Low Prevalence of BK Virus Nephropathy on Nonprotocol Renal Biopsies in Iranian Kidney Transplant Recipients: One Center's Experience and Review of the Literature

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Abstract

Background: **BK virus-associated nephropathy in renal transplant recipients has been increasing in frequency in recent years. This rise is probably because of widespread use of highly potent immunosuppressive regimens, and increased immunosuppression load leads to inability of the recipients to increase a successful antiviral immune response. The incidence of BK virus-associated nephropathy in different reports is between 1% and 10%, with an allograft loss in significant numbers of patients, especially when timely diagnosis and treatment is not restored. We report our experience on BK virus nephropathy in our institute.**

Materials and Methods: **All renal transplant biopsies performed at our center between 2001 and 2006 were immunohistochemically screened for the presence of PV-specific protein (SV40 Ag). The histologic diagnosis of BK virus-associated nephropathy was made upon the observation of morphologic changes in tubular epithelium and confirmation with immunohistochemical staining. We reviewed the clinical records of the subjects for demographic, clinical, and laboratory data.**

Results: **BK virus nephropathy was found in 0.93% of all investigated allograft biopsies (1/108) and in 1.04% of all recipients (1/96; mean age of recipients, 36.48 ±14.10 years; age range, 13-74 years); 54 of them were male (57%). Type of kidney transplant was living-unrelated donor 76 (79%), living-related donor 13 (14%), and deceased donor 7. Seventeen patients (18%) were transplanted for a second time. Immunosuppressive drugs in 87 of recipients (90%) were cyclosporine, mycophenolate mofetil, and prednisolone. Our patient who developed BK virus-associated nephropathy 9 months after transplant was a 37-year-old man on prednisone, cyclosporine, and azathioprine immunosuppresion. He lost his graft 4 months after diagnosis.**

Conclusions: **Although BK virus nephropathy after renal transplant is uncommon, it is a serious complication causing loss of the allograft. It should be included in the clinical differential diagnosis of transplant dysfunction.**

Key words: *Polyoma virus, Renal transplant, Renal failure*

Polyoma BK viruses are widespread double-stranded, nonencapsulated DNA viruses comprising BK and JC strains that are pathogenic in humans (1, 2). Approximately 60% to 90% of adult people worldwide are seropositive for the BK virus. Primary infections usually occur early in childhood through oral and/or respiratory exposure (3, 4). These infections usually are asymptomatic, but they have tropism for renal tubular and transitional cells and remain latent within the genitourinary tract (5-8). These viruses need immune modulation and host cell activation for replication. Diseases caused by reactivation of latent BK virus is typically found in patients with impaired immune system and is prevalent in renal transplant patients (10% to 60%) (9). Such activation is determined by the detection of free viral particles in the urine (by electron

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Acknowledgements: *This research has been supported by Tehran University of Medical Sciences & Health Services granted by Urology Research Center, Sina Hospital.*

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Experimental and Clinical Transplantation (2010) 4: 297-302

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microscopy or polymerase chain reaction [PCR] techniques), intranuclear viral inclusion bearing cells, so-called decoy cells in urine cytology samples, and plasma PCR test for viremia (10, 11). Only 1% to 10% of affected patients change from reactivated infection to histologically manifest BK virus nephropathy (9, 12), usually at a mean period of 10 to 13 months posttransplant (range, 6 days to 5 years) (13-15).

The aim of this study was to determine the frequency of BK virus nephropathy in renal transplant patients who had a renal biopsy for graft dysfunction at our center.

Methods

All renal transplant biopsies performed at our center from April 2001 to March 2006 were reviewed. A total of 108 specimens from 96 renal transplant recipients who presented with allograft dysfunction were screened. All protocols, experimental studies, and clinical trials involving human subjects were approved by the ethics committee of the institution before the study began, and that the protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Written informed consent was obtained from patients or their guardians. A careful histologic analysis of the biopsy specimens was performed on hematoxylin and eosin and periodic acid-Schiff stained slides. A careful search was made for features suggestive of BK virus infection including nuclear atypia of tubular epithelial cells, smudging of nuclei with hyperchromasia, amorphous basophilic or amphophilic intranuclear inclusions of nuclei of the tubular cells, and inflammatory infiltrates. All specimens also were subjected to immunohistochemical staining by a standard method using anti-SV40 large T antigen (cat No: DPo2-calbiochem, anti SV40 T antigen). We also reviewed the clinical records of the subjects (n=96) for demographic, clinical, and laboratory data.

