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Case Report Open Access

Successful Renal Re-transplant in a Patient with Alport Syndrome: A Case Report

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Abstract

This case report is of a sensitized patient with Alport syndrome, who received second kidney transplant from HLA-DQB1 incompatible living donor after excluding two unrelated donors. Four months after transplant he developed BK virus allograft nephropathy, from which he recovered and has excellent renal function-four years post-transplant. The findings highlight that HLA incompatible renal transplant can be performed successfully with prudent pre, and post-transplant evaluation complemented by suitable immunosuppression in sensitized recipients. It is presented on account of its rarity and is possibly the first documented case of re-transplant across a HLA-DQB1 barrier in India as defined by positive Luminex cross matches.

Keywords: Alport syndrome; Re-transplant; Luminex crossmatch; BK virus allograft nephropathy

Introduction

Alport syndrome is a rare heterogeneous group of X-linked (85%) or autosomal recessive (15%) disorder with a prevalence of 1:50000, which affects the glomerular basement membrane and most patients require renal replacement therapy [1,2]. Luminex crossmatch (LXM) has been used successfully for both pre and post -transplant evaluation of kidney recipients, including for monitoring response to immunosuppressants [3]. Here we report a case of HLA incompatible retransplant in which the recipient developed BK virus nephropathy but could be salvaged with prudent titration of immunosuppression and now four years post-transplant has normal serum creatinine.

Case Report

The 45-year-old male patient was one of six affected male children in extended joint family, first became symptomatic at the age of six years and received first renal transplant at the age of 24, years which functioned for 20 years.

Category	Test/ Method	Date	HLA-Class I	HLA-Class II	Remarks
Donor 1	R-SSO	26/05/12	A*24,*33; B*44,*57	DRB1*07	DQB1 not typed
Cross match	CDC	June-2012	T and BCXM negative	-	-
-	Luminex (MFI)	17/12/12	918	923	CDXM-negative
-	Luminex (MFI)	08/05/13	1144	663	Donor excluded
SAB & PRA ID I	Class I (MFI)	26/09/12 09/05/13 27/02/14	A24-DSA 3711 A24-DSA 11613 A24-DSA 8788	DRB1*07 negative Not done	Rise in DSA MFI PRA ID(I) -4237 Jan 14
Donor 2	CDC	20/05/13	A29,-; B7,-Bw6;Cw-	DR10, 15; DR51	No repeat SAB Class II
HLA typing	CDC	12/06/13	A29,-; B7,40,-Bw6;Cw-	Not done	Donor excluded
Crossmatch	CDC	11/06/13	TCXM negative	BRXM weak positive	(After donor exclusion)
PRA ID I	Luminex (MFI)	22/06/13	353	6420	DR15 3542, DR51 3127

Table 1: HLA typing and antibody workup for two rejected donors.

None of the female siblings had any disease manifestation. He was on maintenance haemodialysis for four years before a suitable donor was identified. Comprehensive immunogenetic evaluation including Human Leukocyte Antigen (HLA) typing on multiple samples and extensive antibody workup was carried out (Table 1).

Methods

The third donor was typed for eight loci (HLA-ABCDRB1DQA1DQB1DPA1DPB1) by reverse SSO (LIFECODES HLA SSO). HLA-ABDRB1 typing of the recipient was carried out by reverse-SSO. Additional typing for HLA-C and -DQB1 alleles was done on a second sample. Verification typing for eight loci was carried out HLA-ABCDRB1DQA1DQB1DPA1DPB1 on an additional sample in another laboratory, and all results were concordant. CDC crossmatch which was outsourced was performed, against all the three donors, by augmented Anti Human Globulin method. LXM was performed against all three donors as mentioned previously [3]. Phenotype bead assay was done for both HLA-Class I and II in Dr Lal Path Labs.

Results

HLA typing results of the donors and patient along with antibody profile are shown in Tables 1 and 2. Class I/II percentage panel reactive antibody (PRA) of 62/75% as detected by Luminex phenotype assay (LIFECODES Class I and Class II ID). CDC crossmatch was negative, against the first donor, but LXM tested positive for Class I and II donor specific antibodies- the former was substantiated by single antigen bead assay leading to exclusion of the first donor. DSA was detected against the second donor by CDC crossmatch which was weakly B-Cell positive and strongly positive for Class II antibodies by LXM (LIFECODES DSA) leading to exclusion of the second donor (Table 2).

SAB assay was done for the first time in 2012. It showed DSA against first donor (A 24-MFI 3711; 2nd donor (DR15 MFI 1080); and against third donor (DQ5 MFI 14-19000). HLA-class II reactivity was directed against DQB1 except anti DQ2. Repeat SAB class I assay done in 2013 showed nearly threefold rise in MFI against donor allele A24. SAB class I was again tested in May 2014 also corroborated strong reactivity against HLA-A24 (Table 2).

