Human polyomavirus BKV and renal disease

Keerti V. Shah

Department of Molecular Microbiology and Immunology, Johns Hopkins School of Public Health, Baltimore, USA

Human and non-human polyomaviruses

In 1971, two human polyomaviruses were discovered, BK virus (BKV) from the urine of a renal transplant recipient (whose initials were B.K.) and JC virus (JCV) from the brain of a patient (whose initials were J.C.) with progressive multifocal leukoencephalopathy (PML). The polyomavirus subfamily of the papovavirus family also includes viruses of monkeys (rhesus and cynomologus macaques, African green monkey, baboon), cattle, rabbit, mouse, rat and parakeet [1]. The viruses have a 5 kb double-stranded, circular, supercoiled, DNA genome. Polyomaviruses are highly species-specific and have probably co-evolved with their natural hosts. Primary infections are essentially harmless but the viruses tend to persist indefinitely in the infected individual.

BKV and JCV biology

Primary BKV infections occur in early childhood and primary JCV infections in late childhood. Both viruses remain latent in the kidney and in B lymphocytes after primary infection. Almost all illnesses attributable to BKV and JCV occur in the background of immunodeficiency, most often as a result of reactivation of the latent virus. JCV is the aetiologic agent of PML, a fatal, subacute, progressive demyelinating disease of the brain, which occurs as a complication of AIDS and other immunosuppressive conditions. In contrast to the tropism of JCV for brain, BKV-related pathology is largely confined to the urinary tract.

Some simian polyomaviruses produce illnesses in their natural hosts which closely resemble human illnesses caused by JCV and BKV. Simian virus 40, an indigenous polyomavirus infection of rhesus macaques, produces a PML-like neurological disease in animals which are immunosuppressed by infection with simian immunodeficiency virus [2]. The renal pathology caused by infection with the newly described cynomolgus polyomavirus [3] in animals undergoing experimental renal transplantation is very similar to the BKV-associated human disease described in a recent issue of this journal [4].

BKV-related urinary tract pathology

Urinary shedding of BKV is increased in immunocompromising conditions. BKV infection has been linked to occasional cases of cystitis in immunocompetent children, to glomerulonephritis in immunodeficient children, and to haemorrhagic cystitis in bone marrow transplant recipients. While BKV infections and BK viruria have been frequently documented in renal transplant recipients, conclusive evidence of significant BKV-related kidney pathology has been recognized only recently. Reports from several groups clearly define BKV nephropathy, a clinical condition in renal transplant recipients, in which extensive BKV multiplication in the tubular epithelium results in loss of allograft function [5–7]. The disease occurs in about 2–3% of renal transplant recipients [4,7] and is correlated with the shedding of a large number of virus-infected epithelial cells in the urine [7] and with the presence of BKV DNA in the serum [2]. The disease may be, in part, a result of the introduction of new immunosuppressive drugs [6]. Reduction in the immunosuppressive therapy often leads to improved clinical outcome.

Role of donor kidney

BKV in donor kidney is a determinant of BKV infection in the recipient. Previous studies of paired serum specimens have shown that about a quarter of BKV infections (as determined by a 4-fold or greater rise in BKV antibody titer) in renal transplant recipients occur in individuals who have no detectable antibodies in their first serum, i.e. they are primary infections [8]. This is in contrast to BKV infections in bone marrow

Table 1. BKV infection in renal transplant recipients

<table>
<thead>
<tr>
<th>Donor/recipient</th>
<th>BKV antibody status*</th>
<th>Number</th>
<th>Number (%) of recipients with BKV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>BKV</td>
<td>Number</td>
<td>Number</td>
<td>BKV infection</td>
</tr>
<tr>
<td>+/-</td>
<td>44</td>
<td>19 (43%)</td>
<td></td>
</tr>
<tr>
<td>-/+</td>
<td>21</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>+/+</td>
<td>229</td>
<td>50 (22%)</td>
<td></td>
</tr>
<tr>
<td>+/-</td>
<td>48</td>
<td>6 (13%)</td>
<td></td>
</tr>
</tbody>
</table>

*Data rearranged from ref. [8].

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transplant recipients and in pregnant women, which are almost always due to reactivation of latent BKV. Furthermore, as shown in Table 1, BKV infection in renal transplant recipients occurs most frequently when kidney from a BKV-seropositive donor is transplanted into a BKV seronegative recipient. Such a donor/recipient antibody combination may be a risk factor for BKV nephropathy.

References