Polyomaviruria in Renal Transplant Patients Is Not Correlated to the Cold Ischemia Period or to Rejection Episodes

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Received 20 August 1999/Returned for modification 28 September 1999/Accepted 20 October 1999

Polyomaviruria was observed in one-third of all renal transplant patients, irrespective of whether their renal grafts came from a living or cadaver donor, and was not correlated to graft rejection episodes. This suggests that the renal graft ischemia period is not the major cause of polyomavirus reactivation and that reactivation of polyomavirus is not a dominant cause of graft rejection.

BK virus (BKV) and JC virus (JCV) are widely spread human polyomaviruses that remain latent in the kidney and, possibly, also in the blood and the brain (5, 9, 11, 19). Reactivation can be manifested as symptom-free viral excretion in the urine and is more frequently observed in immunosuppressed patients (10). In such patients BKV can also be associated with hemorrhagic cystitis or ureteral stenosis, while JCV can cause progressive multifocal leukoencephalopathy (PML) (1, 6, 8, 17).

In renal transplant recipients the incidence of BK and JC viruria has been reported to be in the range of 14 to 65%, and reactivation has been speculated to be of donor or recipient origin (7, 13, 15, 16, 18, 19). In half the patients viruria occurs within the first 3 months after transplantation and can be transient or last for weeks or years (13). Ureteral stenosis, graft rejection, rise in serum creatinine level, impaired renal function, and PML have been described in renal transplant patients with polyomaviruria (2, 6, 8, 19). Nevertheless, it has been difficult to assess the clinical significance of viral infection for disease development. It has been suggested that damage of the ureter by ischemia or by inflammation may reactivate latent polyomavirus infection in the ureteric epithelium and cause ureteral stenosis (6, 8). In line with this hypothesis are recent findings in a murine experimental system in which reactivation of polyomavirus is observed in adult mice after occlusion of the renal artery (3). However, so far none of the previous reports have focused on the fact that the renal graft ischemic period (i.e., the period after removal of the renal graft from the donor and until transplantation, when the renal graft is kept at about 4°C in an icebox) may influence polyomaviruria. Hence, polyomaviruria may vary between living donor (LD) and cadaver donor (CD) graft recipients. This could partly explain the marked difference in graft survival rates between LD grafts (1-year graft survival rate, 90 to 95%) and CD grafts (1-year graft survival rate, 75 to 80%) (12). Furthermore, the difference in survival rates are independent of HLA matching since the same rates are observed among both related and spouse donors (12).

To study if polyomaviruria is correlated to renal graft ischemia, we investigated if the presence of polyomaviruria varied in two groups of patients with different renal graft ischemia times. Thus, one group of patients received renal grafts from LDs and the ischemia period was only about 30 min, whereas the second group of patients received renal grafts from CDs and the average cold ischemia time was 17 h in our department.

Three hundred eighty-three urine samples were collected during the period from 1995 to 1998 from 170 patients (of northern European origin and of 2 to 73 years of age) from 1 week to 2 years after transplantation and were analyzed for the presence of polyomaviruses. The majority of all urine samples were analyzed shortly after collection. If possible, the samples were analyzed within 24 to 48 h; otherwise, they were stored at −20°C and were analyzed within a week by a nested PCR for simultaneous detection of BKV and JCV DNA (4). The 176-bp fragment of BKV DNA and the 173-bp fragment of JCV DNA obtained after amplification with the inner primer pair could easily be distinguished after restriction enzyme digestion with BamHI or HinII (4, 14). One hundred four patients received a kidney from a CD, while 66 received a kidney from an LD. Data concerning ureteral stenosis or graft rejection were collected from the patients’ records. As a control group for comparison, urine samples from 14 laboratory staff were included (4).

Of 170 patients, 55 (33%) were found to be positive for human polyomavirus in their urine samples at some time point after transplantation. A detailed description of the data is presented in Table 1. After restriction enzyme cleavage, BKV DNA was found in the urine samples of 12 (7%) patients, JCV DNA was found in the urine samples of 37 (22%) patients, and both BKV and JCV DNAs were found in the urine samples of 6 (3.5%) patients (Table 1). There was no significant difference between excretion of human polyomaviruses in recipients of

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<table>
<thead>
<tr>
<th>Source of donor</th>
<th>Total</th>
<th>No. (%) of urine samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BKV positive</td>
<td>JCV positive</td>
</tr>
<tr>
<td>LD</td>
<td>66</td>
<td>5 (7.5)</td>
</tr>
<tr>
<td>CD</td>
<td>104</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Total</td>
<td>170</td>
<td>12 (7)</td>
</tr>
</tbody>
</table>
TABLE 2. Presence of polyomaviruria and rejection episodes in patients receiving LD or CD renal grafts

<table>
<thead>
<tr>
<th>Source of polyomaviruria</th>
<th>LD grafts</th>
<th>CD grafts</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With rejection</td>
<td>Without rejection</td>
<td>With rejection</td>
</tr>
<tr>
<td>BKV</td>
<td>1/5 (20)</td>
<td>4/5 (80)</td>
<td>3/7 (43)</td>
</tr>
<tr>
<td>JCV</td>
<td>3/15 (20)</td>
<td>12/15 (80)</td>
<td>10/22 (45)</td>
</tr>
<tr>
<td>BKV and JCV</td>
<td>1/4 (25)</td>
<td>3/4 (75)</td>
<td>1/2 (50)</td>
</tr>
<tr>
<td>Neither BKV nor JCV</td>
<td>25/42 (60)</td>
<td>17/42 (40)</td>
<td>27/73 (37)</td>
</tr>
</tbody>
</table>

Total: 30/66 (45) 36/66 (55) 41/104 (40) 62/104 (60) 71/170 (42) 99/170 (58)

REFERENCES


The Karolinska Institute and the Swedish Cancer Society supported this work.