In the name of God

Evaluation the prevalence of Cytomegalovirus glycoprotein B genotypes in kidney transplant patients in IRAN

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Introduction

Cytomegalovirus (CMV) is a DNA virus belongs to Herpes virus family. CMV infection continues to be a major clinical problem after solid organ transplantation with a significant morbidity and mortality. Although gancyclovir and related drugs reduce almost 50-70% of CMV disease incidence and its mortality, the toxicity associated with currently antiviral agents remains a significant problem. research has shown that the presence of only one CMV strain compared with more than ones, in the first year after transplantation in these patients is associated with different clinical outcomes.Previous study have been shown that immune response against CMV may strongly depend on the virus strain And re-infection with another strain may be completely clinically different from relaps of first strain. For example it has been demonstrated that mixed CMV-strain infection in organ transplant patients could associate with more transplant rejection, delayed virus clearance from blood and faster disease development.

Introduction

CMV strains classification usually is done based on virus glycoprotein B (gB) genotype which could be done by either sequencing or restriction fragment length polymorphism (RFLP).

We designed this work regards to that no study has been done yet in our country to evaluate the most prevalent CMV genotype strains in CMV-infected renal transplant patients. We also correlated different demographic as well as clinical characteristics of the patients to such genotypes.

Methods and materials

80 kidney transplant patients were randomly chosen from all 400 ones in 2014 at Baqiyatallah hospital which is a referral hospital for kidney transplantation in Iran. Such sample size had statistically enough power to answer proposed questions.

All of the patients consecutively and as a routine program were monitored every 1-2 weeks for CMV infection through immunofluorescence. Serum of all infected patients evaluated through RFLP to identify the four genotypes of gB1, gB2, gB3, and gB4 according to their specific pattern

All the patients were recipient and donor CMV negative and were followed up to 6 months after transplantation.

Statistical analysis

The results were expressed as mean ± SD. The groups were compared by chi-square and ANOVA tests. Normality test was performed for the examined variables. Pearson and Spearman rho coefficient was determined to correlate between the variables with normal and non-normal distribution, respectively. P values less than 0.05 were considered significant. All analyses were made by the SPSS 18 package

Results

From all 80 renal transplant recipients, 34 (48%) patients showed CMV infection during 6 months. The most infection rate with CMV happened during the first and second month (11% and 9%, respectively).

Table 1: the prevalence of gB genotypes in CMV infected patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	12	35.3	35.3	35.3
	2	5	14.7	14.7	50.0
	3	6	17.6	17.6	67.6
	4	6	17.6	17.6	85.3
	mix	5	14.7	14.7	100.0
	Total	34	100.0	100.0	

gB1 was the most common (35.3%) and then, gB3 and gB4 (each with 17.6 %), gB2 and mix including gB1,3 and gB1,2 (each with 14.7%) were placed in further lines (Table 1).

Table 2: The frequency of different variables according to gB CMV genotypes

		gB					
		1	2	3	4	mix	P
		Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	
Sex	female	5(41.7)	3(60)	3(50)	3(50)	3(60)	0.968
	male	7(58.3)	2(40)	3(50)	3(50)	2(40)	
Age	Mean±SD	12(35.3) 47.58±7.82	5(14.7) 39.4±5.64	6(17.6) 49.33±11.13	6(17.6) 34.17±8.18	5(14.7) 43.60±13.32	0.037
Time of infection	Mean±SD (months)	4.67±1.44	2.60±2.19	3.67±1.63	2.33±1.03	1.80±1.79	0.011
BK	no	11(91.7)	4(80)	4(66.7)	5(83.3)	4(80)	0.897
	yes	1(8.3)	1(20)	2(33.3)	1(16.7)	1(20)	
UTI	no	58.3	3(60)	3(50)	2(33.3)	0(0)	0.240
	yes	5(41.7)	2(40)	3(50)	4(66.7)	5(100)	

Table 2: The frequency of different variables according to gB CMV genotypes

		gB					
		1	2	3	4	mix	P
		Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	
Respiratory infection	no	6(50)	2(40)	5(83.3)	3(50)	2(40)	0.606
	yes	6(50)	3(60)	1(16.7)	3(50)	3(60)	
Rejection	no	11(91.7)	2 (40)	5(83.3)	2(33.3)	1(20)	0.012
	yes	1(8.3)	3(60)	1(16.7)	4(66.7)	4(80)	
Family relation	no	8(66.7)	4(80)	2(33.3)	5(83.3)	3(60)	0.432
	yes	4(33.3)	1(20)	4(66.7)	1(16.7)	2(40)	

Evaluating the frequency of different variables according to gB CMV genotypes, we found that rejection showed a significant relationship to gB strains (P: 0.012) (Table 2) in such a way that the most and least transplantation rejection happened in gB mix (80%) and gB1 (8.3%) groups, respectively. The relationship between CMV gB genotype and age (P=0.037) as well as the time of genotype incidence after transplantation (P=0.011) was also statistically significant (Table 2).

