Relationship between HLA donor specific antibodies (DSAs) detected by complement dependent cytotoxicity (CDC), Luminex single antigen bead (SAB) and C1q assays, and antibody mediated rejection (AMR) and C4d deposition, in renal transplants

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Introduction

To evaluate the clinical significance of DSAs detected by CDC, SAB and C1q assays we examined the relationship between DSAs and biopsy findings, i.e. AMR and C4d staining. Samples from 37 renal recipients, taken close to biopsy, because of likely AMR, were tested by CDC using B-cells (with/without DTT), also Class I and II SAB (with serum EDTA pre-treatment) and the C1q assay (One Lambda).

Results

CDC detected DSA (Class II) in only one patient with biopsy proven AMR and C4d deposition. In contrast, SAB and C1q assays detected 55 (14 Class I, 41 Class II) and 16 (2 Class I, 14 Class II) DSA specificities, respectively (both covering HLA-A, -B, -C, -DR, -DR51/2/3,-DQ,-DP). Overall, HLA-DQ specificities predominated: 23/55(42%) by SAB; 13/16(81%) by C1q.

C4d deposition was significantly associated with biopsy proven AMR ($p < 0.001$). Eleven patients had biopsy proven AMR and C4d deposition. 82% (9/11) had DSA by the SAB assay but only 50% (5/10) had C1q binding DSA. Conversely, in the AMR and C4d negative group of 20 patients, 40% (8/20) had DSAs by the SAB assay and 1 patient had C1q binding DSAs – Table 1.

Table 1: No. of patients with DSAs detected by various assays and the occurrence of AMR and C4d deposition

Biopsy findings		CDC DSA		SAB DSA		C1q DSA*	
		Pos	Neg	Pos	Neg	Pos	Neg
AMR pos	C4d pos	1	10	9	2	5	5
	C4d neg	0	3	2	1	1	2
AMR neg	C4d pos	0	3	3	0	2	1
	C4d neg	0	20	8	12	1	16

*Four patients with invalid C1q results were not included in the C1q DSA analysis.

Conclusion

The C1q assay showed moderate sensitivity (46% and 54%) but high specificity (85% and 90%) for AMR and C4d deposition, respectively. In contrast, the SAB assay was more sensitive (79% and 86%) but less specific (52% and 57%) for both AMR and C4d deposition.

Importantly, no significant association was observed between DSA detected by the CDC, Luminex SAB and/or C1q assay and biopsy findings.