From Hesitancy to Certainty: A Case of Successful Desensitization in High Risk HLA Incompatible Kidney Transplantation

Sir,

Single antigen bead assay (SAB) is a semi-quantitative estimation of the amount of human leukocyte antigen (HLA) antibodies present in recipient plasma, and mean fluorescence intensity (MFI) generated gives a semi-quantitative estimation of the antibodies present in recipient. The presence of donor specific antibodies (DSA) increases the risk of antibody mediated rejection (ABMR) after kidney transplantation. The relevance of antibodies to HLA (class I and II) antigens in kidney transplantation has been found to play a role in graft rejection.[1] Despite improved desensitization regimes, nephrologists still hesitate to cross the HLA barrier, especially in recipients who possess DSA with high MFI; primarily due to the higher rates of ABMR and graft failure. We present a case of successful kidney transplantation in a patient who expressed DSA with high MFI.

A 32-yr-old female, a chronic kidney disease (CKD) patient on regular maintenance hemodialysis, opted for kidney transplant with her sister as donor and was referred to the department of Transplant Immunology for histocompatibility testing. Patient had a history of more than 20 units of blood transfusion and her obstetric history revealed three spontaneous abortions after the birth of her first child. Pre transplant compatibility testing algorithm has been illustrated in Figure 1a. The results of HLA typing and compatibility testing for this patient has been listed in Table 1 along with multiple DSA identified by SAB. Patient was explained about the test reports and the high risk of rejection associated with it. However, she wanted to undergo this transplant. Hence, an informed consent for desensitization and high-risk transplant was taken, and she was counselled about the desensitization protocol which included rituximab, mycophenolate mofetil, tacrolimus, steroid, IvIg, and therapeutic plasma exchange (TPE). SAB was repeated after the 7th session of TPE which revealed highest MFI of 6167. Another 5 sessions of TPE were performed and the highest MFI on SAB after a total of 12 sessions was found to be 822. Anti-thymocyte globulin (ATG) was administered on the day of transplant along with intravenous steroid. The timings of immunosuppression and TPE with respect to transplant are illustrated in Figure 1b.

Patient did not have any complications in the immediate post-operative phase. No bleeding complications were observed. However, a prophylactic post-transplant TPE was performed on post-operative (POD-1) day 1 and the patient was closely monitored for graft function. The immunosuppression was gradually tapered and all

