SIGNIFICANT ALLOSENSITISATION DESPITE EARLY, WITHIN 24 HOUR, GRAFT NEPHRECTOMY

Gaetano Lucisano¹, Paul Brookes², Eva Santos-Nunez², Nicola Firmin², Nicola Gunby², Sevda Hassan¹, Alexander Gueret-Guardle¹, Michelle Willicombe¹, David Taube¹

¹ Renal and Transplant Centre, Imperial College Healthcare NHS Trust, London

² Histocompatibility and Immunogenetics, Imperial College Healthcare NHS Trust, London

INTRODUCTION

Allograft nephrectomy (NX) is a well recognised cause of HLA sensitisation after graft failure [1] and even after a short transplant period, donor specific antibodies (DSAs) and non-DSA anti-HLA antibodies develop immediately after NX [2, 3]. Patients who present with early kidney allograft loss are frequently candidate for retransplantation [4], and the presence of pre-formed DSAs is known to be associated with a poor kidney allograft outcome [5]. Currently there are no large studies investigating the class and tempo of DSA formation according to the timing of NX in a selected cohort of previously unsensitised patients with a first failed kidney graft.

AIM

This is a single centre, retrospective study aiming to investigate the short and long-term effects of NX performed at different times after the graft failure on HLA sensitisation and DSA formation.

METHODS

263/1,714 (15.3%) patients transplanted at our Centre between August 2004 and October 2015 lost their grafts and 106 underwent NX. Only patients returning to dialysis after the failure of their first graft and without detectable DSA at the time of NX or transplant failure were included. Patients were divided into three groups according to the timing of the NX: within 24h from implantation (group I), 1-30days (group II) and >30days (group III) from transplant failure. Sera were taken for class I HLA (A/B/Cw) and class II (DR/DP/DQ) at the time of NX and after 3, 6, 12 and 24 months using the single antigen Luminex assay. A mean fluorescence intensity value of >1,000 was considered positive. Statistical analysis was performed using IBM SPSS Statistics ver. 20 and GraphPad Prism ver. 6.0.

RESULTS

63 patients were studied and assigned to the three groups (Table 1). We observed a rising prevalence of DSA positive patients with time in all groups (Figure 1). This was associated with an increasing breadth of HLA class I and II specificities with time in all groups, expressed as PRA% (Figure 3). Both class I and II DSA were produced. Surprisingly, Group I showed a higher rate of patients developing both class I and II DSAs at 6 months (p=0.03, Figure 2), which seemed to be linked to a higher prevalence of class II DSA positive patients compared with the other two groups, although this did not reach the statistical significance (p=0.056). Eight patients in the Group I did not receive induction immunosuppression. These patients were compared with a subgroup of patients (n=9) who underwent graft NX within 7 days after implantation and received induction. No difference in the rate of DSA production was detected.

Table 1	<24 hours (N=13)	1-30 days (N=27)	>30 days (N=23)	p
Female (%)	15.4	44.4	33.3	0.192
Pre-emptive (%)	23.1	25.9	19.0	0.854
Live-donor (%)	30.8	44.4	47.6	0.607
Alemtuzumab (%)	30.8	77.8	71.4	0.011
No steroids or MMF after Nx	11/13 (84.6)	17/27 (63.0)	7/23 (30.4)	0.002
Steroids alone after Nx	2/13 (15.4)	7/27 (25.9)	16/23 (69.6)	
Steroids + MMF after Nx	0/13 (0.0)	3/27 (11.1)	0/23 (0.0)	
Pre-Tx RRT, months	25.5 (0.1-91.2)	16.8 (0.0-77.6)	18.1 (5.2-47.7)	0.732
Tx vintage, days	0 (0-0)	26 (9-513)	956 (615-1,447)	<0.001
Nx timing after failure, days	0 (0-0)	0 (0-4)	265 (86-360)	<0.001
IS stopped at the time of Nx (%)	92.3	77.8	75.0	0.443
Rejection in Nx (%)	0.0	40.7	71.4	<0.001
NHSBT MM:				0.801
«000»	7.7	7.4	4.8	
«Favourable»	61.5	70.4	81.0	
«Unfavourable»	30.8	22.2	14.3	
Total MM, median	3 (3-4)	3 (2-4)	3 (2-4)	0.964

CONCLUSIONS

In our cohort of previously unsensitised patients undergoing NX of their first failed graft, even a very brief exposure to the allograft led to the early production of DSAs and significant sensitisation despite monoclonal antibody induction, which persisted up to 24months. Our data suggest that NX performed within 24h after implantation might be a particularly strong immunogenic event resulting in a more pronounced early development of class II DSA compared with late NX. This group of patients require further investigation and development of strategies to prevent sensitisation, particularly if they are suitable for retransplantation.

REFERENCES

[1] Khakhar AK et al, *Transplant Proc* 2003; 35: 862
[2] Leaners J et al, *Transplantation* 2006; 81: 614
[3] Del Bello A et al, *Transplantation* 2012;93:936-941
[4] Ojo A et al, *Transplantation* 1998;66:1651
[5] Lefaucheur et al, *American Journal of Transplantation* 2008; 8-324