CASE REPORT

BK virus as a potential oncovirus for bladder cancer in a renal transplant patient

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Renal transplant patients have high risk for bladder cancer. The reactivation of BK virus is common in renal transplant patients especially in the urinary tract. There was some evidence suggesting that the reactivation of BK virus (BKV) in renal transplant patients may associate with the development of bladder cancer. Here we demonstrated that a patient that had persistent elevated BKV viruria (urine BKV DNA concentration more than \(10^{11}\) copies/ml) after renal transplantation. Then, bladder cancer was found in 13 months after kidney transplantation. The urine BKV DNA concentration was detected by real-time PCR and the BKV DNA in the bladder tumor was detected by PCR. BKV DNA was found in the marginal and central part of the bladder tumor. After removal of the bladder cancer, the urine BKV viral load in this patients dropped dramatically to \(<10^2\) copies/ml. However, the urine viral load had increased modestly to \(10^6\) copies/ml in 3 months after surgery. Since there is a close correlation between the urine BK viral load and the presence of bladder cancer, we suggested that there might be a causal relationship between the reactivation of BKV and the development of bladder cancer in renal transplant patient.

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A 39-year-old woman underwent cadaveric renal transplantation in November 2005. After the transplantation, the patient was given a drug regimen that consisted of cyclosporin A, mycophenolic acid, and prednisolone. The trough level of cyclosporin was adjusted to about 400–600 ng/mL in the 1st postoperative month, 300–500 ng/mL in the 1st half-year, and 200–300 ng/mL thereafter. Quantitative real-time polymerase chain reaction demonstrated that the patient’s urine was positive for BK virus (BKV) DNA (Fig. 1A). In the year 2007, the urinary BK viral load in this patient was persistently elevated for 1 year. In January 2008, due to persistent hematuria, bladder cancer was detected, and transurethral curettage was done in February 2008. After surgery, the urinary viral load dropped to <10^2 copies/mL. Since April 2008, the urinary BKV viral load increased modestly. We found the genome of BKV by polymerase chain reaction in the bladder cancer specimen from the central and marginal zone in this case (Fig. 1B). The drop in BK viral load after tumor removal indicated that high urine BK viral load came from the bladder cancer. During the post-surgery period, the patient was maintained on the same dose of immunosuppressant and showed no occurrence of bladder cancer until now.

Bladder cancer is a common cancer in adults, but the role of exposure to virus such as human papillomavirus or polyomavirus in bladder cancer has been a controversial subject. Since the urogenital tract is the main site of BKV latency, BKV could transform cells based on in vitro studies. It has been speculated that BKV could have a potential role in bladder cancer development. In fact, the prevalence and titer of antibodies to BKV was higher in individuals with bladder cancer, and there is a higher percentage of BKV genome present in patients with bladder cancer compared to normal controls. However, other studies failed to demonstrate the correlation of BKV and bladder cancer. We speculated that although most of the general population has been infected with BKV, significant BKV reactivation with clinical manifestations is mostly limited to immunocompromised patients especially renal transplant patients. It is already known that BKV contributes to BKV-associated nephropathy, hemorrhagic cystitis, and ureteral stenosis in renal transplant patients. The incidence of bladder cancer is around 2- to 4-fold in patients undergoing renal transplantation and with impaired immune surveillance due to medication. In addition, virus infection/reactivation such as BKV could play a role, and in fact BKV genome with large T-antigen has been found in bladder cancer from renal transplant patients. In this case, we have specifically demonstrated that there is a close time correlation between high urinary viral loads of BKV and the occurrence of bladder cancer.

Taking these facts together, our report suggests that BKV may be a transforming agent particularly in renal transplant patients. In addition, a thoughtful examination for bladder cancer is critical in renal transplantation patients with persistent elevated urine BKV viral load.

References