

NK-cell subset distribution, renal function and biopsy findings in kidney transplant recipients with HLA donor-specific antibodies

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Background

Detection of post-transplant donor-specific anti-HLA antibodies (DSA) constitutes a risk factor for kidney transplant (KT) allograft loss. NK-cell antibody-dependent cell mediated cytotoxicity (ADCC) has been proposed to contribute to microvascular damage associated to antibody-mediated rejection (ABMR).

Aims

Assessment of peripheral NK-cell subsets in KT recipients with circulating HLA DSA and the potential relationship with clinical outcomes or histological changes.

Methods

Prospective cross-sectional study of 38 patients with HLA DSA compared with KT patients with HLA no DSA and with patients without antibodies. We collected information from the patients and performed studies.

- Clinical data
- Analysis of HLA antibodies (Luminex® screening & SAB)
- Peripheral CD3-CD56+ NK-cells IF (NKG2A, NKG2C, KIR, ILT2, CD161)
- Histological data

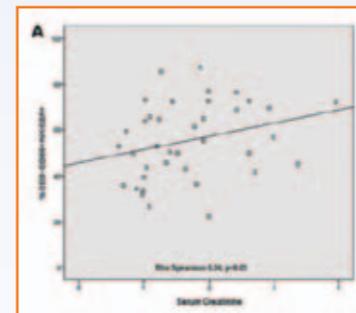
Results

Table 1: Clinical characteristics at study time of KT patients comparing those with DSA vs. HLA non DSA vs. no antibodies.

	No antibodies (n=300)	Anti-HLA non-DSA (n=55)	Anti-HLA DSA (n=38)	p ₁	p ₂	p ₃
Creatinine (mg/dL) (mean ± SD)	1.5 ± 0.6	1.6 ± 0.8	1.7 ± 0.8	0.19	0.82	0.17
MDRD-4 eGFR (mL/min) (mean ± SD)	54.9 ± 20.6	45.7 ± 18.1	51.6 ± 26.3	0.002	0.2	0.46
Urinary protein:creatinine (mg/mg) (median, IQR)	158 (94.8-158)	183.6 (83.8-404.9)	238.2 (105.5-463.6)	0.58	0.247	0.05
Steroid treatment (%)	53%	63.6%	68.4%	0.14	0.63	0.07
Tacrolimus treatment (%)	77.7%	80%	65.8%	0.7	0.12	0.1
Cyclosporine treatment (%)	9.3%	10.9%	13.2%	0.71	0.74	0.45
mTOR inhibitors treatment (%)	8.3%	3.6%	15.8%	0.32	0.06	0.13
Mycophenolic treatment (%)	78.8%	72.7%	78.9%	0.4	0.49	0.98
Follow-up months after tests: median (IQR)	21 (8-27)	21 (8-25)	21 (18-24.2)	0.46	0.49	0.16
Graft loss at last followup (death censored)	3%	7.3%	13.2%	0.12	0.47	0.008

p₁, p-value for statistical differences between No antibody and anti-HLA non-DSA;
p₂, p-value for statistical differences between anti-HLA non-DSA and DSA;
p₃, p-value for statistical differences between No antibody and DSA groups.

Figure 2. Correlation of creatinine and NKG2A% cells



Conclusions

Our study shows that the percentage of circulating NKG2A cells in KT recipients with DSA correlate with graft function and histological damage, thus probably selecting a subgroup of patients with stronger histological injury or different mechanisms of graft damage.

Figure 1A. NK cells in KTr with DSA vs. HLA non DSA vs. no antibodies

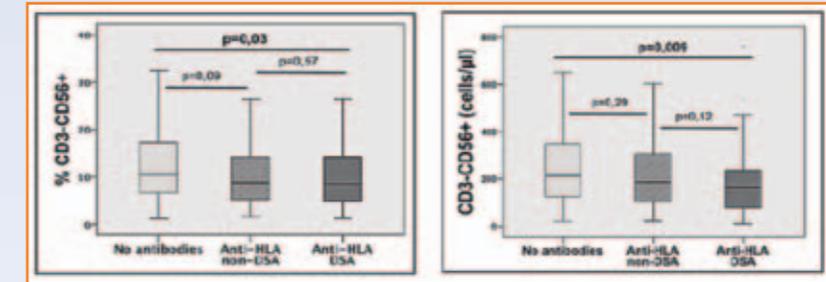
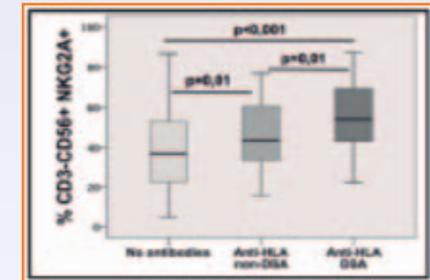
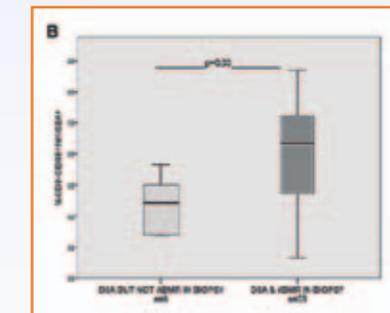
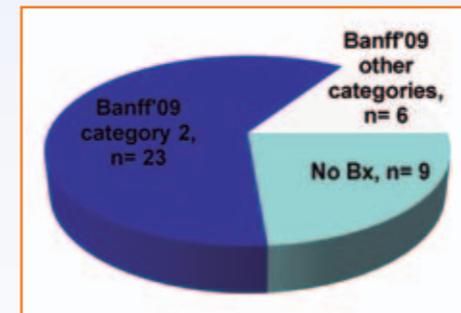


Figure 1B. Analysis of NK subpopulations showed that NKG2A% is significantly higher in DSA KT than HLA no DSA KT and than KT without HLA antibodies.



Figures 3 and 4: Biopsies in DSA patients and relationship of Bx findings and NKG2A%.



References

1. Haas et al. AJT 2014.
2. Hirohashi et al. AJT 2012.

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