



## CASE REPORT

# BK Virus-Associated Hemorrhagic Cystitis in Children Suffering from Malignancies: Report of Three Cases

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## ABSTRACT

BK virus-associated hemorrhagic cystitis (HC) is frequent in patients undergoing bone marrow transplantation, but it rarely occurs among other immunosuppressed patients particularly in those who are receiving chemotherapy for hematologic malignancies. Herein, we report three children with malignancies suffering from hemorrhagic cystitis due to BK virus infection who were successfully improved.

Early detection of BK virus using RT-PCR technique was undertaken. With administration of antiviral agents; specifically, IVIG or leflunomide, BK virus-associated HC could be successfully managed in children affected by malignancies and consequently, chemotherapy of underlying disorder might be continued after virus elimination.

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## Introduction

HC is a common problem complicating those suffering from different kinds of cancers particularly hematologic malignancies which occurs mainly following chemotherapy or bone marrow transplantation with the incidence varying from 7% to 70%.<sup>1</sup> This condition results in severe morbidity that is seldom life-threatening. It has been shown that main causes of HC include chemotherapeutic agents or viral infections such as polyomaviruses or adenoviruses.<sup>2</sup> BK virus; a member of polyomaviruses has been shown to be strongly associated with HC.<sup>3</sup> Herein, we describe our experience with three children with malignancy under chemotherapy suffering from HC due to BK virus infection who were successfully recovered.

## Case Report

A 3-year-old boy, known case of burkitt lymphoma developed hematuria and dysuria along with mild fever

two months after starting chemotherapy. Complete blood count showed a white blood cell count  $0.200 \times 10^9/\text{mm}^3$ , Hemoglobin 8.9 g/dL and platelet  $207 \times 10^9/\text{mm}^3$ . Ultrasound showed the bladder with thickened and irregular wall, containing floating and vesicular echogenic pattern which raised the suspicion for HC. The positivity for BK virus was thus checked in urine using real-time polymerase chain reaction (RT-PCR) which was positive with a copy number of  $1 \times 10^6/\text{ml}$ . Therefore, the patient was treated with ciprofloxacin and IVIG. After three days, hematuria was disappeared; however, dysuria was not completely resolved. Ten days later, BK virus in urine was rechecked which copy numbers were reduced to 395,245/ml. IVIG was prescribed again that led to complete disappearance of symptoms and thus chemotherapy was continued. Final assessment of BK virus by PCR one month later showed negative results.

The second case was a 5-year-old girl with acute lymphoblastic leukemia since 18 months of age who

was receiving chemotherapy. She experienced an episode of dysuria and hematuria between the sessions of chemotherapy. As a result, BK virus was checked for her that reported to be positive in urine. She was planned to receive leflunomide while chemotherapy was discontinued for the patient. Leflunomide was continued for one month. After one month of treatment, symptoms completely were resolved and BK virus was rechecked in urine that was revealed to be negative.

The third case was a 7-year-girl with astrocytoma who underwent surgery for her mass. After one year, the mass relapsed and the patient was scheduled to receive radiotherapy and chemotherapy. During chemotherapy, the patient complained of dysuria and hematuria. Urine analysis revealed many RBCs without bacteria. We assessed for BK virus in the urine by RT-PCR that was positive in urine. Treatment started with leflunomide and IVIG. Severity of dysuria was reduced, however hematuria was persistent. Accordingly, we prescribed AryoSeven™, (Iranian Recombinant activated factor VII) which after 3 days hematuria was resolved. On month later, all symptoms completely resolved and BK virus in the urine was revealed to be negative.

### Discussion

HC is a complication associated with HSCT. HC is characterized by hemorrhagic inflammation in urinary tract mucosa. The symptoms vary from asymptomatic microscopic hematuria to gross hematuria with clot formation and urinary tract obstruction.<sup>4</sup>

BK virus; primarily isolated in 1971, has been identified as the main risk factor for nephropathy due to immunosuppression during kidney transplantation.<sup>5</sup> Routine screening for the virus along with reducing immunosuppression remain mainstay of prevention and treatment of BK virus-related conditions.<sup>6</sup> In most cases, the acquisition of the virus is asymptomatic until the body undergoes immunosuppression that can lead to severe morbidities in affected patients. Major clinical manifestations of infection with BK virus include non-specific symptoms of renal dysfunction such as raised creatinine or those due to bladder inflammation containing dysuria or hematuria.<sup>7</sup> An abnormal urinalysis can reveal renal tubular cells and inflammatory cells.<sup>8</sup>

BK virus-associated HC is frequent in patients undergoing bone marrow transplantation, but it rarely occurs among other immunosuppressed patients particularly in those who are receiving chemotherapy for hematologic malignancies.<sup>9</sup> HC can deteriorate the course of the underlying disease leading to poorer outcome, longer hospitalization, higher morbidity and mortality and increased financial burden.

Early diagnosis of BK virus using RT-PCR technique can successfully help better control of HC and prevent its adverse consequences. As the first attempt to control viremia and its sequel, immunosuppression should be reduced. Along with this approach, IVIG and leflunomide is suggested as the second line to eliminate the virus and relief of symptoms of HC. Leflunomide has a powerful antiviral activity by inhibiting virus replication in urinary

system.<sup>10</sup> The beneficial effects of IVIG for treating BK virus have also been described.<sup>11</sup>

### Conclusion

Early detection of BK virus using RT-PCR technique and administration of antiviral agents mainly; IVIG or leflunomide, are mainstay of management of BK virus-associated HC in children affected by hematologic malignancies. Obviously, chemotherapy could be continued after virus elimination.

**Conflict of Interest:** None declared.

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