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Research Article

BK virus in kidney transplantation: A single center experiences

Abstract

Background: BK virus is the most common infectious causes of nephropathy and graft loss after kidney transplantation. In our study, we investigated the factors that may affect positive BK virus in the blood in patients with kidney transplantation.

Material and method: Between April 2014 and April 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 30 patients with positive BK virus in urine after kidney transplantation were studied retrospectively. In these patients were divided into two groups; Group 1: Patients with BK virus positive in the blood. Group 2: Patients with BK virus negative in the blood. Between these two groups, factors that may affect positivity in blood were compared.

Results: The mean age was 37.1±16.1 years. 21 (70%) patients were male and 9 (30%) patients were female. During follow-up, there were 16 (53.3%) patients with BK virus positive in the blood. BK virus positive in the blood was statistically significantly more common in patients given high dose immunosuppressive therapy due to acute rejection (p:0.021).

Conclusions: BK virus in the blood appears to be more common in patients given high dose immunosuppressive therapy.

Introduction

The only definitive treatment of end-stage kidney disease is kidney transplantation [1]. BK virus is the most common infectious cause of nephropathy and graft loss after kidney transplantation [2]. The most important risk factor known is high dose immunosuppressive therapy. Also, older age, male sex, HLA mismatches, ischemic injury, acute rejection episodes are other risk factors [3]. BK virus is seen first urine. End organ damage is nephropathy developing after viremia [2]. Reduction of immunosuppression is the key point of BK virus Treatment [4].

In this study, we investigated the factors that may affect positive BK virus in the blood in patients with kidney transplantation.

Material and Method

Between April 2014 and April 2017 at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey, 30 patients with positive BK virus in urine after kidney transplantation were studied retrospectively. In these patients were divided into two groups; Group 1: Patients

with BK virus positive in the blood. Group 2: Patients with BK virus negative in the blood. Between these two groups, factors that may affect positivity in blood were compared.

Immunosuppression

All patients received quadruple sequential immunosuppression consisting of induction with ATG, followed by triple immunosuppressive therapy. All this patients were given ATG at the intraoperative period and continues postoperative 2 days. The patient will be used as a standard immunosuppressive therapy for life-long calcineurin inhibitors (tacrolimus or cyclosporine). Targeted tacrolimus level was between 8-10 nanogram/milliliter (ng/mL). Targeted cyclosporine a level was between 100 and 200 nanogram/ milliliter (ng/mL).

Mycophenolate Mofetil or Mycophenolate Sodium to be used in the first year, Prednisolone to be used in the first third months.

Follow up protocol

Patients received control once a week for the first month after discharge, and once every 15 days for the second month and monthly for the following months.

BK virus was looked from urine + blood at each control (BK PCR-DNA). A positive urine test (Viruria) was defined as urine BK PCR-DNA count of ≥ 25 million copies/mL. A positive blood test (viremia) was defined as blood BK PCR-DNA count of 1000 copies/ml.

In patients with BK virus positive in the only urine, the only we reduced immunosuppressive drug (Tacrolimus or cyclosporine A) dose. Whereas in patients with BK virus positive in the urine + blood, we reduced immunosuppressive drug (Tacrolimus or cyclosporine A) dose and we started Levofloxacin. In these patients, Levofloxacin was given 2×500 mg ten days.

In patients with BK virus-positive, targeted tacrolimus level was less than 6 nanograms/ milliliter (ng/mL) and targeted cyclosporine A level was less than 80 nanograms/ milliliter (ng/mL).

Statistical analysis

SPSS 22.0 (SPSS for Windows, 2007, Chicago) was used for statistical analysis. Continuous variables which have normal distribution were presented as mean \pm Standard deviation. Statistical analysis for the parametric variables was performed by the Student's T-test. The qualitative variables were given as percent and the correlation between categorical variables was investigated by the chi-square test and Fisher's exact test. Statistical significance level was defined as $p < 0.05$.

Results

Mean age of the patients with BK virus positive in the blood were 33.5 ± 17.6 years, in patients with BK virus negative in the blood were 41.1 ± 13.5 years ($p: 0.327$). There were ten (62.5%) males and six (37.5%) females in patients with BK virus positive in the blood, there were eleven (78.5%) males and three (21.5%) females in patients with BK virus negative in the blood ($p: 0.355$).

The indications for kidney transplantation were; 11 (36.7%) patients had unknown, 8 (26.7%) had diabetes mellitus, 5 (16.7%) had hypertension, 4 (13.3%) had chronic glomerulonephritis, 1 (3.3%) patient had polycystic kidney disease and 1 (3.3%) other causes (Alport syndrome, vesicoureteral reflux, etc.).

Mean body mass index of in patients with BK virus positive in the blood were 28.8 ± 6.8 kg/m², in patients with BK virus negative in the blood were 23.4 ± 4.9 kg/m² ($p: 0.326$).