Results

BK virus nephropathy was found in 0.93% of all investigated allograft biopsies (1/108) and in 1.04% of all recipients (1/96). Ninety patients were transplanted in our center and 6 patients in other centers. Mean age of recipients was 36.48 ± 14.10 years (range, 13-74 years), and 54 of them were male (57%) (Table 1).

Table 1. Demographic, clinical, and laboratory data of 96 studied patients.

Mean age (year)	36.48 ±14.10 (range: 13-74)
Men, No. (%)	54 (57%)
Second transplant, No. (%)	17 (18%)
Living-unrelated donors, No. (%)	76 (79%)
Living-related donors, No. (%)	13 (14%)
Deceased donors, No. (%)	7 (7%)
Mean serum creatinine at baseline (μmol/L)	136.14 ± 44.20
Mean serum creatinine 6 months before biopsy (μmol/L)	173.26 ± 121.11
Mean serum creatinine at biopsy time (μmol/L)	338.57 ± 212.16
Mean time between transplant and biopsy (mo)	2.75 (range: 1-20.75)
DGF (need for dialysis first week posttransplant), No. (%)	12 (12.5%)

Abbreviations: DGF, delayed graft function

Seventy-one of the patients (74%) had received methylprednisolone pulses, 48 patients (50%) had received antithymocyte globulin (for delayed graft function, second transplant, deceased transplant and rejection), both methylprednisolone pulses and antithymocyte globulin were given to 37 of the patients (38%). Maintenance immunosuppressive therapy was cyclosporine, mycophenolate mofetil, and prednisolone in 87 patients (90%); cyclosporine, azathioprine, and prednisolone in 9 patients (10%); and tacrolimus in 19 patients (20%), sometimes during the posttransplant period (mostly for rejection).

The recipient with BK virus nephropathy was a 37-year-old man with a female living-unrelated donor. He received a kidney transplant in October 2001 without any complications. He was discharged with a serum creatinine level of 106.08 μmol/L (1.2 mg/dL). His maintenance immunosuppressive therapy was cyclosporine, azathioprine, and prednisolone with a stable serum creatinine. Nine and a half months after transplant, he presented in other centers with a serum creatinine of 159.12 μmol/L (1.8 mg/dL) and 185.64 μmol/L (2.1 mg/dL) for which he received 2 courses of methylprednisolone pulses within 3 weeks with no dramatic responses, and azathioprine was replaced by mycophenolate mofetil. Five weeks later, he referred to this center with a serum creatinine of 309.40 μmol/L (3.5 mg/dL), and renal biopsy (H&E and PAS staining) demonstrated nuclear atypia and anisonucleosis of tubular epithelial cells with interstitial inflammation suggestive of viral infection (Figures 1 and 2). Unfortunately, despite reduction in immunosuppression, progressive deterioration in renal function was noted. Four months later, the maintenance hemodialysis was instituted and

because of fever and kidney tenderness, the transplanted kidney was removed. He received the second kidney transplant in our center in 2005. After 2 years, his serum creatinine was 91.94 μmol/L (1.04 mg/dL).

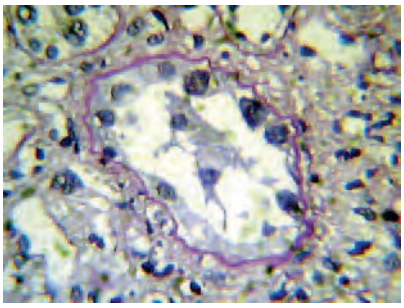

Figure 1. Polyoma virus infection: Tubular epithelial cells show irregularity of the nuclear contour with abnormal coarse chromatin and anisonucleosis. PAS stain. (Original magnification ×640)

