CMV-specific T Cell Response and eGFR identify Patients at High Risk of Infection after Renal Transplantation

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INTRODUCTION AND OBJECTIVES

Assessing the risk of Cytomegalovirus (CMV) viremia in kidney transplant recipients (KTR) may be helpful to indicate in which patient it is worth to start antiviral treatment during preemptive strategy.

THEREFORE, WE EVALUATED WHETHER MONITORING T CELLS DIRECTED AGAINST PP65 AND IE-1 ANTIGENS, COULD PREDICT THE ONSET OF VIREMIA.

METHODS

In 40 consecutively CMV-seropositive KTR preemptively treated with ganciclovir, we used IFN-γ Elispot to measure CD4+ and CD8+ anti-CMV specific T cells at 30, 90, 180 and 360 days after transplantation. CMV DNAemia was monitored to identify viral infection.

RESULTS

Baseline characteristics are showed in Table 1. CMV viremia occurred in 24 patients (60%) within 120 days after transplantation, so time points used for viral infection prediction were 30 and 90 days.

Non-viremic patients had higher anti-pp65, anti-IE-1 T cells and eGFR in the first 90 days post-transplantation (Figure 1). Early CMV specific immune response was significantly correlated to CMV DNAemia and eGFR.

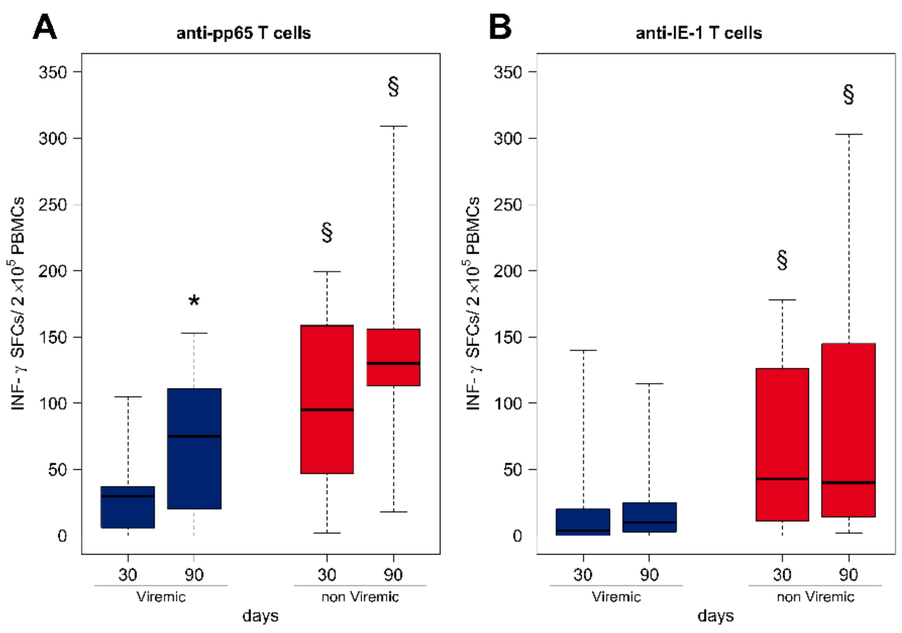
At logistic regression anti-pp65, anti-IE-1 T cells and eGFR measured at 30th day were significantly associated to CMV infection (OR: 0.33, 0.32, 0.03 respectively). Cut-off values of 15 SFCs/200000 PBMCs for anti-IE, 40 SFCs/200000 PBMCs for anti-pp65 and 46.6 ml/min/1.73m2 for eGFR respectively predicted the risk of CMV infection with high sensitivity and specificity (AUC > 0.75).

Using a classification tree model we identified as high-risk patients, those showing anti-pp65 < 42 SFCs/200000 PBMCs and eGFR < 62 ml/min/1.73m2 as well as anti-pp65 ≥ 42 and anti-IE-1 < 6.5 SFCs/200000 PBMCs (Figure 2).

Table 1. Main demographic and baseline characteristics of the study group.

