Prevalence and Impact of Donor Specific anti-HLA Antibodies in the setting of Myeloablative Haploidentical Transplant for Malignant Hematological Diseases, *single-center experience*

Majed Altareb, Moheeb Alawwami, Mahmoud Aljurf, Riad El Fakih
King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

Introduction

The presence of Donor Specific Antibodies (DSA) correlates with poor graft function and graft failure (GF) in mismatched HLA transplantation. Despite the availability of multiple potential donors, transplant physicians still facing scenarios where the recipient has DSA against the appropriate donor. If alternative donors are not available, desensitization to remove the alloantibodies from the serum of recipient ahead of transplant is recommended to minimize the risk of GF.

Objective

To study the outcomes, prevalence and impact of DSA and anti-HLA of myeloablative haploidentical transplant for malignant hematological diseases.

Materials & Methods

This study is a retrospective analysis of our BMT Data base. We identified 107 patients who received myeloablative Haplo-HCT between January 2013 and December 2020. at KFSHRC. Sixty-two recipients were males (58%) and 45 were females (48%) with a median recipient age of 22 (range 1-56). The majority of pairs had matched ABO blood groups (76 pairs [71%]). The graft source was BM in 83 patients (78%). The median infused CD34 cell dose was 4.02 × 10^6 per Kg of recipient weight (range 1.3-13.1). Sixty-one recipients (57%) had positive anti-HLA of these 17 patients had DSAs (15% of the total number of patients, or 28% of patients who have anti-HLA antibodies). The median age of the 17 patients who had DSA was 36 (range: 8 - 48). The median cumulative MFI was 2062 (IQR: 1038 - 6500).

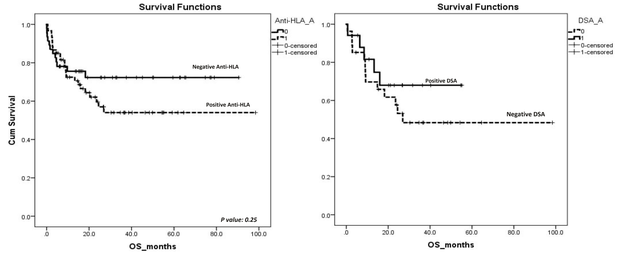
Results

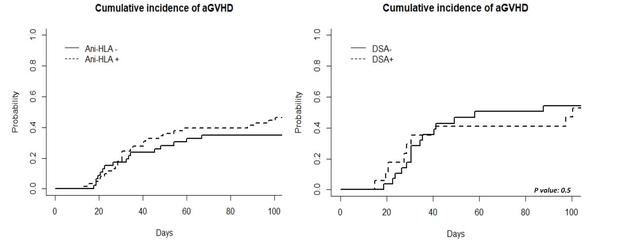
OS, CIR, aGvHD and cGvHD were comparable between patients with anti-HLA antibodies and those without, nor between patients with DSA and those without DSA. Recipient and donor gender as well as recipient/donor gender mismatch showed statistical association with the incidence of anti-HLA antibodies but not with DSA. Of the 17 patients with DSA, five patients underwent desensitization with three of them converting to DSA negative (although one of them developed new DSA but at a low level) and one of them achieving significant reduction in the intensity of DSA after desensitization.

Patients Characteristics	All patients 107 (%)	Anti-HLA		DSA	
		61 (57%)	P value	17 (15%)	P value
Recipient (R):					
Male	62 (58%)	28 (46%)	0.004	7 (41%)	0.56
Female	45 (42%)	33 (54%)		10 (59%)	
Donor (D):					
Male	70 (65%)	35 (57%)	0.044	10 (59%)	0.48
Female	37 (35%)	26 (43%)		7 (41%)	
R/D Gender Mismatch:					
MF	25 (23%)	16 (26%)	0.012	5 (30%)	0.41
FM	17 (16%)	9 (15%)		1 (6%)	
MM	45 (42%)	19 (31%)		5 (30%)	
FF	20 (19%)	17 (28%)		6 (35%)	
R Median age:	22 (1- 56)	22 (1- 56)	0.66	36 (8-48)	0.23
D Median age:	31 (5-60)	32 (5-60)	0.12	30 (16-60)	0.48
R/D relationship:					
Father	18 (17%)	11 (18%)	0.07	3 (18%)	0.064
Mother	14 (13%)	12 (20%)		1 (6%)	
Sibling	62 (58%)	30 (49%)		8 (47%)	
Offspring	13 (12%)	8 (13%)		5 (29%)	
ABO mismatch:					
Major	16 (15%)	9 (15%)	0.68	3 (18%)	0.94
Minor	15 (14%)	8 (13%)		2 (12%)	
Diagnosis:					
AML	62 (58%)	36 (59%)	0.52	9 (53%)	0.33
ALL	29 (27%)	14 (23%)		3 (17%)	
MDS	7 (6.5%)	5 (8%)		2 (12%)	
CML	7 (6.5%)	5 (8%)		2 (12%	
Others	2 (1.8%)	1 (1.6%)		1 (6%)	
Infused Cell Dose CD34	4.02 (1.3-13.1)	3.7 (1.5-13.1)	0.42	3.31 (1.99-4.86)	0.76

Results *(Continue)*

C1q assay was done on three patients pre desensitization and on all five patients post desensitization, and crossmatch was done on four patients post desensitization, one of them was negative and 3 were positive. Three patients only developed GF (2.8%), one was primary (0.9%) due to low CD34 dose and the other two had secondary GF (1.9%). None of the GF cases was in patients with anti-HLA antibodies or DSA. The median time from transplant to GF was 2.23 months (range: 0.8 – 2.89). The median time from transplant to ANC & platelets engraftment was 16 days for the whole cohort.





	Desensitization Protocol	Desensitization level						Cross-match
		Pre			Post			
		MFI	Conv.	C1q Assay	MFI	Conv.	C1q assay	
1	3 PEX, Rituximab, IVIG and Buffycoat	Anti-DR51 (7373) Anti-Cw4 (1769) Anti-DR15 (5911) Anti-DQ6 (8756) Cumulative MFI (23809)	Yes	No	Negative	Yes	Yes	N/A
2	3 PEX, Rituximab, IVIG and Buffycoat	Anti-DQ8 (19953)	Yes	Yes	Anti-DQ8 (4816)	Yes	Yes	Negative
3	3 PEX, Rituximab, IVIG and Buffycoat	Anti-DR17 (26427) Anti-DR52 (21977) Anti-DQ2 (1568) Cumulative MFI (49972)	Yes	Yes	Anti-DR17 (42071)	Yes	Yes	Positive
4	IVIg	Anti-B58 (5303) Anti-A2 (999) Cumulative MFI (6302)	Yes	No	Negative	Yes	No	Positive
5	5 PEX, Rituximab & IVIg	Anti-A2(6699)	Yes	Yes	DQB1*05:02 (735)	Yes	Yes	Positive

Conclusion

Our study validate the importance of desensitization strategy in presence of high DSA titer, despite insignificant OS, CIR, aGvHD and cGvHD results, that warranting prospective studies in these patients.

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