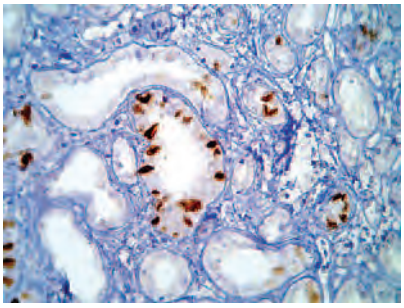

Figure 2. Immunohistochemical staining shows positive reaction of the tubular epithelial cell nuclei for SV-40 T antigen. (Original magnification ×640)

Discussion

Asymptomatic urinary shedding of BK virus BK virus with low urine viral loads of less than 105 copies per mL is noticed in up to 10% of healthy BK virus seropositive immunocompetent individuals (16). In patients with impaired immune function, especially after hematopoietic stem cells transplant or solid-organ transplant, a high level of urine viral load of more than 107 copies/mL is observed (11, 17-19). At this time, sloughing of decoy cells is seen in urine cytology, and virions can be detected by negative staining electron microscopy (20-22). In nonrenal solid organ transplant patients, BK viruria is due to reactivating the endogenous BK virus, (18, 23-26), but in renal transplant recipients, BK virus is most likely reactivated in tubular epithelial cells of the donor kidney, which is then amplified in the urothelial layer (19, 20, 27). Approximately 30% to 50% of kidney transplant recipients with high level of viruria going to BK virus viremia and polyoma-associated nephropathy (11, 28-30). BK virus nephropathy BK virus nephropathy-induced graft loss would be reduced to 10% or less by extensive screening of BK virus. before irreversible tissue damage (31, 32).

The key feature in pathogenesis of BK virus nephropathy is imbalance between BK virus reactivation in renal tubular epithelial cells and BKV-specific cellular immune response (33-35). Risk factors for BK virus nephropathy are not entirely understood, and BK virus nephropathy is also reported in centers using conventional cyclosporine and azathioprine therapy, or calcineurin inhibitor-free protocols comprising sirolimus and mycophenolate mofetil (14, 36). One prospective study noticed that the incidence of BK viruria and viremia were similar in patients randomly designated to tacrolimus or cyclosporine (17). In a recent longitudinal study, only antithymocyte globulin induction and steroid maintenance therapy were independent risk factors for BK virus replication (37). Older age, male sex, and number of HLA mismatches also are denoted as risk factors for BK virus nephropathy (12, 15, 38).

There are no specific clinical symptoms or signs to diagnose BK virus nephropathy, and an increase in serum creatinine is frequently the first clinical sign of BK virus nephropathy with associated kidney damage (20). Discovery of decoy cells in urine cytology, which are cells with an enlarged hyperchromatic nucleolus occasionally containing single basophilic intranuclear inclusion, are useful for screening and diagnosis of BK nephropathy. The positive predictive value of a positive decoy cell analysis (more than 10 cells per cytospin) for the diagnosis of BK virus nephropathy is 25% to 30%, and the negative predictive value is greater than 99% (21, 38, 39-41). The overall positive predictive value of a positive quantitative plasma PCR test to predict BK virus nephropathy is 50%, and the negative predictive value is 100%; the plasma viral load levels of greater than 104 copies/mL have a positive predictive value of greater than 80% (38). A retrospective, single center study reported that the presence of cast like 3-dimensional polyoma aggregates (Haufen) by negative staining electron microscopy of the urine had a sensitivity and specificity for BK virus nephropathy of 100% and

99% (42). A conclusive diagnosis of BK virus nephropathy needs the establishment of viral cytopathic changes in tubular epithelium on a renal biopsy (taking at least 2 biopsy cores including the medulla). Diagnostic confirmation of BK virus nephropathy and rolling out other viral infections is generally accomplished by immunohistochemistry (antibodies against SV40-T antigens). Stages A, B, and C have been determined according to increasing intensity and duration of the involvement and regarding adverse effects on graft survival (9, 43).

