Transfusion reactions related with hematopoietic stem cell infusions: Are they more frequent than we think?

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Background

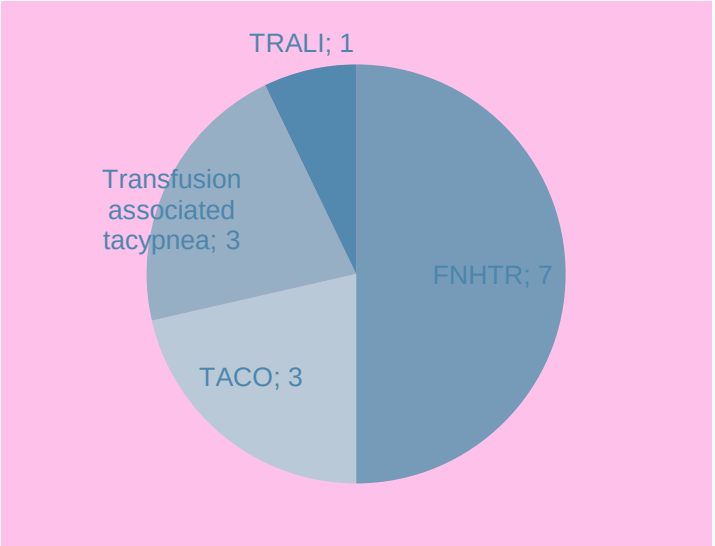
- Despite the frequent reporting of transfusion reactions related to blood transfusion, transfusion reactions related to hematopoietic stem cell infusions are usually underestimated as the patients may have comorbid diseases causing symptoms that would make clinicians to misdiagnose transfusion reactions
- After transfusion related acute lung injury (TRALI) that occured in a 8 year old patient with aplastic anemia who was transplanted from a 10/10 HLA-matched A,B,O matched 22 year old female sister donor, we planned to retrospectively evaluate the transfusion reactions associated with stem cell products from female donors

Background

- 45 patients who were transplanted from >18 years female donors between 2000-2021 were included at the study.
- Transfusion reactions during stem cell infusion were diagnosed according to the report of ISBT Working Party On Hemovigilance Report (July 2011)
- The relationship between transfusion reactions and the time from last pregnancy of the donor, the number of parity, the blood group mismatch, HLA-mismatch, the manipulation of the stem cell product, the conditioning regimen and HSCT complications were evaluated.

Results

- The total group included 45 pediatric HSCT patients.
- The mean age of the transplant recipients(F/M:21/24) and donors were 6.5± 5.25 (0-19 ages) and 28.60 ±7.13 (17- 47 ages)respectively.
- Tranplantation data is given in Table 1.
- Among the 45 patients, 14 patients (31.1%) had experienced transfusion reactions that can be attributed to stem cell infusion.



Transplant Data

Parameters	Patients (n=45) %
Age of the recipient (years) (mean ± SD) (Minimum-maximum)	6.5 ± 5.25 (0-19)
Gender	
Male	24 (40%)
Female	21 (60%)
Diagnostic Group	
Hematological disease	22 (48.9%)
Immunological disease	13 (28.9%)
Hematological malignancy	8 (17.8%)
Metabolic disease	2 (4.4%)
Conditioning regimen	
MA	32 (71.1%)
NMA	9 (28.9%)
Non-available	4 (4.4%)
Stem cell source	
Bone marrow	37 (82.2%)
PBSC	8 (17.8%)
Stem cell manipulation	
None	24 (53.3%)
Erythrocyte depletion	9 (20%)
Plasma depletion	8 (17.7%)
CD34 selection	2 (4.5%)
TCR αβ depletion	2 (4.5%)
Immunosupression	
CSA-MTX	42 (93.4%)
CSA only	1 (2.2%)
CSA-MMF	1 (2.2%)
None	1 (2.2%)
ABO mismatch between patient and donor	
None	21 (46.7%)
Minor incompatibility	14 (31.1%)
Major incompatibility	10 (22.2%)
Bidirectional incompatibility	None

Results

- 35/45 of the donors have given birth previously, 62.2% were multiparous.

We could not show any correlation between parity and nsfusion reactions with stem cell infusion ($p>0.05$).

- We also investigated the relation between time from last birth (≤6 months in 13.3 % of donors and and > 6 months in 64.4% of donors) stem cell donation among parous donors (n=35), there was no difference regarding stem cell transfusion reactions in groups with time from last birth >6 months versus ≤6 months ($p>0.05$).
- The only patient who had experienced TRALI had a sister donor who gave birth 6 months ago, and anti-HLA DPB1 antibody was detected as the cause of TRALI.
- We could not find any relation between transfusion reactions with MA vs NMA regimen, stem cell source, donor parity, time from last pregnancy of the donor, recipient-donor HLA and ABO mismatch and product manipulation ($p>0.05$).

Results

	Transfusion reaction with stem cell infusion (+) n(%)	Transfusion reaction with stem cell infusion (-) n(%)	p
Presence of HSCT			
Complication			
Any complication	11 (24.4)	18 (40)	0.160
Acute GVHD	3 (6.7)	13 (28.9)	0.160
Chronic GVHD	1 (2.2)	8 (17.8)	0.147
VOD	2 (4.4)	6 (13.3)	0.518
CMV Infection	2 (4.4)	5(11.1)	0.626
Hemolytic anemia	2 (4.4)	2 (4.4)	0.366
Fungal disease	2 (4.4)	3 (6.7)	0.5
Hemorrhagic cystitis	2 (4.4)	2 (4.4)	0.366
Engraftment syndrome	4 (8.9)	4 (8.9)	0.195
Outcome			
Alive	13 (28.9)	24 (53.3)	0.207
Exitus	1(2.2)	7 (15.6)	

Discussion

- The infusion of hematopoietic stem cells in stem cell transplantation is generally considered a safe procedure; however, our study indicates that transfusion reactions related to hematopoietic stem cell infusions might be more frequent than traditionally perceived. Our findings show a 31.1% incidence rate of transfusion reactions among pediatric patients, which is significant and warrants closer scrutiny.

- Our results align with those of Truong et al. , who reported on adverse reactions during the infusion of cellular therapy products (CTPs) in both autologous and allogeneic stem cell transplants .Their study, which analyzed 361 infusion episodes in 213 patients, found that reactions occurred in both settings, highlighting that transfusion reactions are not uncommon and should be carefully monitored and documented.

Discussion

- Our study did not find significant correlations between transfusion reactions and factors such as donor parity, time from last pregnancy, HLA mismatch, ABO incompatibility, or product manipulation. Despite there are many studies regarding the risks of clinically severe graft-versus-host disease, graft failure and mortality are increased in the presence of multilocus mismatching, we could not find a study evaluating HLA mismatch with advese events with stem cell product infusion.
- Our study did not find a significant correlation between donor parity or the time from the last pregnancy and the frequency of transfusion reactions.
- **In conclusion, our study underscores the importance of recognizing and accurately diagnosing transfusion reactions and other stem cell product infusion-related adverse events.**

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