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CASE REPORT | LIVER

Hemorrhagic Cystitis in a Liver Transplant Recipient Secondary to BK Virus

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ABSTRACT

The association between BK virus infection and hemorrhagic cystitis (HC) in hematopoietic stem cell transplant (HSCT) recipients is well established. However, BK virus-associated HC has not been described in liver transplant (LT) recipients. We present a case of BK virus-associated HC in a LT recipient. Our patient presented with worsening liver function tests 2 years after transplantation and was found to have acute cellular rejection. He was treated with increased immunosuppression and subsequently developed hematuria. He was eventually diagnosed with BK virus-associated HC.

INTRODUCTION

BK viruses belong to a class of viruses called human polyomaviruses. Infection in immunocompetent individuals usually has a subclinical course and nonspecific influenza-like symptoms. However, in immunocompromised patients, BK virus can cause specific syndromes with significant morbidity. Hemorrhagic cystitis (HC) secondary to BK virus in hematopoietic stem cell transplant (HSCT) has been well characterized.[1,2] There have been some case reports showing the association between HC and BK virus in solid organ transplant recipients such as kidney transplant and lung transplant.[3,4]

CASE REPORT

A 53-year-old man with a history of liver transplantation (LT) for hepatitis C (HCV)-related cirrhosis. His postoperative course was significant for chronic kidney disease (CKD) stage 3 and recurrent HCV. He was treated for HCV posttransplant with sofosbuvir (400 mg daily) and simeprevir (150 mg daily) for 20 weeks and achieved sustained virological response. His immunosuppression was based on tacrolimus 0.5 mg twice daily and mycophenolic acid 720 mg twice daily. He had good allograft function for 2 years after transplantation before he presented with abnormal liver function tests. A liver biopsy showed severe acute cellular rejection.

The patient was treated with 2 cycles of 3 doses of intravenous methylprednisolone (each dose 500 mg) and 4 doses of intravenous thymoglobulin (each dose 125 mg). The dose of tacrolimus was increased to 2 mg twice daily, and mycophenolate was changed to everolimus 1.5 mg twice daily. When he showed no improvement in liver function tests, a repeat liver biopsy revealed features of persistent severe acute rejection as well as an element of humoral rejection. He was managed with 9 sessions of plasmapheresis and 9 doses of intravenous

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immunoglobulin (each dose 200 mg/kg). His liver function tests gradually improved, and he was subsequently maintained on tacrolimus (1 mg twice daily), everolimus (2.25 mg twice daily), and prednisone (10 mg daily).

The patient developed gross hematuria, dysuria, and abdominal pain secondary to bladder spasms 5 weeks after the onset of acute cellular rejection. At that time, he had received 4 sessions of plasmapheresis and 4 doses of intravenous immunoglobulin. The urinary symptoms developed 2 weeks after the last dose of intravenous thymoglobulin and 4 weeks after the last dose of intravenous steroids. Urinalysis revealed moderate blood and pyuria. The patient was then started on broad-spectrum antibiotics. Urine cultures did not grow any microorganisms. A retroperitoneal ultrasound was negative for abnormalities. Cystoscopy showed diffuse inflammation of the bladder mucosa and was negative for any mass or stricture. However, bladder mucosa was not biopsied. Because his symptoms failed to resolve with an antibiotic course, we evaluated the urine for BK and adenovirus titers. High titers of BK virus (>5,000,000 copies/mL) were identified in urine. The patient also had low-level of BK viremia (1,200 copies/mL). Adenovirus was ruled out by negative polymerase chain reaction.

Supportive care with intravenous hydration and pain control resulted in gradual resolution of symptoms over 2 weeks. Kidney function remained stable throughout the duration of hematuria and dysuria and were at baseline at time of discharge. He was discharged on tacrolimus (1 mg twice daily), everolimus (2.25 mg twice daily), and prednisone (10 mg daily). On follow-up 7 months after his initial presentation with HC, the patient remains clinically stable with resolution of his genitourinary symptoms. His liver and renal function remain stable. BK virus is undetectable in blood but still present in urine at low levels (1,200 copies/mL).

DISCUSSION

This is a unique case of BK virus infection associated with HC in a LT recipient. To our knowledge, this is the first reported case of this association. The prevalence of BK viremia and viruria in LT recipients is low when compared to other solid organ transplant recipients.[5] The prevalence of BK viruria in LT recipients has been reported to be 7.8% compared to 26.5% in kidney transplant recipients and 25.5% in heart transplant recipients. The prevalence of BK viremia was 0% in LT compared to 12.2% in kidney transplant recipients and 7% in heart transplant recipients.[6]

The risk factors that have been identified for BK virus infection in LT recipients include CKD, immunosuppression and previous episode(s) of rejection.[7,8] One study found that LT recipients with a history of rejection had BK viremia more frequently (40%) than those without rejection (10.6%).[8] Although immunosuppression is a risk factor for BK virus infection, none of the studies have identified any specific immunosuppressive regimen that leads to increased risk. While LT and kidney transplant recipients may use a similar immunosuppressive regimen, the lower prevalence of BK virus infection in LT recipients may be explained by other factors, such as CKD and the intensity of immunosuppression, which is higher for kidney transplant recipients.[5]