The main treatment of BK virus nephropathy is a reduction in maintenance immunosuppression. The recent uprising in the prevalence of BK virus nephropathy is due to extensive use of highly powerful immunosuppressive drugs. It is the overall immunosuppression rather than specific drugs that leads to the inability of the recipient to raise a successful antiviral immune response (14, 17, 36, 37, 44, 45). A period of more than 12 weeks of decreased immunosuppression and measuring of viral load every 2 to 4 weeks is usually needed for viral clearance (46, 47). Different immunosuppression reduction strategies including changing tacrolimus to low-dose cyclosporine, and mycophenolate mofetil to azathioprine; discontinuation of tacrolimus or mycophenolate mofetil or azathioprine; lowering dosages of mycophenolate mofetil and tacrolimus have been advised (13, 15, 17, 38, 48). Switching mycophenolate mofetil to leflunomide (a drug with both immunosuppressive and antiviral actions) (49, 50), or use of low-dose cidofovir (an antiviral agent with potential nephrotoxicity) might be recommended in cases unresponsive to reduction of immunosuppression (51-54). Treatment with steroid pulses followed by modification of immunosuppression 2 weeks later should be recommended in patients with simultaneous acute rejection (9, 12), and use of intravenous immunoglobulins may be last resort in case of treatment failure (17, 53, 55, 56).

Screening for BK virus BK virus replication by urine cytology for decoy cells or by urine quantitative PCR for BK virus DNA or VP1 mRNA (12, 20, 21, 29, 30, 57, 58) should be performed at least once every 3 months during the first 2 years posttransplant, and then annually until the fifth year posttransplant (12). Recipients with significant decoy cells or urine viral loads more than 107 copies/mL should be tested for plasma BK virus DNA loads. In patients with sustained plasma viral loads > 104 copies/mL for more than 3 weeks, a diagnosis of presumptive BK virus nephropathy is made and an allograft biopsy should be considered for a diagnosis of definitive BK virus nephropathy (12). In case of definitive or even presumptive BK virus nephropathy, judicious reduction of immunosuppression and follow-up by measuring serum creatinine every week and plasma viral loads every other week until clearance of virus (usually within 8 to 12 weeks) is recommended (46, 47).

It has been suggested that the clearance of BK replication should be established before retransplant. Surgical removal of the first renal graft is not required unless pre-emptive retransplant is considered during ongoing BK virus replication (46). Because BK virus nephropathy is supposed to be donor-origin, it is in favor to select the donor with the lowest anti-BK antibody titer among candidate donors (12).

In the present study, we reported 1.04% incidence (1 of 96 recipients) of BK virus nephropathy. We are not aware of the underlying reasons behind of this low incidence in our patients, considering that risk factors for BK virus nephropathy are still incompletely understood. We used more live donors (93%) with subsequently fewer complications (such as delayed graft function) and lower overall immunosuppression. However, our patient with BK virus nephropathy diagnosis also had uncomplicated course after transplant, and he was on maintenance immunosuppression consisting of prednisolone, cyclosporine, and azathioprine. He received a second live-donor kidney transplant 19 months after first kidney transplant nephrectomy with an uneventful posttransplant course and drugs comprising prednisolone, cyclosporine, and mycophenolate mofetil. After 2 years, his serum creatinine was 91.94 μmol/L (1.04 mg/dL).

In conclusion, although BKV nephropathy after renal transplant is unusual, it is a serious complication causing loss of the allograft. To date, there is no specific treatment for BKN; therefore, vigorous patient screening strategies seem to be the main effective approach.

References

1. Gardner SD, Field AM, Coleman DV, Hume B. New human papovavirus (B.K.) isolated from urine after renal transplantation. Lancet. 1971;1(7712):1253-1257.

