	341
Pre-donation WBC count (/µl)	36,600	32400	27000	33,200
Post-donation WBC count(/µl)	28,100	28,300	24000	27,500
Volume collected (ml)	450	420	416	410
Total blood volume processed (ml)	11000	8240	8226	10004
PMN (final product) yield ($\times10^{10}$)	2.6	1.14	0.75	1.3
WBC yield (final product) ($\times10^{10}$)	2.9	1.7	0.90	2.0
RBC incompatibility	Weak +	1+	1+	Weak+
Any adverse effect (in donor)	Nil	Nil	Nil	Nil
GC transfusion	Uneventful	Uneventful	Uneventful	Uneventful
Pre-transfusion ANC count (/µl)	90	140	190	610
Post-transfusion ANC count (/µl)	800	620	600	2310

PMN: polymorphonuclear, WBC: white blood cells, RBC: red blood cells, GC: granulocyte concentrate, ANC: absolute neutrophil count

Monospecific DAT was positive (2+) for IgG. Any drug interference causing a positive DAT was ruled out. She had received multiple PRBC transfusions in last four months with no history of adverse reaction. Of the multiple PRBC units crossmatched, two least incompatible units (wk+ to 1+) were transfused under close monitoring uneventfully. In addition, ABO and RhD identical 10 random donor platelet concentrates, and 4 single donor apheresis platelets were also transfused uneventfully during her course of treatment.

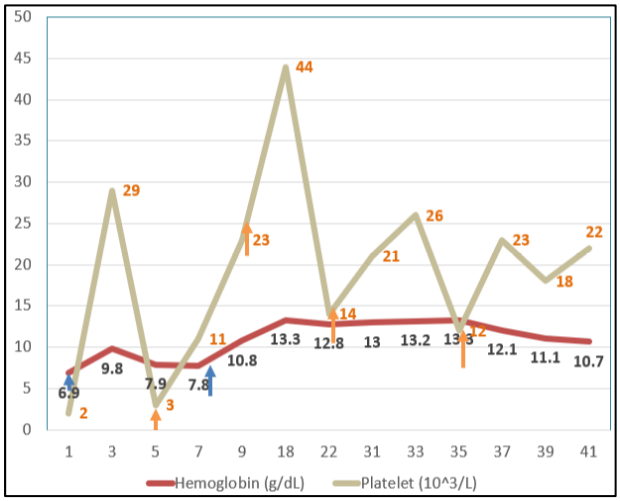

Figure 1: Hemoglobin and platelet count trend with transfusion (↑) support (Blue arrows indicate PRBC transfusion, orange arrows indicate platelet transfusion). Horizontal axis indicates the day of hospital stay.

The Hb and platelet (PLT) count trends are shown in figure 1. As her ANC dropped from 1310/µl to 90/µl, there was a need for GTx. Autoantibody interference in compatibility testing was a limitation to get a compatible donor. After screening 10 group specific (AB RhD positive) donors, 4 least incompatible (wk+ to 1+) donors were selected. The GC products (table 2) were irradiated (25Gy) and transfused within 24 hours of collection without any adverse event. The patient began to improve clinically. The blood culture was sterile on day 33 and subsequently she remained afebrile and discharged on day 41. The hemogram was- Hb:10.7g/dl, total leucocyte count (TLC): 5610/µl, ANC: 4375/µl, PLT: 22000/µl.

DISCUSSION

FN in the setting of sepsis is one of the indications for GTx. This is a unique case given the immunohematological presentation and therapeutic challenges posed due to multiple comorbidities. Finding donors for granulocyte donation was itself challenging as the patient's blood group was AB RhD positive which has a low frequency (7.74%) amongst Indian population.[7] Further, motivating donors for getting G-CSF injection and relieving their apprehension for long duration procedures was also demanding. We had to adopt selection of a least incompatible donor(s) with respect to RBC compatibility testing, due to autoantibody interference. Only 7 out of the 10 donors screened were found to be least incompatible and were considered for donations, however, 3 of them did not turn up due to their time constraints for the procedure and/or possible apprehension of the procedure. Thus, there needs to be strategy donor recruitment and motivation for granulocyte donors as well. Strauss et al, in a study of collection modalities in GC preparation via apheresis, found that 3 out of 4 respondents emphasized the use of leucocyte antibody screening along with ABO and Rh matched granulocytes.[8] However, in a developing country like India, screening for the presence of anti-HLA and anti-HNA in every donor and recipient is not always a feasible option, due to limited availability of these testing platforms and sometimes because of cost-constraints. GCs would invariably have RBC contamination which is typically ameliorated by RBC sedimenting agents like hydroxyethylstarch.[9] Strauss et al in their study found pervasive use of sedimenting agents across the centers.[8] We avoided use of sedimenting agents owing to donor safety issues. All the GTx were uneventful. There was no correlation between strength of incompatibility and granulocyte increment in recipient after transfusion. The trigger for development of autoantibody in this patient could be due to an antibody targeted against an infectious etiology and having cross reactivity with RBC antigens due to molecular mimicry of the epitope. Strength of this autoantibody was not strong (2+). The autoantibody was detected during a transient phase and was cleared off on further testing later. Most of the literature mentions about development of autoimmune hemolytic anemia (AIHA) in lymphoproliferative disorders especially in chronic lymphocytic leukemia, but there are no reports in the setting of T-cell ALL.[10] We could not establish the diagnosis of AIHA due to confounding factors in the setting of sepsis.

CONCLUSION

Our case highlights the significance of serological testing with respect to donor selection for granulocyte collection in a patient with RBC autoantibodies. Also, the setting of GTx requires an integrated approach between the treating physician and transfusion services for an optimal therapeutic benefit to the patient.

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