ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Mini Review

Polyoma Virus Nephropathy and Renal Transplant Recipients; A Mini Review

Emmanuel E Siddig*

Mycetoma Research Center, Faculty of Medical Laboratory Sciences, Unit of Applied Basic Sciences, University of Khartoum, Khartoum, Sudan

***Corresponding Author:** Emmanuel E Siddig, Mycetoma Research Center, Faculty of Medical Laboratory Sciences, Unit of Applied Basic Sciences, University of Khartoum, Khartoum, Sudan.

Received: May 24, 2018; **Published:** July 23, 2018

Abstract

Kidney transplantation had significantly increased over years. Two factors were considered as a corner stone for better outcome for kidney transplantation, the first factor was the better prevention of the infectious agent and the second one was better treatment of the infectious agents. Infectious complications are common in renal transplant recipients. Additionally, polyoma virus nephritis is considered an increasing problem and is posing a threat to improving renal transplant graft survival. The pathogenesis of polyoma virus inducing nephritis remains a mystery and need further investigation. Higher prevalence of polyoma virus infection in recent years has been correlated with declining acute rejection rates and the use of potent immunosuppressive agents. treatment strategies

Keywords: *Polyoma Virus; Renal Transplant; Decoy Cells*

Historical Background of PVAN

Polyomavirus associated nephritis was first described in 1970s after detecting the virus in urine sample from a patient with ureteric stenosis after transplantation [1,2]. Interestingly, a significant incidence of Polyoma virus infection in the renal transplant population has only been seen in recent years. A reemergence [3] of this viral infection became obvious after 1995 with the initial report by Pappo and his associates and was confirmed by several subsequent reports from different centers [4,5]. Although awareness of the clinico- pathologic features of Polyoma virus nephritis (PVN) undoubtedly resulted in an increase in the diagnosis of this infection in the past few years, these may be attributed to presence of new risk factors. A clear temporal association between the increase in PVN and the use of newer more potent immunosuppressive drugs [6,7] has proposed that these agents have not only dramatically reduced the acute rejection rates but have also likely created an environment more permissive for viral reactivation.

Polyomavirus associated nephropathy (PVAN) occurs in 1 - 10% of kidney transplant recipients, usually manifesting in the first year following transplantation and associated with the graft loss in about 15% - 80% BKVN cases within 5 years [8-13]. Active replication of BKV in urothelial cells and subsequent tissue damage cause release of Polyoma virus (BK) into urine and blood that can be checked by molecular techniques. Monitoring of BK viruria and viremia can facilitate early diagnosis of BK replication, guide management of immunosuppressive therapy, and monitor response to intervention. Molecular monitoring has been increasingly used as a noninvasive tool for diagnosis and monitoring of BKVN [8-10].

Laboratory Diagnosis

Histopathology

Histopathological diagnosis considered as a gold standard method for the definitive diagnosis of PVAN, Macroscopical appearance will show a streaky fibrosis of the medulla and circumscribed cortical scars [13]. Under the light microscope the histological section will show viral cytopathic effect which can be noticed by careful examination of the slides which may shows dense intranuclear inclusion that occupy almost the entire nuclear area of the renal tubular cells. no perinuclear halo is present.

Urine Cytology

Urine cytology considered as the most inexpensive method for the screening for the presence of polyomavirus among renal transplant recipient by detection the cytopathic effect of the virus in the infected cells. The infected cells characterized by the presence of large homogeneous basophilic nuclear inclusion that may mimic the nuclear changes that associated with urothelial carcinoma.

The abnormalities were first recognized in the 1950s by Mr. Andrew Ricci a cytotechnologist at Memorial Sloan-Kettering Cancer Center, who named these cells Decoy cells which is descriptive term for epithelial cell with intranuclear viral inclusion bodies that can have different phenotype (type 1-4) depending on the state of viral replication and maturation as well as cellular preservation.

The most common occurrence of decoy cells in urine cytology were classical decoy cells or type 1 which characterized by large intranuclear inclusion bodies with condensation of chromatin at nuclear border the nucleus has a ground glass appearance. Moreover, in certain cases decoy cells reveal granular intranuclear inclusions surrounded by a clear halo, i.e., cytomegalovirus (CMV)-like (type 2). Additionally, multinucleated decoy cells with granular chromatin are detected (type 3). Furthermore, the most conspicuous presentation of decoy cells that it can show vesicular nuclei, with clumped chromatin and nucleoli which should differentiated from malignant cells [15].

Sensitivity and Specificity of Urine cytology in detection of Decoy cells

Rarely, polyomavirus causes clinically evident tubulointerstitial disease in renal allograft recipients after reactivation of latent virus in the renal epithelium. In these cases, urine cytology detects numerous cells with intranuclear inclusions, but the final diagnosis is made by renal biopsy. However, preliminary studies suggest that urine cytology is more sensitive for the diagnosis [16]. The sensitivity of urine cytology in detection of polyomavirus cellular changes were ranges from 25% till 61%, and specificity ranged from 70% - 85% [17].

Ancillary Testing

Interestingly, measuring of polyoma virus DNA using Real time PCR and conventional PCR from urine and blood samples can be used as a monitoring tool for transplant patients and it used since 2001. Currently there is no US Food and Drug Administration – approved or standardized BK viral load assay. Various testing protocols can have significant differences in the limit of quantitation and dynamic ranges, leading to different conclusions regarding the cutoffs and predictive values of BKV viruria and viremia for Polyoma virus nephropathy [18-19].