2. Gardner SD, MacKenzie EF, Smith C, Porter AA. Prospective study of the human polyomaviruses BK and JC and cytomegalovirus in renal transplant recipients. J Clin Pathol. 1984;37(5):578-586.
3. Shah KV, Daniel RW, Warszawski RM. High prevalence of antibodies to BK virus, an SV40-related papovavirus, in residents of Maryland. J Infect Dis. 1973;128(6):784-787.
4. Mackenzie EF, Poulding JM, Harrison PR, Amer B. Human polyoma virus (HPV)–a significant pathogen in renal transplantation. Proc Eur Dial Transplant Assoc. 1978;15:352-360.
5. Chesters PM, Heritage J, McCance DJ. Persistence of DNA sequences of BK virus and JC virus in normal human tissues and in diseased tissues. J Infect Dis. 1983;147(4):676-684.
6. Nickeleit V, Singh HK, Gilliland MGF, Thompson D, Romeo C. Latent polyomavirus type BK loads in native kidneys analyzed by TaqMan PCR : what can be learned to better understand BK virus nephropathy? J Am Soc Nephrol 2003;14:424A
7. Polo C, Pérez JL, Mielnichuck A, Fedele CG, Niubò J, Tenorio A. Prevalence and patterns of polyomavirus urinary excretion in immunocompetent adults and children. Clin Microbiol Infect. 2004;10(7):640-644.
8. Nickeleit V, Gordon J, Thompson D, Romeo C. Antibody titers and latent polyoma-BK virus loads in the general population: potential donor risk assessment for the development of BK-virus nephropathy posttransplantation. J Am Soc Nephrol 2004;15:524A
9. Hirsch HH, Steiger J. Polyomavirus BK. Lancet Infect Dis. 2003;3(10):611-623.
10. Tani EM, Montenegro MR, Viana de Camargo JL. Urinary bladder washings in autopsies. A cytopathologic study of 63 cases. Acta Cytol. 1983;27(2):128-132.
11. Binet I, Nickeleit V, Hirsch HH, Prince O, Dalquen P, Gudat F, et al. Polyomavirus disease under new immunosuppressive drugs: a cause of renal graft dysfunction and graft loss. Transplantation. 1999;67(6):918-922.
12. Hirsch HH, Brennan DC, Drachenberg CB, Ginevri F, Gordon J, Limaye AP, et al. Polyomavirus-associated nephropathy in renal transplantation: interdisciplinary analyses and recommendations. Transplantation. 2005;79(10):1277-1286.
13. Howell DN, Smith SR, Butterly DW, Klassen PS, Krigman HR, Burchette JL Jr, et al. Diagnosis and management of BK polyomavirus interstitial nephritis in renal transplant recipients. Transplantation. 1999;68(9):1279-1288.
14. Sachdeva MS, Nada R, Jha V, Sakhuja V, Joshi K. The high incidence of BK polyoma virus infection among renal transplant recipients in India. Transplantation. 2004;77(3):429-431.
15. Ramos E, Drachenberg CB, Papadimitriou JC, Hamze O, Fink JC, Klassen DK, et al. Clinical course of polyoma virus nephropathy in 67 renal transplant patients. J Am Soc Nephrol. 2002;13(8):2145-2151.
16. Egli A, Köhli S, Dickenmann M, Hirsch HH. Inhibition of polyomavirus BK-specific T-Cell responses by immunosuppressive drugs. Transplantation. 2009;88(10):1161-1168.
17. Brennan DC, Agha I, Bohl DL, et al. Incidence of BK with tacrolimus versus cyclosporine and impact of preemptive immunosuppression reduction. Am J Transplant. 2005;5(3):582-594. Erratum in: Am J Transplant. 2005;5(4 Pt 1):839.
18. Randhawa P, Uhrmacher J, Pasculle W, Vats A, Shapiro R, Eghtsead B, et al. A comparative study of BK and JC virus infections in organ transplant recipients. J Med Virol. 2005;77(2):238-243.
19. Funk GA, Gosert R, Comoli P, Ginevri F, Hirsch HH. Polyomavirus BK replication dynamics in vivo and in silico to predict cytopathology and viral clearance in kidney transplants. Am J Transplant. 2008;8(11):2368-2377.
20. Nickeleit V, Hirsch HH, Binet IF, Gudat F, Prince O, Dalquen P, et al. Polyomavirus infection of renal allograft recipients: from latent infection to manifest disease. J Am Soc Nephrol. 1999;10(5):1080-1089.
21. Drachenberg CB, Beskow CO, Cangro CB, Bourquin PM, Simsir A, Fink J, et al. Human polyoma virus in renal allograft biopsies: morphological findings and correlation with urine cytology. Hum Pathol. 1999;30(8):970-977.