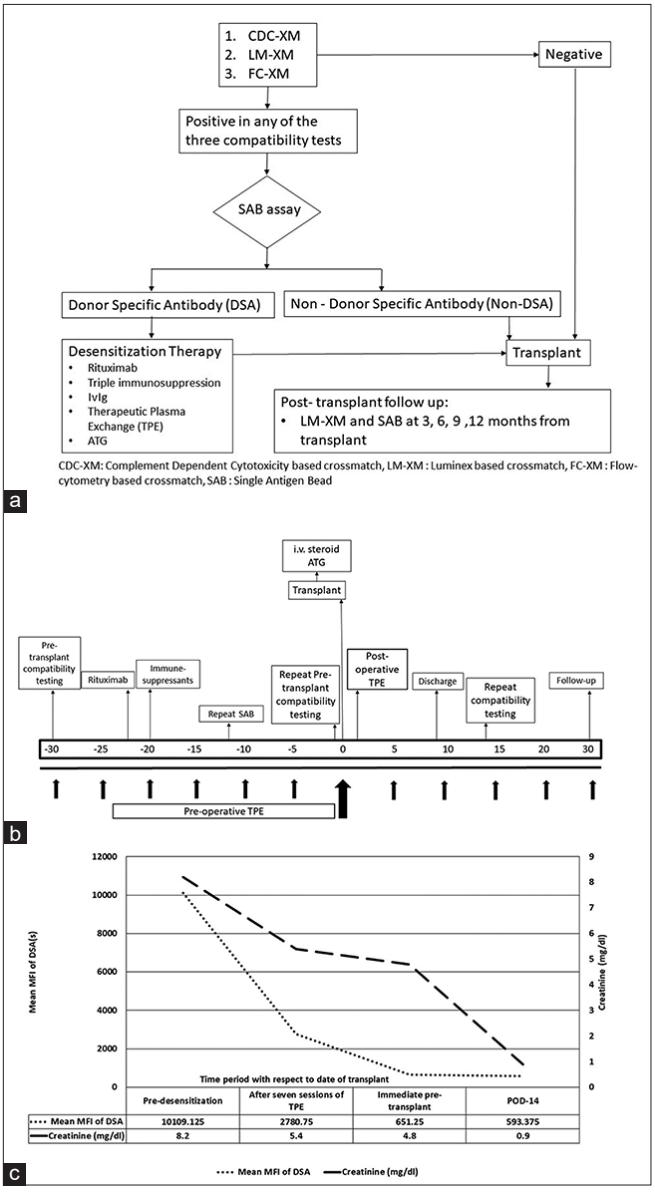

Figure 1: (a) Pre-transplant compatibility testing algorithm. (b) Schematic illustration of treatment protocol followed. (c) Change in creatinine and MFI of DSA with desensitization

investigations like kidney function tests, tacrolimus levels, ultrasound, and doppler were performed. Patient was discharged on POD-9 and an additional SAB was performed on POD-14 (MFI<1000). Change in the mean MFI of all DSA(s) with desensitization over different time periods with respect to the date of transplant has been demonstrated in Figure 1c. At the time of writing this letter the patient continues to do well; after 3 months in the post-operative phase.

Table 1: Pre-transplant HLA typing and histocompatibility test results

HLA typing of recipient	A*02,31 B*52,40 C*16,06	DR*14,15 DQA1*02,01 DQB1*01,06 DPA1*02,02 DPB1*11,11

	Before desensitization	After seven sessions of TPE	Immediate pre-transplant (After twelve sessions of TPE)	Post-transplant (POD - 14)
CDC-XM	Strong Positive	NP	NP	NP
FC-XM	T-Cell - Positive	NP	NP	Negative
	B-Cell - Positive	NP	NP	Negative
LM-XM	Class I - Positive (MFI-4095)	Positive	Negative	Negative
	Class II - Positive (MFI-3606)	Positive	Negative	Negative
SAB				
Donor HLA	**MFI of DSA**	**MFI of DSA**	**MFI of DSA**	**MFI of DSA**
A*02:01	23440	6167	822	621
A*33:03	ND	ND	ND	ND
B*18:01	9544	5430	665	627
B*58:01	15916	1217	511	594
C*03	1147	502	512	506
C*07	ND	ND	ND	ND
DRB1*12:02	3987	1903	749	655
DRB1*03:01	6656	3264	646	576
DQA1*05:01	10157	2245	783	665
DQB1*02:01	ND	ND	ND	ND
DQB1*03:01	10026	1518	522	503
DPA1*01:03	ND	ND	ND	ND
DPA1*04:01	ND	ND	ND	ND
DPB1*105:01	ND	ND	ND	ND
DPB1*28:01	ND	ND	ND	ND
Median channel shift for FC-XM: T cell-52, B cell-146	Cut-off for LM-XM: ≥500		Cut-off for SAB: ≥1000	

ND - Not detected, NP - Not Performed

Kidney transplantation is the best modality of treatment that can be offered to patients suffering from CKD on hemodialysis for a better quality of life.[2] Successful renal transplantation in the presence of an impediment in the form of DSA in sensitized individuals has been on the rise during the past decade primarily due to the evolution of desensitization regimes. More often than not, a suitable donor may be deferred due to the presence of DSA in recipient plasma with high MFI. Although, using MFI as a measure of antibody strength has important limitations like inter-laboratory variations and complement interference but most studies use MFI as a marker of antibody strength because there is no consensus on anti-HLA antibody quantification. Zecher *et al*. concluded from their study that simultaneous presence of class I and class II DSA is associated with an increased risk for ABMR and that monitoring DSA 14 days after transplantation is a very good prognostic indicator.[3] In the present study, SAB was repeated at POD-14 for the same reason and was found to be negative, which was considered as a predictor of good graft outcome. Song *et al*. reported a case where the maximum MFI reported before re-transplant was 14,454 and concluded that clinically significant HLA antibodies may develop in the post-transplant phase, the evaluation for which can prevent ABMR.[4] In the present case, there were multiple donor specific antibodies with a high MFI of up to 23,440. Desensitization regime and close monitoring of the graft in the post-operative phase helped in improving the odds of ABMR. The authors thus conclude that the option of a high risk HLA incompatible kidney transplant can be offered to recipients with high MFI DSA, who wish to undergo transplantation for end stage renal disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands

that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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