Role of cell-mediated immune monitoring using Interferon-γ Enzyme-linked Immunosorbent Spot Assay to predict CMV infection within six months after kidney transplantation

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INTRODUCTION

- CMV infection can cause substantial morbidity and mortality in kidney transplant (KT) recipients due to an impairment in cell-mediated immunity (CMI) from immunosuppressive drugs

AIMS

- To investigate the role of CMI monitoring prior to and after transplant to predict CMV infection after KT

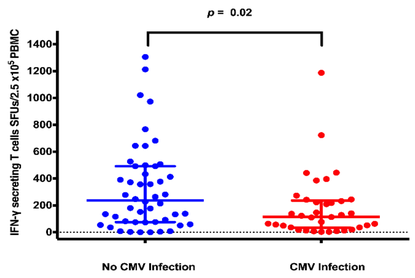
METHODS

- A prospective study was performed between December 2020 and December 2021
- All adult KT recipients underwent CMI measurement by investigating IFN-γ-producing T cells using enzyme-linked immunosorbent (ELISpot) assay before and one month post-transplant
- The incidence of CMV infection within six months after transplant was reported, and predictors of CMV infection were analyzed using the Cox proportional hazard model

RESULTS

- We included 93 KT recipients with a mean (SD) age of 44 (11) years; 59.1% were male, and 98.9% were CMV seropositivity
- Twenty-two (23.7%) participants received anti-thymocyte globulin (ATG) for induction therapy
- A median (IQR) of IFN-γ-producing T cells measured one month after transplant was significantly lower compared to before transplant (148 [54-389] vs. 763 [409-1,067] SFUs per 2.5 x 10^5 PBMCs, p <0.001)

Figure IFN-γ ELISpot distribution plots in KT recipients with and without CMV infection



- Forty (42.9%) KT recipients who developed CMV infection had less IFN-γ-producing T cells compared to those did not develop CMV infection (47.1%) (115 [33-237] vs. 238[76-492] SFUs/2.5x10^5 PBMCs, p=0.019)
- In univariate analysis, predictors for CMV infection included higher panel-reactive antibody (HR 1.02 [95%CI, 1.01-1.03], p<0.001), ATG induction therapy (HR 3.45 [95%CI, 1.82-6.56], <0.001) and lack of CMI one month after transplant; IFN-γ-producing T-cells of <250 SFUs/2.5x10^5 PBMCs (HR 3.11 [95%CI, 1.36-7.10], p=0.007)
- In multivariate analysis, lack of CMI one month after transplant remained independently associated with CMV infection (HR 3.1 [95%CI 1.2-7.80], p=0.019)

Table Factors associated with infection in KT recipients

Factors	Univariate analysis			Multivariate analysis		
	HR	95%CI	P-value	HR	95%CI	P-value
Female sex	0.72	0.37-1.39	0.326			
Age	1.03	1.00-1.06	0.087			
BMI	1.03	0.95-1.12	0.484			
Hypertension	1.58	0.62-4.03	0.342			
Diabetes mellitus	1.19	0.46-3.04	0.721			
Hyperparathyroidism	1.19	0.61-2.32	0.606			
DDKT	2.01	0.89-4.56	0.095			
Retransplantation	1.79	0.64-5.05	0.270			
HLA mismatch	0.99	0.76-1.28	0.923			
PRA	1.02	1.01-1.03	<0.001	1.01	0.99-1.03	0.572
Anti-thymocyte globulin for induction therapy	3.45	1.82-6.56	<0.001	4.20	0.87-20.22	0.074
ALC at 1-month posttransplant ≤ 500 cells/mm^3	1.68	0.74-3.81	0.215			
IFN-γ ELISpot at 1-month posttransplant < 250 SFUs/2.5x10^5 PBMCs	3.11	1.36-7.10	0.007	3.06	1.20-7.80	0.019

CONCLUSIONS

✓KT recipients with low IFN-γ-producing T cell responses are more likely to develop CMV infection post-transplant

✓ Quantification of CMI using ELISpot assay could potentially predict those at risk of CMV infection after KT

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