

Urine Cytology: Useful Screening Method for Polyoma Virus Nephropathy in Renal Transplant Patients

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Abstract

Polyoma virus nephropathy occurs in 3% to 4% of renal transplant recipients, causing graft loss in 50% of cases. The objective of the present study was to explore the effects of age, sex, post-transplantation period and plasma creatinine levels on the polyoma virus infection in kidney transplanted patients. Urine samples were collected from 362 patients, centrifuged and microscopic slides prepared using Papanicolaou staining method. The slides then examined and decoy cells were identified in 96 (27%) patients. The prevalence of the infection increased with increased post-transplantation period and the age of the patients. Moreover, patients with positive decoy cells had more abnormal plasma creatinine levels than those with negative for such cells. In conclusion identification of decoy cells might be of value for the diagnosis of nephropathy, especially if the presence of such cells is accompanied with the elevated plasma levels of creatinine.

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Keywords • Polyoma virus • renal transplant • urine cytology

Introduction

Human polyoma viruses are the members of the papovavirus family which have a double strand DNA-genome.¹ The most known species of this kind are BK-virus (BKV), JC-virus (JCV) and Simian-virus (SV-40).² The documented worldwide rate of seroprevalance in adults is 60-80 percent.³ Primary infection, which has a flu-like course and occurs in childhood, is associated with urinary excretion of BKV in 4-6% of immunocompetent patients.³ Furthermore, BKV has been implicated in auto-immune diseases and in cancer.^{1,4}

BKV remains latent in urogenital tract and is rarely activated spontaneously. However, its reactivation is estimated to occur in 10-60% of immunosuppressed renal transplant patients, due to immunosuppressive therapy, which is accompanied by shedding of urothelial cells. BKV is recently recognized as a cause of severe renal allograft dysfunction and potential graft loss.⁵ The BKV-induced shedding can be detected in the urine of patients by the presence of cells containing viral inclusion bodies known as decoy cells.⁵ The objective of the present study was to examine the incidence of polyoma virus infection in renal transplant recipients, using the presence of decoy cells in their urine as a marker.

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Patients and Methods

The study was performed using 362 renal transplant recipients (241 males and 121 females) at Nemazee Hospital of Shiraz University of Medical Sciences. One thousand and eighty six urine samples (3 samples from each patient) were collected from the second early morning void using the clean catch midstream method. The samples were cytocentrifuged for five minutes, followed by the preparation of microscopic slides using Papanicolaou staining.

The slides were examined for the presence of decoy cells. Decoy cells were characterized by an increased nuclear volume, basophilic nucleus, condensed chromatin and perinuclear halo. Urine samples with more than one decoy cell and patients with at least one urine sample positive for decoy cells were considered as virus-positive. Renal function was also evaluated by measuring plasma creatinine at the time of urine cytology were also recorded. Plasma creatinine levels above 1.25 mg/dl for men and 1.1 mg/dl for women were considered abnormal.

Results

Decoy cells were observed in 96 patients (26.6%). The number and the rate of decoy cell occurrences were 72 (29.9%) in male and 24 (20%) female patients. Urine cytology for decoy cells was positive in five patients (12.2% of 41) within less than one month after transplantation. This positivity was seen in 18.5% of patients (10 of 54) during one to three months and in 15.4% of the patients (3 of 13) during 3-6 months, and after transplantation respectively. Urine cytology for decoy cells was positive in 96 patients. Seventy eight (31.2%) patients (n=253) with more than six months after transplantation were positive for decoy cells.

The numbers and rates of patients positive or negative for decoy cells stratified based on their ages are shown in Table 1. Urine cytology was most frequently positive in patients aging 40-49 (30.2%) and least for patients under 20 (17.6%). Twenty five (26%) of patients with positive urine cytology (n=96) had elevated plasma creatinine levels. However, for those with negative urine cytology (n=266), 36 (13.5%) patients had elevated plasma creatinine level.

Table 1: The number of patients with positive or negative for decoy cells stratified based on their ages.

Age (yrs)	Urine Cytology		Total
	Positive	Negative	
<20	6	28	34
20-29	26	76	102
30-39	25	66	91
40-49	29	67	96
>50	10	29	39

Discussion

The presence of decoy cells (26.6%) in kidney transplant recipients was similar to those previous reports showing the presence of decoy cells in 20-40% of patients.^{5,6} Similarly increased prevalence of decoy cells was observed in males (29.9%) as compared to females (20%). This might show, as indicated in previous studies, that male gender is a risk factor for polyoma virus infection.¹

The present study showed that the incidence of decoy cells in urine samples of patients aged fewer than 20 was less than that from those aging above 20-yrs-old. Previous investigation indicated that prevalence of polyoma virus infection increased in higher age groups because they became more immunocompromised with the same doses of immunosuppressive medications as compared to younger patients.¹ Moreover, the prevalence of polyoma virus infections increased with increasing time after transplantation which is similar with the reports of Liu et al.⁷

This study also showed that the incidence of elevated plasma creatinine was higher in patients positive for decoy cells which is similar to a previous study demonstrating that patients with BK-virus nephropathy had high serum creatinine that mimicked either tubular necrosis or rejection.¹

Despite a low positive predictive value of decoy cells in urine, its absence has a negative predictive value of 100%, because almost all of those patients who did not have decoy cells had normal renal functions. Therefore, the absence of decoy cells in urine might be an indicative of the absence of BK-virus active infection. As urine cytology is easy to perform and of low cost, it is a useful tool for the investigation of active polyoma virus infection. In conclusion, the findings of the present study suggest that considering the risk of graft loss due to polyoma virus infection, routine urine cytology might be used as a screening method for the detection of polyoma virus infection. While absence of decoy cells in urine excludes the presence of polyoma virus infection, their presence might be suggestive of the presence of active viral infection. Moreover, the findings suggest that the presence of decoy cells along with high creatinine is a better indicator of the virus presence.

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