Mean warm ischemia time of in patients with BK virus positive in the blood were 88.4 ± 20.6 seconds, in patients with BK virus negative in the blood were 91.3 ± 19.5 seconds ($p: 0.548$).

Mean cold ischemia time of in patients with BK virus positive in the blood were 52.5 ± 13.8 minutes, in patients with BK virus negative in the blood were 53.3 ± 12.8 minutes ($p: 0.476$).

The acute rejection rate was 31.2% (5 patients). In this patients, taken high dose immunosuppressive therapy (Methylprednisolone 5 mg/kg/day + ATG 2 mg/kg/day) for acute rejection. All these patients were in the group of patients

with BK virus positive in the blood ($p: 0.021$). In this group, a transplant kidney biopsy was performed in 4 patients with increased creatinine levels. All biopsy results were a recurrent acute rejection.

Mean follow-up was 26.1 ± 11 months. During follow-up, there was not developed BK virus nephropathy and graft loss in the group of patients with BK virus positive in the blood.

Table 1 shows comparison of positive BK virus in blood and negative BK virus in the blood.

Table 1: Comparison of BK Virus in Blood.

	BK Virus Positive in the Urine (n:30)		p
	BK Virus Positive in the Blood (n:16)	BK Virus Negative in the Blood (n:14)	
Age (Years)	33.5 \pm 17.6	41.1 \pm 13.5	0.327
Sex (Male/Female) (n/%)	10 (62.5%) /6 (37.5%)	11 (78.5%) /3 (21.5%)	0.355
Body Mass Index (kg/m ²)	28.8 \pm 6.8	23.4 \pm 4.9	0.326
Warm Ischemia Time (Second)	88.4 \pm 20.6	91.3 \pm 19.5	0.548
Cold ischemia Time (Minute)	52.5 \pm 13.8	53.3 \pm 12.8	0.476
Acute Rejection (n/%)	5 (31.2%)	-	0.021

kg: kilogram, m²: square meters.

Discussion

Kidney transplantation is the treatment of choice in patients with end-stage renal disease [1]. BK virus is an important risk factor for graft dysfunction and graft loss after kidney transplantation [2,5]. First human polyomavirus was seen in 1971 urine sample of a kidney recipient [6]. Subsequently, BK virus had exactly identified in 1995 with a made biopsy for evaluation of acute rejection after kidney transplantation [7].

BK virus is usually reactivated by immunosuppression. Viral shedding in the urine, viremia and finally result in tubulointerstitial nephritis [8].

BK shedding with urine can be seen in 20–60% of patients after kidney transplantation. Incidence of BK viremia is about 13%, the incidence of nephropathy is about 8% after kidney transplantation. Nephropathy can result in graft loss [9–14]. In our study, BK shedding rate was 30.6%, BK viremia rate was 16.3%. Also, there was not developed BK virus nephropathy and graft loss after BK viremia.

BK detection by of urine and blood BK DNA by PCR. Transplant kidney biopsy remains the gold standard for the diagnosis of BK virus nephropathy [15,16]. In our clinic, for the BK detection BK PCR-DNA (urine-blood) and transplant kidney biopsy was used.

The BK virus infections risk factors were included high dose immunosuppression, older age, male sex, number of HLA mismatches, ischemic injury, acute rejection episodes

[17,18]. In our study, the only risk factor was high dose immunosuppressive therapy for acute rejection. All these patients were in the group of patients with BK virus positive in the blood.

In our clinic, all patients received quadruple sequential immunosuppression consisting of induction with ATG, followed by triple immunosuppressive therapy. In our protocol, the ATG induction begins in the intraoperative period and continues postoperative 2 days. In patients whose *creatinine* levels are increasing (acute rejection suspect patient) additional 5 daily doses (1.5–2 mg/kg) of ATG was administered. Also, calcineurin dose was increased. The biopsy was performed in patients whose creatinine value did not decrease despite treatment. Reduction of immunosuppression is the key point of BK virus treatment [4]. Other treatment alternatives can include use of Leflunomide, Cidofovir, Fluoroquinolones (Ciprofloxacin, levofloxacin), Rapamycin or Intravenous Immunoglobulin [19–25]. In our study, in patients with BK virus positive in the urine, the only we reduced immunosuppressive drug dose. Whereas in patients with BK virus positive in the blood, we reduced immunosuppressive drug dose and we started Levofloxacin. Levofloxacin was given 2 × 500 mg ten days.

Through this treatment, there was not developed BK virus nephropathy and graft loss after BK viremia.

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

Conclusions

Despite the limitations described in discussion; Positive BK virus in blood was more common in patients given high dose immunosuppressive therapy due to acute rejection. Need to be more careful in these patients for BK virus nephropathy.

Author contributions

GE and TY collected, analyzed, interpreted the data, and wrote the manuscript. All authors read and approved the final manuscript.

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