# Reversible Ureteral Obstruction due to Polyomavirus Infection after Percutaneous Nephrostomy Catheter Placement

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BK virus (BKV) is a human polyomavirus that remains latent in the urinary tract epithelium in most individuals. However, in immunocompromised states, including after hematopoietic stem cell transplantation (HSCT), BKV may reactivate and cause infection predominantly affecting the bladder, commonly manifested as hemorrhagic cystitis. Renal insufficiency, occasionally requiring hemodialysis, is not uncommon and was previously attributed to medications or the development of tubulointestitial nephritis. We report a series of 6 HSCT recipients who developed obstructive uropathy of the upper urinary tract system secondary to inflammation and hemorrhage involving the upper uroepithelium, causing ureteral stenosis. Temporary placement of a percutaneous nephrostomy catheter relieved the obstruction and significantly improved kidney function, successfully preventing progression to more advanced renal disease in these patients.

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**KEY WORDS:** BK virus infection, Allogeneic stem cell transplantation, Obstructive nephropathy

## INTRODUCTION

BK virus (BKV) is a human polyomavirus infecting approximately 60%-80% of the adult human population. Most individuals remain seropositive and asymptomatic throughout the lifespan; however, in immunocompromised states, including after hematopoietic stem cell transplantation (HSCT), the virus may become reactivated, causing primarily BKV-associated hemorrhagic cystitis [1]. More rarely, BKV infection can present or progress to tubulointerstitial nephritis, complicating treatment outcomes [2]. Several reports have documented direct kidney injury from BKV in immunosupressed solid organ transplantation and HSCT recipients [3-9]. Most cases of BKV nephropathy have been reported in renal transplant recipients, and the risk factors for progression from asymptomatic reactivation to BKV cystitis or nephropathy are incompletely defined [10]. Non–renal transplant recipients receive similar immunosuppressive regimens as kidney transplant recipients, including calcineurin inhibitors, which might account for, at least in part, the renal dysfunction observed in these patients.

There is no established therapy for BKV infection. Intravenous or intravesicular cidofovir and leflunomide have in vitro BKV inhibitory activity; however, cidofovir is highly nephrotoxic, and leflunomide is hepatotoxic and is rarely tolerated at full doses after HSCT because of its myelosuppressive adverse effects [11]. More commonly, treatment is symptomatic and includes pain control, antispasmodics, platelet transfusions to limit associated hematuria, and continuous bladder irrigation to prevent ureteral obstruction from blood clots [12].

We hypothesize that kidney dysfunction in patients with BKV cystitis may result from obstructive uropathy involving the upper urinary tract system, and suggest that temporary nephrostomy catheter placement may relieve the obstruction and improve kidney function in these patients.

## PATIENTS AND METHODS

### Selection of Patients

A retrospective chart review was undertaken of all HSCT patients who developed BKV cystitis treated in

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the Department of Stem Cell Transplantation and Cellular Therapy of the University of Texas M.D. Anderson Cancer Center between March 2009 and February 2010. A total of 421 patients underwent allogeneic HSCT during this period (including transplants from matched related, matched unrelated, cord blood, and haploidentical donors), of whom 87 (21%) developed BKV cystitis. The presence of BKV in the urine was confirmed by quantitative polymerase chain reaction (PCR), with results reported as the number of viral copies/mL. Detection of any virus in the urine was considered a positive test result. Six patients who demonstrated a significant increase in creatinine level (ie, doubling from baseline levels) or a >50% decrease in creatinine clearance underwent evaluation for obstructive uropathy and had a temporary nephrostomy catheter placed to relieve obstruction. A data review protocol that included a waiver of informed consent was approved by the University of Texas M.D. Anderson Cancer Center's Institutional Review Board for this study.

