Pre-transplant Compatibility Tests in Kidney Transplants: Case Report on Significance of Epitope-based Analysis in Donor Selection

Sir,

Detection of alloantibodies is one of the main objectives of compatibility work-up before transplantation. One of the common strategies employed in India is to perform complement-dependent cytotoxicity cross-match (CDC) and flow cytometry-based cross-match (FCXM) tests.[1] If either or both of these tests are positive, Luminex-based single antigen bead (SAB) assay is performed to identify specific antibodies. These antibodies are then matched with human-leukocyte antigens (HLA) of prospective donor to determine donor-specific antibody (DSA), called virtual cross-match.[2] Routinely matching is done at antigen level; not at epitope level. Antibodies positive at antigen level can be negative at epitope level and vice versa.[3,4] Epitopes are configurations of polymorphic amino acid residues that are recognized by B cells, and antibodies reactive with these epitopes lead to rejection and/or premature allograft loss. we report our experience of two cases having history of sensitization, where class II (DPA1) antibody was ruled out as a DSA, only because of epitope analysis. Since this has a clinical implication of deciding the prospective kidney donor, epitope analysis may be used routinely in all SAB test interpretation.

Recipient serum samples were collected for Luminex SAB assay (LIFECODES LSA™ Kit Immucor Transplant Diagnostics, Inc. USA.) to identify the DSA. Luminex software (Match IT antibody) was used for antigen-based analysis (cut-off; BCM ≥1000/positive by machine) and Epitope-based analysis was done with the help of freely available online software 'HLA Matchmaker' (http://www.epitopes.net).

As described in Table 1, we presented two cases where both the patients and prospective donors were females, having history of sensitization. All three tests (CDCXM, FCXM, and SAB) were performed for pre-transplant workup. In the first case, CDC cross-match was negative and FCXM was positive for both T and B cells and in the second case CDC and B cell FCXM were negative; T cell FCXM was positive. DSA was identified in class I and class II in both cases. DSA allele matching at antigen and epitope level was performed. In both cases, epitope analysis revealed that antibody against DP locus was not DSA.

Both these patients had significant DSA in class I (case I - B*44:03 and case II - B*44:02) and class II (case I-DRB1*10:01; DPA1*02:01- DPB1*04:01 and case II DPA1*01:03-DPB1*06:01). Case 2 underwent desensitization by therapeutic plasma exchange (TPE) followed by retesting for median fluorescence intensity MFI. The patient (case 2) underwent successful renal transplant once MFI below 500[5] was achieved. However, what we would like the readers of journal know that if we had considered antigen-based analysis only and if these Class II (case I- DPA1*02:01-DPB1*04:01 and case II; DPA1*01:03-DPB1*06:01) were the only antibodies present in the recipient; it would have led to donor deferral. The epitope-based analysis resolved that DPA1*02:01- DPB1*04:01 in case I and DPA1*01:03-DPB1*06:01 in case II were not DSA and these patients could have undergone successful transplant even without TPE. India is a predominantly live-related transplant setting where only close relatives can be organ donors as per Transplantation of Human Organs and Tissues Act (THOTA) 2014.[6] To have a willing donor in the family, by itself is difficult and any unnecessary deferral would be catastrophic for the recipient and her/his family. It is in this light, that epitope-based analysis assumes even greater significance.

Table 1: HLA typing, pretransplant compatibility testing, and DSA on the basis of epitope matching.

		HLA typing					CDC	FCXM		DSA antigen matching				Epitope matching	Result after epitope analysis
								T	B	Class I			Class I		
		A	B	DR	DQA	DQB	DPA	DPB	-VE	+VE	+VE	Alleles	MFI	Alleles	
Case 1	Recipient	02,11	13,18	07,11	ND	ND	ND	ND				B*44:03	1018	DRB1*10:01	5349	B*44:03 (Epitope 162GLS) DRB1*10:01 (Epitope 13FE) DPB1*04:01 (Epitope 33EA)	1) No DSA in DP locus. 2) DSA found in B and DRB1 locus.
	Age/Sex Sensitization													DPA1*02:01-DPB1* 04:01	1930		
	47/F Yes																
	Donor	A	B	DR	DQA	DQB	DPA	DPB									
	Age/Sex Relationship	02,11	13,44	07,10	ND	ND	02,02	17,26									
	27/F Daughter																
Case 2	Recipient	A	B	DR	DQA	DQB	DPA	DPB	-VE	+VE	-VE	Alleles	MFI	Alleles	MFI	B*44:02 (Epitope 82LR + 145R) DPB1*06:01 (Epitope 84DEAV)	1) No DSA in DP locus. 2.) DSA found in B locus.
	Age/Sex Sensitization	02,11	13,18	07,11	ND	ND	ND	ND				B*44:02	1694	DPA1*01:03-DPB1 *06:01	3344		
	30/F Yes																
	Donor	A	B	DR	DQA	DQB	DPA	DPB									
	Age/Sex Relationship	02,02	40,44	15,15	01,01	06,06	01,01	02,04									
	54/F Mother																

CDC: Complement-dependent cytotoxicity cross-match; FCXM: Flow cytometry-based cross-match; DSA: Donor-specific antibodies

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Conflicts of interest

There are no conflicts of interest.

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