22. Drachenberg RC, Drachenberg CB, Papadimitriou JC, Ramos E, Fink JC, Wali R, et al. Morphological spectrum of polyoma virus disease in renal allografts: diagnostic accuracy of urine cytology. Am J Transplant. 2001;1(4):373-381.
23. Thomas LD, Vilchez RA, White ZS, Zanwar P, Milstone AP, Butel JS, et al. A prospective longitudinal study of polyomavirus shedding in lung-transplant recipients. J Infect Dis. 2007;195(3):442-449.
24. Doucette KE, Pang XL, Jackson K, Burton I, Carbonneau M, Cockfield S, et al. Prospective monitoring of BK polyomavirus infection early posttransplantation in nonrenal solid organ transplant recipients. Transplantation. 2008;85(12):1733-1736.
25. Haririan A, Ramos ER, Drachenberg CB, Weir MR, Klassen DK. Polyomavirus nephropathy in native kidneys of a solitary pancreas transplant recipient. Transplantation. 2002;73(8):1350-1353.
26. Barber CE, Hewlett TJ, Geldenhuys L, Kiberd BA, Acott PD, Hatchette TF. BK virus nephropathy in a heart transplant recipient: case report and review of the literature. Transpl Infect Dis. 2006;8(2):113-121.
27. Bohl DL, Storch GA, Ryschkewitsch C, Gaudreault-Keener M, Schnitzler MA, Major EO, et al. Donor origin of BK virus in renal transplantation and role of HLA C7 in susceptibility to sustained BK viremia. Am J Transplant. 2005;5(9):2213-2221.
28. Nickeleit V, Klimkait T, Binet IF, Dalquen P, Del Zenero V, Thiel G, et al. Testing for polyomavirus type BK DNA in plasma to identify renal-allograft recipients with viral nephropathy. N Engl J Med. 2000;342(18):1309-1315.
29. Drachenberg CB, Hirsch HH, Papadimitriou JC, Gosert R, Wali RK, Munivenkatappa R, et al. Polyomavirus BK versus JC replication and nephropathy in renal transplant recipients: a prospective evaluation. Transplantation. 2007;84(3):323-330.
30. Viscount HB, Eid AJ, Espy MJ, Griffin MD, Thomsen KM, Harmsen WS, et al. Polyomavirus polymerase chain reaction as a surrogate marker of polyomavirus-associated nephropathy. Transplantation. 2007;84(3):340-345.
31. Wadei HM, Rule AD, Lewin M, Mahale AS, Khamash HA, Schwab TR, et al. Kidney transplant function and histological clearance of virus following diagnosis of polyomavirus-associated nephropathy (PVAN). Am J Transplant. 2006;6(5 Pt 1):1025-1032.
32. Drachenberg CB, Papadimitriou JC, Wali R, Nogueira J, Mendley S, Hirsch HH, et al. Improved outcome of polyoma virus allograft nephropathy with early biopsy. Transplant Proc. 2004;36(3):758-759.
33. Comoli P, Azzi A, Maccario R, Basso S, Botti G, Basile G, et al. Polyomavirus BK-specific immunity after kidney transplantation. Transplantation. 2004;78(8):1229-1232.
34. Comoli P, Hirsch HH, Ginevri F. Cellular immune responses to BK virus. Curr Opin Organ Transplant. 2008;13(6):569-574.
35. Comoli P, Binggeli S, Ginevri F, Hirsch HH. Polyomavirus-associated nephropathy: update on BK virus-specific immunity. Transpl Infect Dis. 2006;8(2):86-94.
36. Lipshutz GS, Flechner SM, Govani MV, Vincenti F. BK nephropathy in kidney transplant recipients treated with a calcineurin inhibitor-free immunosuppression regimen. Am J Transplant. 2004;4(12):2132-2134.
37. Dadhania D, Snopkowski C, Ding R, Muthukumar T, Chang C, Aull M, et al. Epidemiology of BK virus in renal allograft recipients: independent risk factors for BK virus replication. Transplantation. 2008;86(4):521-528.
38. Hirsch HH, Knowles W, Dickenmann M, Passweg J, Klimkait T, Mihatsch MJ, et al. Prospective study of polyomavirus type BK replication and nephropathy in renal-transplant recipients. N Engl J Med. 2002;347(7):488-496.
39. Nickeleit V, Steiger J, Mihatsch MJ. BK virus infection after kidney transplantation. Graft 2002; 5 (December Supplement): S46.
40. Drachenberg CB, Papadimitriou JC, Hirsch HH, Wali R, Crowder C, Nogueira J, et al. Histological patterns of polyomavirus nephropathy: correlation with graft outcome and viral load. Am J Transplant. 2004;4(12):2082-2092.
41. Boldorini R, Brustia M, Veggiani C, Barco D, Andorno S, Monga G. Periodic assessment of urine and serum by cytology and molecular biology as a diagnostic tool for BK virus nephropathy in renal transplant patients. Acta Cytol. 2005;49(3):235-243.