### Definitions

Engraftment was defined as achieving an absolute neutrophil count of $>0.5 \times 10^9$/L for at least 3 consecutive days before day 28 post-HSCT, with donor-derived cells detected by DNA microsatellite analysis. Myeloablative conditioning was defined as regimens including busulfan >520 mg/m$^2$, melphalan >140 mg/m$^2$, or total body irradiation >6 Gy, with doses below these values considered reduced-intensity conditioning [13]. Acute graft-versus-host disease (aGVHD) was defined and graded according to previously described criteria [14]. BKV infection was diagnosed if typical symptoms of hemorrhagic cystitis (ie, dysuria, urinary frequency, hematuria, bladder pain/spasms) were associated with a positive PCR for BKV in the urine of the transplant recipient.

### Statistical Analysis

Data were double-entered and analyzed in Stata 11.0 (StataCorp, College Station, TX) and Microsoft Excel (Microsoft Corp, Redmond, WA) on February 22, 2011. Results are presented as median (range) frequencies.

## RESULTS

Characteristics of the patients and treatment outcomes are summarized in Table 1. Transplantation was performed mostly for acute and chronic leukemias, with grafts from unrelated donors (in 4 patients) or cord blood (in 2 patients). Three patients had a reduced-intensity conditioning regimen, and the other 3 patients received myeloablative conditioning (Table 1). All patients received anti-thymocyte globulin. The median follow-up for survivors (n = 4) was 608 days (range, 440-715 days). All patients achieved remission after HSCT, and only 1 patient (with acute myeloid leukemia) relapsed. Four patients developed grade II-IV aGVHD, and none developed chronic GVHD. The patients with aGVHD were treated with systemic corticosteroids, with therapy tapered and then discontinued after the resolution of GVHD. Two patients died, at 64 and 177 days post-HSCT, due to recurrence of primary disease and multiorgan failure, respectively.

Six patients (7%) with documented BKV infection demonstrated an elevated serum creatinine level and were evaluated for obstructive uropathy. These patients underwent temporary nephrostomy tube placement by an interventional radiologist. BKV viruria was detected by PCR at a median of 36 days post-HSCT (range, 12-67 days). The median number of viral copies was 119 million/mL (range, 30-500 million/mL). Two out of 3 tested patients were also positive for adenovirus. The earliest and most common symptom was dysuria (present in all 6 patients); hematuria, which occurred initially in 5 patients, was the second most common complaint. Other symptoms included urgency/frequency in 4 patients and flank pain in 3 patients.

All patients were initially managed with continuous bladder irrigation. Those patients presenting with excessive hematuria and blood clots received intravesical formalin or bladder fulguration in an attempt to achieve hemostasis. Other conservative strategies involved antiviral therapy, such as intravenous cidofovir in 4 patients, and hyperbaric oxygen therapy (100% oxygen concentration at 2 atmospheric absolute pressures for 60 minutes a day) in 2 patients. If a patient developed upper urinary tract symptoms (eg, flank pain) and/or a doubling of serum creatinine level over a period of up to 7 days (or a creatinine clearance decrease by >50% from baseline), then retroperitoneal ultrasonography was performed to evaluate for hydronephrosis. Bilateral percutaneous insertion of a temporary nephrostomy catheter was used to relieve obstruction in all patients, except 1 patient who had unilateral obstruction and 1 patient who had only a single kidney (Table 1). The median time from detection of BKV viruria to nephrostomy tube placement was 44.5 days (range, 7-84 days). Catheters were kept in place for a median of 38.5 days (range, 30-91 days) and were removed after symptoms (and/or viruria) resolved and the creatinine level returned to normal or decreased significantly (Table 1). Creatinine values improved from a median of 3.25 mg/dL (range, 1.5-4 mg/dL) before catheter insertion to a median of 1.1 mg/dL (range, 0.8-1.7 mg/dL) after catheter insertion. Creatinine clearance also improved, from a median of 30 mL/min to 74.5 mL/min, an increase of 124% (Table 1). The median creatinine level at 4 months after catheter placement remained at 1.1 mg/dL (range, 0.7-1.94 mg/dL) (n = 5). No complications