Management of a Patient Post-BMT and Pre-heart Transplant

Kevin Billand[1], Gail Crowther[1], Kristin Gay[1], Maria P Bettinotti[1], Alison J Gareau[1]

[1] Johns Hopkins Immunogenetics Laboratory, Department of Pathology, Johns Hopkins School of Medicine, Baltimore, MD, United States.

Introduction

The management of transplant patients requires thorough evaluation not only from an HLA viewpoint, but also requires careful attention to comprehensive medical history with a particular emphasis on previous transplants. An increasing number of bone marrow transplant (BMT) recipients are successfully engrafting and surviving longer post-transplant, with some proceeding to solid organ transplantation. Here, we present a case of a patient under evaluation for a heart transplant who previously received a haploidentical BMT. The patient, a 63 year-old female, had a history of breast cancer with secondary acute myelogenous leukemia for which she underwent BMT in 2010 with her daughter as a donor. She had no donor-specific antibody at the time of transplant and successfully engrafted, showing 100% chimerism post-transplant. The patient developed chemotherapy-induced cardiomyopathy and evaluation for heart transplant was initiated in March 2024. During the evaluation, a buccal swab was requested to determine the patient's pre-BMT constitutional typing. A peripheral blood sample was also received as part of the standard evaluation protocol and donor antigens were detected using rSSO at all HLA loci with the exception of HLA-DQA1 and -DQB1, where the patient and donor were matched. The evaluation report provided the patient's constitutional and the donor's pre-BMT typing. It was recommended to list the patient's constitutional typing in UNet and to consult Transfusion Medicine for blood group type listing. They advised listing genetic Type A positive, which was the result of the current screening and the blood group shared by both patient and donor pre-BMT. The patient had only one low-level class I antibody (A3, CPRA = 22.41) and was transplanted within 5 days of listing from a donor with no DSA. Of interest, the heart donor shared DR11 and DR52 antigens with the BMT donor and these were reported as shared mismatches on the virtual XM to the clinical care team.

Materials and Methods

DNA was isolated using the EZ1& 2 DNA Tissue and Blood kits from Qiagen. HLA high resolution typing was performed using the CareDx AlloSeqTx17 next generation sequencing platform and intermediate resolution typing was performed with OneLambda LABType™ SSO DNA typing system. Antibody testing was performed with OneLambda Single Antigen assays in conjunction with Werfen LIFECODES Phenotype assays.

Objectives

Determine the patient's constitutional typing and antibody profile to be able to list the patient in UNet for heart transplantation.

Results

	A	B	Bw	C	DR	DRB3	DRB4	DRB5	DQA	DQB	DPA	DPB
Patient	68	71	6	10	15			51	1	6	1	18:01
	30	7		15	8						3	04:01
Bone Marrow Donor	68	71	6	10	15			51		6		
	74	72		2	11	52						

Figure 1— HLA typing of patient and BMT donor
The patient's constitutional typing performed in 2009 compared to the haploidentical bone marrow donor.

Possible Allele Code: A*68:XX1 A*74:XX2

XX1:=:68:02/68:18N/68:34/68:44/68:49N/68:53/68:60/68:62/68:64/68:67/68:74/68:77/68:78/68:80/68:81/68:82/68:86/68:92/68:97/68:110/68:124/68:125/68:128/68:138/68:140/68:147/68:160/68:163/68:169/68:170/68:174/68:186/68:187/68:193/68:198/68:201/68:216N/68:219/68:236N/68:237/68:242/68:259/68:272/68:274/68:275/68:278/68:291/68:292N/68:299/68:304

XX2:=:74:01/74:02/74:03/74:09/74:11/74:14N/74:15/74:17/74:18/74:22/74:24/74:25/74:26/74:31/74:32N/74:34/74:36/74:38/74:40/74:44/74:45

Figure 2 — HLA-A low-resolution typing of patient blood sample post-BMT
Donor alleles were detected at all mismatched loci in 2024 with the exception of DQA1 and DQB1, where the patient and donor were matched.

	A	B	Bw	C	DR	DRB3	DRB4	DRB5	DQA	DQB	DPA	DPB
Patient	68	71	6	10	15			51	1	6	1	18:01
	30	7		15	8						3	04:01
Heart Donor	2	27	4	15	11	52			5	7	1	04:01
	24	55	6	9								

Figure 3 – HLA typing of patient and potential heart donor
Patient's constitutional typing that was listed in UNet vs the typing of the deceased donor heart. Note the shared mismatches DR11 and DRB3 with the BMT donor.