Table 3: Adjusted association of different variables with different CMV genotypes

Genotype	Variable	B	SE	Wald	Sig.	OR
gB1	Sex	-0.393	0.629	0.390	0.532	0.675
	Age	.0480	0.030	2.527	0.112	1.049
	Family relation	1.417	0.714	3.938	0.047	4.126
	HLA mismatch	0.806	0.326	6.101	0.014	2.240
gB2	Sex	-1.317	1.007	1.708	0.191	0.268
	Age	-0.062	0.059	1.076	0.300	0.940
	Family relation	0.505	1.273	0.157	0.692	1.657
	HLA mismatch	0.738	0.482	2.350	0.125	2.093
gB3	Sex	-1.158	0.996	1.351	0.245	0.314
	Age	0.066	0.042	2.489	0.115	1.069
	Family relation	2.838	1.109	6.546	0.011	17.087
	HLA mismatch	0.671	0.516	1.694	0.193	1.957

Table 3: Adjusted association of different variables with different CMV genotypes

Genotype	Variable	B	SE	Wald	Sig.	OR
gB4	Sex	-1.899	1.103	2.962	0.085	0.150
	Age	-0.177	0.075	5.534	0.019	0.838
	Family relation	0.163	1.231	0.018	0.895	1.177
	HLA mismatch	0.804	0.444	3.281	0.070	2.234
mix	Sex	-0.883	0.941	0.880	0.348	0.414
	Age	-0.002	0.047	0.001	0.972	0.998
	Family relation	1.124	1.051	1.144	0.285	3.078
	HLA mismatch	0.343	0.459	0.560	0.454	1.410

Adjusting the association of different variables with different CMV gB genotypes, we showed that some variables have a significant relationship to some gB genotypes. Such relationships include family relation (P=0.047) and HLA mismatch (P=0.014) with gB1, family relation with gB3 (P=0.011), and age with gB4 (P=0.019)(Table 3).

Discussion:

In the study of Madi and colleagues on 42 renal transplant recipients infected with CMV, gB1 was the most the predominant CMVgenotype and then gB2 and gB3 (59%, 29% and 10%)in Kuwait (17)Pang and colleagues observed In 121 plasma specimens from 47 solid organ transplant recipients gB1 was the predominant genotype followed by gB2,mixed gB, gB3 and gB4 (18).

In our study, we evaluated 80 renal transplant recipients that 34 cases were infected with CMV of which gB1 was the most common (35.3%) and then, gB3 and gB4 (each with 17.6 %), gB2 and mix including gB1,3 and gB1,2 (each with 14.7%) were placed in further lines. As the results of studies show that the most common genotype is identical, but the second and third rank in our country is different, even in contrast with neighboring Kuwait, which is probably due to racial differences.

Discussion:

In Madi study also demonstrated that gB1 genotype were significantly more often associated with the development of fever with leukopenia and severe CMV disease than other gB genotypes (17). In a study by Rosen and colleagues on 53 patients receiving liver transplants that had CMV infection showed that genotype (in this study gB1) had significatly higher mean number of acute rejection episodes but not related to rejection severity. (19).In contrast Sarcinella in a research on 58 liver transplant recipients with CMV infection showed that gB genotype did not correlate with peak CMV viral load and with the development of CMV disease or acute rejection (20).

In our study among UTI, respiratory infection, gender,familial relation and rejection only rejection showed a significant relationship to gB strains (P: 0.012). The relationship between CMV gB genotype and age (P=0.037) as well as the time of genotype incidence after transplantation (P=0.011) was also statistically significant . Adjusting the association of different variables with different CMV gB genotypes, we showed that family relation (P=0.047) and HLA mismatch (P=0.014) with gB1, family relation with gB3 (P=0.011), and age with gB4 (P=0.019) had a significant relation.

In conclusion, UTI, respiratory infections, HLA mismatch and family relation between donor and recipient, were risk factors for CMV infection. In our study the most common CMV gB genotype was gB1. age and the time of genotype incidence after transplantation was associated CMV gB genotype and althuogh CMV infection was not an independent risk factor for rejection but in patients infected with CMV, CMV gB genotype was associated with transplant rejection.

Thanks for your attention