BKV - a Challenge for Post-Transplant Patients

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Abstract

BKV infection is widespread as early as infancy and early adolescence. The virus remains persistent at low levels in many tissues of the human body, in particular the urogenital tract. Reactivation and/or reinfection from donors in the post-transplant period may result in severe disease, including BKV-associated nephropathy and graft rejection. The aim of this study is to determine the percentage involvement of BKV in morbidity after kidney transplantation and after allogeneic stem cell transplantation. Eighty-seven studies were performed in a total of 37 post-transplant patients (out of which 59.4% were women) with a mean age of 42.2 years (SD ± 10.6, range 26-70 years). Thirty-three patients after renal transplantation were screened for reactivation (89.2%, CI: 79.2% to 99.2%) in serum, and 4 patients (10.8%; CI: 0.8% to 20.8%) after allogeneic stem cell transplantation in urine samples when clinical evidence of haematuria was present. We used quantitative BKV PCR test kit Anatolia Geneworks, Istanbul, Turkey. We obtained a positive result in 1 patient after renal transplantation (3.03%) and in 3 patients (75%) after allogeneic stem cell transplantation and haematuria. Our data indicate that BKV is involved in morbidity after transplantation. In order to determine the most appropriate PCR sample material (serum, plasma or urine), all three should be tested simultaneously.

Keywords:...

Introduction

Polyomaviruses are ubiquitous, infecting many different mammalian species including humans. Most human polyoma-diseases are caused by JCV and BKV. BKV is a small non-enveloped double-stranded DNA virus. It is a ubiquitous virus with high seroprevalence in the general population (Knowles et al.,...
BKV infection is usually acquired in early childhood. Transmission occurs typically via oral and respiratory routes. Following primary infection, the virus remains latent in the host in different sites, particularly the kidneys, uroepithelial cells and lymphocytes. Reactivation from latency may occur in normal subjects with asymptomatic viruria in about 5%, while it can be associated with nephropathy in kidney transplant recipients (Dolei et al., 2000; Replog et al., 2001; Costa et al., 2012). Under the circumstances of severe immunosuppression, BKV can cause pneumonitis, hepatitis, retinitis, and meningoencephalitis (Bressollette-Bodin et al., 2005; Dropulic et al., 2008). Hemorrhagic cystitis is seen in 25–60% of bone marrow transplant patients, usually 2 weeks after transplantation (Bressollette-Bodin et al., 2005). Up to 80% of renal transplant recipients have BK viruria, and 5%–10% progress to BKV nephropathy (BKVN) (Hirsch et al., 2002). Given that polyomavirus is widely latent in the kidney, kidney transplantation (KT) is believed to be an important mode of infection in patients with end-stage kidney disease. Graft loss rate has been reported to be as high as 30%–50% following the diagnosis of BKVN (Sood et al., 2012; Hirsch et al., 2013). RT-PCR is the method of choice to detect viral replication in urine and blood, for diagnosis and prognosis of BKVN (Dall et al., 2008, Van Din et al., 2017) and screening is recommended every 3 months in the first two post-transplant years or when allograft dysfunction occurs (Posdzich et al., 2016). The aim of present study was to determine the percentage involvement of BKV in morbidity after KT and allogeneic stem cell transplantation (aHSCT).

**Material and Method:**

**Material**

87 tests were performed in a total of 37 post-transplant recipients (out of which 59.4% were women) with a mean age of 42.2 years (SD ± 10.6, range 26-70 years). 33 patients (89.2%, CI: 79.2% to 99.2%) after KT were screened for reactivation in serum and 4 patients (10.8%; CI: 0.8% to 20.8%) after aHSCT in urine samples when clinical evidence of haematuria was present (Fig. 1, Fig. 2).

A total of 87 studies were performed in different post-transplant periods. 28 KT recipients were monitored in more than one sample. One patient after aHSCT was tested twice (Fig. 3).

**Method**

We used quantitative BKV PCR test kit v1 of Anatolia, Geneworks, Istanbul, Turkey.

**Results and Discussion**

A total of five samples from four patients were positive in PCR. We obtained positive results in 1 serum sample from a patient after KT (3.03%), and in the urine samples of 3 patients (75%) after aHSCT and haematuria, where one of them was positive twice (Fig. 4, Table 1).

BKV infection is widespread in the human population. Infection is usually asymptomatic in childhood. After primary infection, the virus remains latent in many tissues and organs, mainly in the urogenital tract mucosa. Immunosuppression after transplantation leads to reactivation of the
latent BKV infection and may cause rejection of the grafted organ or tissue. In a study of 441 organ transplant recipients in Europe 24 days after transplantation, the detected BKV-seroprevalence was 97%. In addition, there was a significant increase in antibody reactivity after the onset of immunosuppression (Antonsson et al., 2013). Viral reactivation during immunosuppression causes cytopathic changes in the uroepithelium and subsequently increases the viral load in the urine. Nucleic acid amplification testing of blood and urine is the main diagnostic and prognostic test for BKV infection. Data show that BKV viruria higher than 10^7 c/ml and plasma BKV viremia of 10^4 c/ml are reported to be typical in patients with BKV nephropathy (Ferreira-Gonzalez et al., 2007). BKV disease is a common complication after aHSCT. Hemorrhagic cystitis is seen in 25–60% of bone marrow transplant patients, usually 2 weeks after transplantation according to the literature (Bressollette-Bodin et al., 2005). According to other authors, BKV was detected in urine in 51.4% of patients 100 days after aHSCT, but only 19.1% of them developed hemorrhagic cystitis (Posdzich et al., 2015).

According to our data, 3 (75%) of the 4 patients after aHSCT developed BKV-associated hemorrhagic cystitis about 1 month after transplantation (Table 1). In our study, the viral load in the urine of these patients was high and ranged from log 7.2 to log 10.5.

<table>
<thead>
<tr>
<th>Date of study</th>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Sample</th>
<th>Type of transplantation</th>
<th>Date of transplantation</th>
<th>BKV PCR (c/ml)</th>
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<tr>
<td>01.12.2015</td>
<td>С И П</td>
<td>39</td>
<td>female</td>
<td>serum</td>
<td>KT</td>
<td>27.10.2014</td>
<td>167 519</td>
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<td>21.09.2018</td>
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<td>female</td>
<td>urine</td>
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<td>03.08.2018</td>
<td>30 198 577 152</td>
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<tr>
<td>16.10.2018</td>
<td>С Х И</td>
<td>43</td>
<td>male</td>
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</tr>
</tbody>
</table>

Our data from the screening program of 33 kidney transplant recipients for BKV viremia after KT showed a positive result in one (3.03%) patient about 1 year after the transplantation. We do not have baseline data on the BKV seroprevalence of the patients studied. Real time PCR results do not show reactivation and viremia in most of them. A limitation of the study is that urine test was not performed for these patients.

In conclusion, BKV is more frequently involved in the morbidity of patients after aHSCT, who undergo more severe immunosuppression as a rule. BKV plays a role in morbidity after KT and aHSCT, but for more accurate determination of the proportion, a more frequent follow-up of the recipients is required simultaneously in both clinical materials - urine and serum/plasma.

References