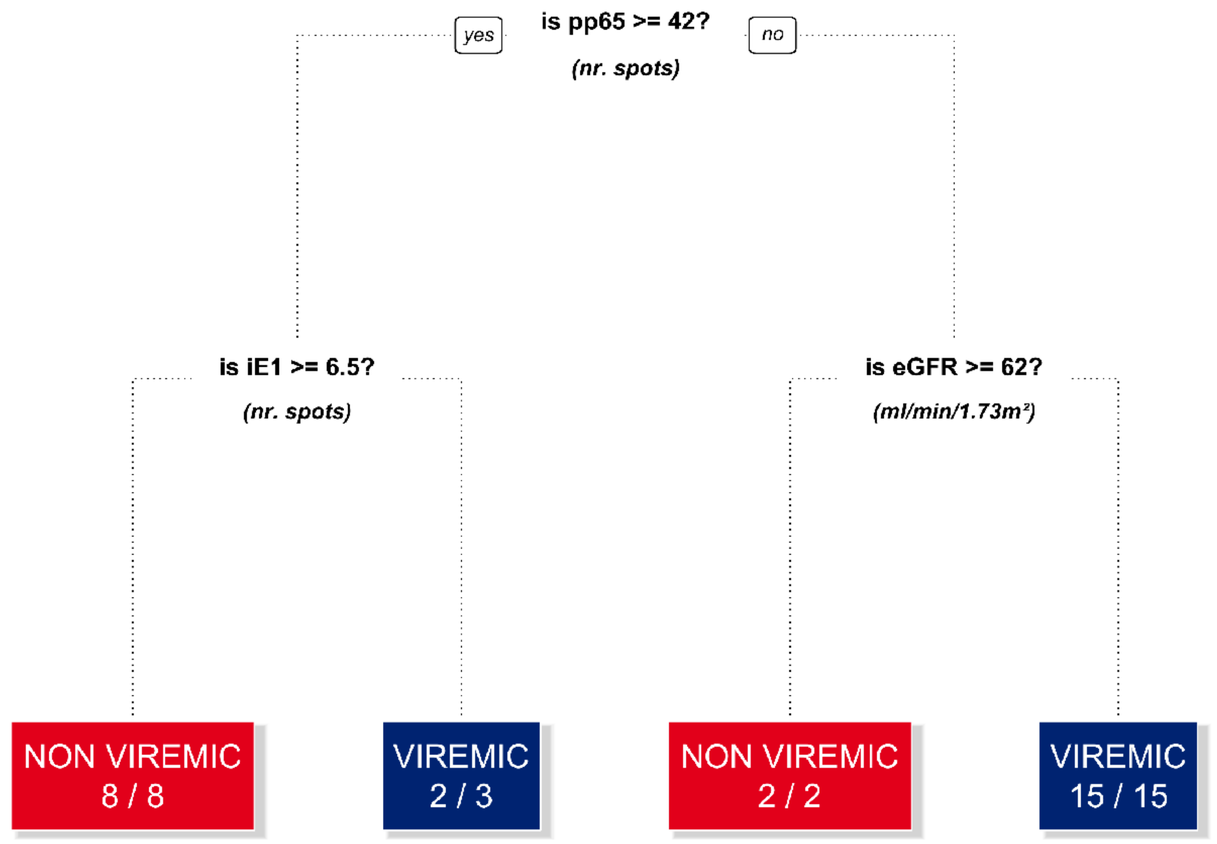
Characteristics	Patients (n=40)
Gender (male/female)	23/17
Age (years)	49 ± 12.16
Donor Age(years)	46.9 ± 12.9
eGFR (ml/min/1.73m²)	53.4 ± 17
DGF (%)	19/40 (47.5
Mismatches ≥ 4 (%)	25/40 (62.5)
BPAR (%)	10/40 (25)
CMV D/R serostatus	
D+/ R+ (%)	27 (67.5)
D-/ R+ (%)	13 (32.5)
Pre-Transplant anti-CMV IgG titers (UA/ml)	190.7 ± 81
CIT (hours)	13.1 ± 4.59
Maintenance Immunosuppression	
FK (%)	34/40 (85)
CsA (%)	6/40 (15)
Post-Transplant CMV DNAemia (%)	24/40 (60)
Antiviral treatment (%)	17/40 (42.5)
CMV disease (%)	3/40 (7.5)

Figure 1. CMV-specific T cell responses at 30 and 90 days after transplantation in viremic and non viremic KTR.



* p < 0.01 vs 30 days. § p < 0.01 vs viremic.

Figure 2. Classification tree for the onset of CMV viremia in the 1st year after transplantation.



CONCLUSIONS

THE HIGH LEVELS OF CD4+/CD8+ CMV-SPECIFIC T-CELLS OBSERVED 6 MONTHS AFTER TRANSPLANTATION, ASSOCIATED WITH A LOWER INCIDENCE OF VIRAL REACTIVATION, INDICATE THE NEED OF AT LEAST 6 MONTHS FOR THE RECONSTITUTION OF CMV-SPECIFIC IMMUNITY.

MONITORING IE-1 CMV-SPECIFIC T-CELL FREQUENCIES AFTER TRANSPLANTATION WOULD HELP TRANSPLANT PHYSICIANS TO GUIDE PREEMPTIVE ANTIVIRAL TREATMENT.

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