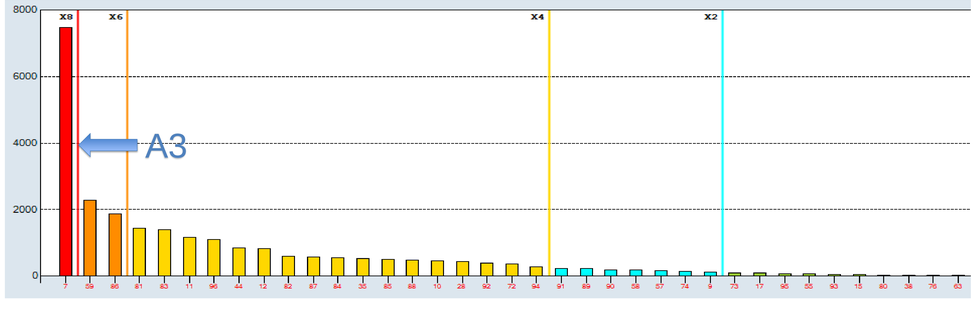
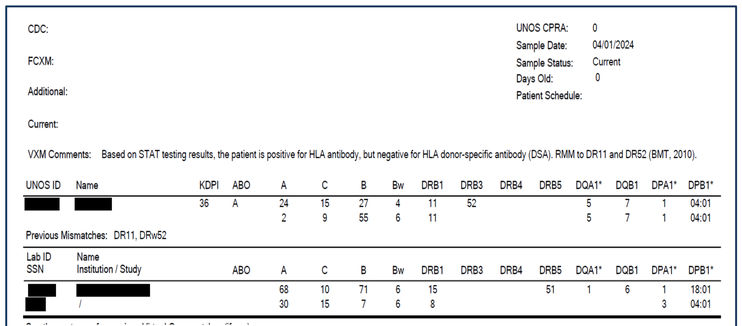


Figure 4 – HLA class I antibody profile pre-heart transplant
A STAT sample was tested prior to transplant. A3 reactivity was seen at ~7,700 MFI and was not listed as an unacceptable antigen in UNet. There were no other antigens considered positive using our laboratory's cutoffs or assignment algorithm and the patient was HLA antibody negative prior to BMT.


CDC:

FCXM:

Additional:

Current:

UNOS CPRA: 0
Sample Date: 04/01/2024
Sample Status: Current
Days Old: 0
Patient Schedule:

VXM Comments: Based on STAT testing results, the patient is positive for HLA antibody, but negative for HLA donor-specific antibody (DSA). RMM to DR11 and DR52 (BMT, 2010).

UNOS ID	Name	KDPI	ABO	A	C	B	Bw	DRB1	DRB3	DRB4	DRB5	DQA1*	DQB1	DPA1*	DPB1*
[redacted]	[redacted]	36	A	24	15	27	4	11	52			5	7	1	04:01
				2	9	55	6	11				5	7	1	04:01

Previous Mismatches: DR11, DRw52

Lab ID SSN	Name Institution / Study	ABO	A	C	B	Bw	DRB1	DRB3	DRB4	DRB5	DQA1*	DQB1	DPA1*	DPB1*
[redacted]	[redacted]		68	10	71	6	15			51	1	6	1	18:01
[redacted]	/		30	15	7	6	8						3	04:01

Figure 5 – Virtual XM results for deceased donor offer
A virtual assessment was performed on the pair using a STAT tested patient sample. The results showed that no DSA was present to the potential heart donor but there was two shared mismatches (DR11 and DR52).

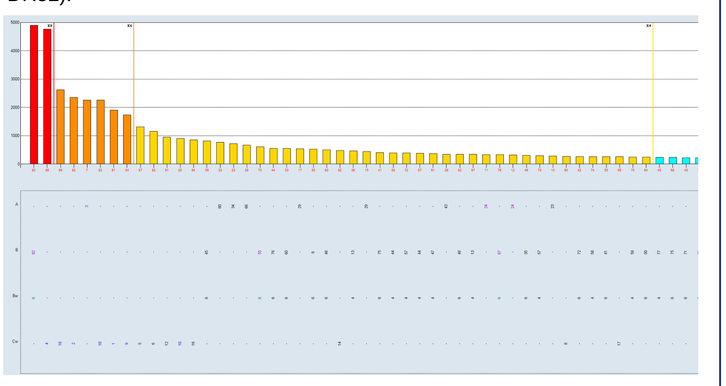


Figure 6 – HLA class I antibody profile post-heart transplant
The patient received blood products 2 days prior to the collection of this sample, which showed an increase in non-specific reactivity but no DSA.

Conclusion

In conclusion, when listing a patient for solid organ transplant with a previous BMT, our practice is to confirm the patient's constitutional HLA typing and current ABO for listing in UNet. This should be done in consultation with Transfusion Medicine.

Post-transplant, there was no significant change in the level of A3 HLA antibody over the course of 4 months. Sadly, the patient passed away 144 days post-transplant due to cardiogenic shock in the setting of a massive pulmonary embolism. There was no DSA or pathological signs of rejection at that time.