It is not possible to evaluate the cumulative DSA against the first two donors as HLA-DQB1 typing of donors was not done and one can comment only on the basis of DRB1- DQB1 association. SAB class I and PRA specification (class I and II) indicate that there was a change in the donor's reactivity pattern which was no correlated with the class II SAB assay. The PRA class II phenotype bead assay showed DSA against second donor HLA-DRB1 alleles (Table 1) which explains the strongly positive LXM result.

Test	Method	Date	Class I	Class II
Recipient	R- SSO	17/04/13	A*02,*03;*18,*40	DRB1*07,*11
HLA Typing	SSP	24/07/13	C*12	DRB1*07,*11: DRB3, DRB4,DQB1*02,*03
Recipient HLA Typing	R- SSO	07/03/14	A*02,*03;*18,*40	DOA1*02:01,*05:;DQB1*02:02,*03 DPA1.01:03,*02:01;DPB1*04:01,*26:01
Donor 3 HLA Typing	R- SSO	07/03/14	A*02,*33;B*44,*50 C*06,07	DRB1*01,1*07,DRB4 DQA1*01,*02:01;DQB1*02;02*05 DPA1*01:03,-;DPB1*02:01,*04:02
Crossmatch	CDC-AHG	27/02/14	B & T cell negative	-
Cross-match (MFI)	Luminex	27/05/13	151	577
-	Luminex	27/02/14	499.5	733
-	Luminex	12/06/14	210	346 (post Bortezomib addition).
Post-transplant	Luminex	17/07/14	130	452
SAB- DSA (MFI)	Luminex	27/02/14	Negative (<self)	Not done

Table 2: HLA typing results of recipient 3rd donor and antibody workup.

Serial evaluation for DSA was done on basis of LXM with the third donor who was initially weakly positive even though the recipient had received plasmapheresis and potent immunosuppression. On addition of Bortezomib he became LXM negative and LXM is negative on post-transplant follow up. No features of rejection were seen on allograft biopsy which showed non-specific interstitial inflammation without evidence of tubular necrosis. Patient initially tested positive for viremia but later became negative although viriuria still persists.

Immunosuppression

Desensitization protocol included Bortezomib, Campath and Rituximab in addition to plasmapheresis. He developed BK Virus nephropathy in the allograft after four months post-transplant, which improved with lowering of immunosuppression. Maintenance drugs include Leflunamide (20 mg), Wysolone (5 mg) in single daily dosage and Pan graph (1 mg) twice daily. At four years post-transplant, the recipient has excellent renal function and continues to be DSA negative.

Discussion

Unlike in United Kingdom, there are no laid down guidelines for pre-transplant evaluation of prospective renal recipients in India [4]. At the time of this patient's work up SAB test had been commenced in very limited centres in the country and they probably had limited experience, so was not used widely [5]. HLA-DQB1 typing was not performed for the first two donors in spite of the fact that HLA-Class II DSA was detected against all the donors on LXM and on phenotype assay. Some studies have suggested that LXM detects only HLA-IgG

directed against HLA-DRB1 alleles [6]. Our findings however suggest that it may detect anti DQB1 antibodies, if the reactivity is very high, as can be inferred by the reactivity against first and third donors. The recipient had no DSA against discrepant DRB1 antigen in the third donor but showed class II LXM positivity even after administration of strong immunosuppression in addition to plasmapheresis which became negative three days prior to transplant. HLA-Class II phenotype assay results showed MFI of 3129 against HLA-DQ5 which can explain positive LXM results.

In the only other available report of HLAi renal transplant from India the DSA MFI was less than 2500 for all three patients, who were first time recipients and responded to single dose of Rituximab with plasmapheresis and [7]. The first SAB class II MFI against mismatched DRB1 antigens of the second donor (DR10 and DR15) which was <1500 albeit with very strong reactivity against the likely mismatched DQ allele (DQ6 or rarely DQ5). The possibility of masked reactivity against mismatched DRB1 alleles is another possibility, which would have become apparent on adding EDTA or testing in dilution [8,9].

It is probably the first documented case of HLA incompatible renal re-transplant in India across HLA-DQB1 barrier. The other interesting aspect of this case is that even after BK Virus allograft nephropathy which was shown to be associated with graft loss in up to 46.1% of recipients and more likely in retransplants and with cytomegalovirus positivity as in the present patient [10]. At the time of submitting this case report the recipient has excellent renal function.

Conclusion

The case report is of a patient with Alport syndrome who received second renal transplant across HLA-DQB1 incompatibility as defined by positive pre-transplant LXM, went on to develop BK Virus allograft nephropathy from which he recovered and has excellent graft function.

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