Treatment and Management

To best of our knowledge there is no specific antiviral therapy for polyomavirus. The treatment strategies implicated the reduction in the doses of immunosuppressive drugs with close monitoring and follow up of the patients. Several antiviral therapy were tested Invitro for their effect against the virus, including cidofovir, leflunomide, and certain quinolone antibiotics. In the clinical setting, the use of these drugs was combined with reduced immunosuppression which limits the evaluation of their efficacy. Amantadine has been used in the treatment of PVAN without discernable effect [20]. Cidofovir has a significant *in vitro* effect inhibiting nonhuman polyomavirus. However, the pronounced nephrotoxicity limits its use particularly in renal transplantation. A number of patients have been treated with a combina-

tion of low-dose Cidofovir and reduced immunosuppression with variable results. In most published reports, its use was associated with a decrease in viremia, but viruria often persisted for prolonged times [21]. Some patients have gone on to develop end-stage renal disease which may, however, be multifactorial. This off-label use of cidofovir is at a low dose of 0.25 mg/kg, administered every two weeks. The patients are usually premeditated, with increased intravenous fluids [22]. Chandraker and his associates have shown that the quinolones also have anti- polyomavirus activity *in vitro* and observed resolution of BKV replication *in vivo* in some of 10 prospectively studied patients [23]. Although the efficacy is less than requested for an anti-polyomavirus agent, these data suggest that the BKV encoded helicase activity may represent a significant drug target for further development.

Disclosure

The author declare no financial conflict of interest.

Bibliography

1. Gardner SD., *et al*. "New human papovavirus (BK) isolated from urine after renal transplantation". *Lancet* 1.7712 (1971): 1253-1257.
2. Scadden JR., *et al*. "Polyoma virus nephropathy in kidney transplantation". *World Journal of Transplantation* 7.6 (2017): 329-338.
3. Hirsch HH. "Polyomavirus BK nephropathy: A (Re-) emerging complication in renal transplantation". *American Journal of Transplantation* 2.1 (2002): 25-30.
4. Pappo O., *et al*. "Human polyoma virus infection of renal allografts: Histopathologic diagnosis, clinical significance, and literature review". *Modern Pathology* 9.2 (1996): 105-109.
5. Binet I., *et al*. "Polyomavirus disease under new immunosuppressive drugs". *Transplantation* 67.6 (1999): 918-922.
6. Randhawa PS., *et al*. "Human polyoma virus-associated interstitial nephritis in the allograft kidney". *Transplantation* 67.1 (1999): 103-109.
7. Randhawa PS and Demetris AJ. "Nephropathy due to polyomavirus BK". *New England Journal of Medicine* 342.18 (2000): 1361-1363.
8. Hirsch HH., *et al*. "Polyomavirus-associated nephropathy in renal transplantation: interdisciplinary analyses and recommendations". *Transplantation* 79.10 (2005): 1277-1286.
9. Brennan DC., *et al*. "Incidence of BK with tacrolimus versus cyclosporine and impact of preemptive immunosuppression reduction". *American Journal of Transplantation* 5.3 (2005): 582-594.
10. Hirsch HH. "BK virus: opportunity makes a pathogen". *Clinical Infectious Diseases* 41.3 (2005): 354-360.
11. Ahuja M., *et al*. "Polyoma virus infection after renal transplantation: Use of immunostaining as a guide to diagnosis". *Transplantation* 71.7 (2001): 896-899.
12. Hussain S., *et al*. "Rapid kidney allograft failure in patients with polyoma virus nephritis with prior treatment with antilymphocyte agents". *Clinical Transplantation* 16.1 (2002): 43-47.
13. Rahamimov R., *et al*. "BK polyoma virus nephropathy in kidney transplant recipient: The role of new immunosuppressive agents". *Transplantation Proceedings* 35.2 (2003): 604-605.
14. Bratt G., *et al*. "BK virus as the cause of meningoencephalitis, retinitis, and nephritis in a patient with AIDS". *AIDS* 13 (1999): 1071-1075.
15. Kitamura T., *et al*. "High incidence of urinary JC virus excretion in nonimmunosuppressed older patients". *Journal of Infectious Diseases* 161.6 (1990): 1128-1133.

16. Drachenberg CB., *et al*. "Human polyoma virus in renal allograft biopsies: morphological findings and correlation with urine cytology". *Human Pathology* 30.8 (1999): 970-977.

17. Bechert CJ., *et al*. "Monitoring of BK viral load in renal allograft recipients by real-time PCR assays". *American Journal of Clinical Pathology* 133.2 (2010): 242-250.

18. Hirsch HH., *et al*. "Prospective monitoring of BK virus load after discontinuing sirolimus treatment in a renal transplant patient with BK virus nephropathy". *Journal of Infectious Diseases* 184.11 (2001): 1494-1495.

19. Hoffman NG., *et al*. "Marked variability of BK virus load measurement using quantitative realtime PCR among commonly used assays". *Journal of Clinical Microbiology* 46.8 (2008): 2671-2680.

20. Trofe J., *et al*. "Polyomavirus in kidney and kidney-pancreas transplant recipients". *Transplant Infectious Disease* 5.1 (2003): 21-28.

21. Kadambi PV., *et al*. "Treatment of refractory BK virus-associated nephropathy with cidofovir". *American Journal of Transplantation* 3.2 (2003): 186-191.

22. Vats A., *et al*. "Quantitative viral load monitoring and cidofovir therapy for the management of BK virus-associated nephropathy in children and adults". *Transplantation* 75.1 (2003): 105-112.

23. Chandraker A., *et al*. "Use of fluorochinolones to treat BK infection in renal transplant recipients". *American Journal of Transplantation* 4 (2004): 587 (Abstract #1564).

Volume 14 Issue 8 August 2018