CKD is considered to be a risk factor for BK virus replication. One study found that the prevalence of BK viremia in cirrhotic patients with CKD on the LT wait list was 56%, while it was 14% in cirrhotic patients without CKD.[7] This higher prevalence of BK viremia in patients with CKD may lead to increased replication of the virus after transplantation once immunosuppression is started. BK virus causes renal dysfunction in kidney transplant recipients, occasionally leading to graft failure, but it is not usually associated with severe manifestations in LT recipients.[9] BK virus infection has a relatively benign course in LT recipients, and infection resolves spontaneously in most cases.[10,11] Although it can cause renal dysfunction in LT recipients, severe renal damage has not been reported, and the long-term outcomes are usually good.[8]

BK virus-associated HC has mostly been described in HSCT recipients.[12] Ruling out other causes of HC, such as bacterial infections and adenovirus, is important in these patients because management is dependent on etiology. The incidence of adenovirus can be as high as 60% in HSCT recipients with HC.[13] In our patient, other possible etiologies of HC were appropriately ruled out by a negative urine culture, negative adenovirus polymerase chain reaction, and an unremarkable retroperitoneal ultrasound and cystoscopy. BK virus is an emerging pathogen causing infections and complications in solid organ transplant recipients.[14] Drake *et al.* reported three cases of BK virus infection in kidney transplant recipients causing renal insufficiency, HC, and microscopic hematuria.[3] BK virus-associated HC has also been described in a pediatric lung transplant recipient.[4] Sandler *et al.* described a case of interstitial pneumonia after an umbilical cord transplant-ation.[15]

Although BK virus infection is common in LT recipients, an association with HC has not been described yet.[8] This case reflects the emerging pathogenic potential of BK virus and shows the importance of considering BK virus-induced HC as differential in LT recipients with gross hematuria. There is an ever-increasing pool of patients with solid organ transplants, and physicians other than transplant specialists are required to be part of care team for these patients. It is imperative that physicians are familiar with potential infectious complications in this group of patients, as delay in diagnosis and treatment can cause significant morbidity.

DISCLOSURES

Author contributions: F. Kamal, B. Ali, and H. Gonzalez wrote and revised the manuscript. M. Barnes and S. Kamal searched the literature. S. Nair critically revised the manuscript. B. Ali is the article guarantor.

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REFERENCES

1. Arthur RR, Shah KV, Baust SJ, Santos GW, Saral R. Association of BK viruria with hemorrhagic cystitis in recipients of bone marrow transplants. *N Engl J Med*. 1986;315(4):230–4.
2. Bedi A, Miller CB, Hanson JL, et al. Association of BK virus with failure of prophylaxis against hemorrhagic cystitis following bone marrow transplantation. *J Clin Oncol*. 1995;13(5):1103–9.
3. Drake KA, Najera L, Reed RC, Verghese PS. Unusual presentations of BK virus infections in pediatric renal transplant recipients. *Pediatr Transplant*. 2013;17(1):E9–15.
4. Elidemir O, Chang IF, Schecter MG, Mallory GB. BK virus-associated hemorrhagic cystitis in a pediatric lung transplant recipient. *Pediatr Transplant*. 2007;11(7):807–10.
5. Umbro I, Tinti F, Muiesan P, Mitterhofer AP. Different behaviour of BK-virus infection in liver transplant recipients. *World J Gastroenterol*. 2016;22(4):1532–40.
6. Muñoz P, Fogeda M, Bouza E, et al. Prevalence of BK virus replication among recipients of solid organ transplants. *Clin Infect Dis*. 2005; 41(12):1720–5.
7. Mitterhofer AP, Tinti F, Umbro I, et al. Polyomavirus BK infection before liver transplantation in patients with chronic kidney disease. *Transplant Proc*. 2012;44(7):1934–7.
8. Loeches B, Valerio M, Pérez M, et al. BK virus in liver transplant recipients: A prospective study. *Transplant Proc*. 2009;41(3):1033–7.
9. Ramos E, Drachenberg CB, Portocarrero M, et al. BK virus nephropathy diagnosis and treatment: experience at the University of Maryland Renal Transplant Program. *Clin Transpl*. 2002:143–53.
10. Amir A, Shapiro R, Shulman LM, et al. BK virus infection and its effect on renal function in pediatric liver-transplant recipients: A cross-sectional, longitudinal, prospective study. *Transplantation*. 2011;92(8):943–6.
11. Doucette KE, Pang XL, Jackson K, et al. Prospective monitoring of BK polyomavirus infection early posttransplantation in nonrenal solid organ transplant recipients. *Transplantation*. 2008;85(12):1733–6.
12. Xie Y, Han Y, Wu DP, et al. [The BK virus load in urine in association with the development of hemorrhagic cystitis after hematopoietic stem cell transplantation]. *Zhonghua Xue Ye Xue Za Zhi*. 2009;30(8):524–7.
13. Akiyama H, Kurosu T, Sakashita C, et al. Adenovirus is a key pathogen in hemorrhagic cystitis associated with bone marrow transplantation. *Clin Infect Dis*. 2001;32(9):1325–30.
14. Mylonakis E, Goes N, Rubin RH, Cosimi AB, Colvin RB, Fishman JA. BK virus in solid organ transplant recipients: An emerging syndrome. *Transplantation*. 2001;72(10):1587–92.
15. Sandler ES, Aquino VM, Goss-Shohet E, Hinrichs S, Krisher K. BK papova virus pneumonia following hematopoietic stem cell transplantation. *Bone Marrow Transplant*. 1997;20(2):163–5.