42. Singh HK, Andreoni KA, Madden V, True K, Detwiler R, Weck K, et al. Presence of urinary Haufen accurately predicts polyomavirus nephropathy. J Am Soc Nephrol. 2009;20(2):416-427.
43. Nickeleit V, Mihatsch MJ. Polyomavirus nephropathy in native kidneys and renal allografts: an update on an escalating threat. Transpl Int. 2006;19(12):960-973.
44. Hirsch HH, Mohaupt M, Klimkait T. Prospective monitoring of BK virus load after discontinuing sirolimus treatment in a renal transplant patient with BK virus nephropathy. J Infect Dis. 2001;184(11):1494-1495; author reply 1495-1496.
45. Lipshutz GS, Mahanty H, Feng S, Hirose R, Stock PG, Kang SM, et al. Polyomavirus-associated nephropathy in simultaneous kidney-pancreas transplant recipients: a single-center experience. Transplant Proc. 2004;36(4):1097-1098.
46. Hirsch HH, Ramos E. Retransplantation after polyomavirus-associated nephropathy: just do it? Am J Transplant. 2006;6(1):7-9.
47. Funk GA, Steiger J, Hirsch HH. Rapid dynamics of polyomavirus type BK in renal transplant recipients. J Infect Dis. 2006;193(1):80-87.
48. Barri YM, Ahmad I, Ketel BL, Barone GW, Walker PD, Bonsib SM, et al. Polyoma viral infection in renal transplantation: the role of immunosuppressive therapy. Clin Transplant. 2001;15(4):240-246.
49. Williams JW, Javaid B, Kadambi PV, Gillen D, Harland R, Thistlewaite JR, et al. Leflunomide for polyomavirus type BK nephropathy. N Engl J Med. 2005;352(11):1157-1158.
50. Josephson MA, Gillen D, Javaid B, Kadambi P, Meehan S, Foster P, et al. Treatment of renal allograft polyoma BK virus infection with leflunomide. Transplantation. 2006;81(5):704-710.
51. Bjorang O, Tveitan H, Midtvedt K, Broch LU, Scott H, Andresen PA. Treatment of polyomavirus infection with cidofovir in a renal-transplant recipient. Nephrol Dial Transplant. 2002;17(11):2023-2025.
52. Vats A, Shapiro R, Singh Randhawa P, Scantlebury V, Tuzuner A, Saxena M, et al. Quantitative viral load monitoring and cidofovir therapy for the management of BK virus-associated nephropathy in children and adults. Transplantation. 2003;75(1):105-112.
53. Keller LS, Peh CA, Nolan J, Bannister KM, Clarkson AR, Faull RJ. BK transplant nephropathy successfully treated with cidofovir. Nephrol Dial Transplant. 2003;18(5):1013-1014.
54. Kadambi PV, Josephson MA, Williams J, Corey L, Jerome KR, Meehan SM, et al. Treatment of refractory BK virus-associated nephropathy with cidofovir. Am J Transplant. 2003;3(2):186-191.
55. Trofe J, Roy-Chaudhury P, Gordon J, Wadih G, Maru D, Cardi MA, et al. Outcomes of patients with rejection post-polyomavirus nephropathy. Transplant Proc. 2005;37(2):942-944.
56. Blanckaert K, De Vriese AS. Current recommendations for diagnosis and management of polyoma BK virus nephropathy in renal transplant recipients. Nephrol Dial Transplant. 2006;21(12):3364-3367.
57. Ding R, Suthanthiran M. Noninvasive diagnosis of BK virus nephritis by measurement of messenger RNA for BK VP1 virus in urine. Transplantation. 2003;76(2):446.
58. Yeo FE, Yuan CM, Swanson SJ, Reinmuth B, Kiandoli LC, Kaplan KJ, et al. The prevalence of BK polyomavirus infection in outpatient kidney transplant recipients followed in a single center. Clin Transplant. 2008;22(5):532-541.