

If the Donor Had an Early-Stage Genitourinary Carcinoma and the Liver Has Already Been Implanted, Should We Perform the Transplantectomy?

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Information regarding the outcome of liver grafts from cadaveric donors with genitourinary cancer is scarce. In some cases, the liver has already been implanted when the tumor is detected. What must we do then? Our goal is to evaluate the outcome of recipients of liver allografts from donors with unsuspected early-stage genitourinary carcinoma. We performed 684 liver procurements from cadaveric donors and 582 liver transplants. A malignant genitourinary tumor was detected in the donor after implantation of the donor liver in six cases (1.03%): four renal carcinomas and two prostate cancers. All donors were elderly (mean age, 64.6 years) and died of a cerebrovascular accident. Four patients are still alive and presently free of malignancy, whereas the two other transplant recipients died of hepatitis C virus recurrence at 14 and 55 months after transplantation without evidence of tumor transmission. We did not observe evidence of tumor transmission in any patient after an average follow-up of 51 ± 20 months. Our results suggest it is not always necessary to perform transplantectomy or use special treatment modalities in recipients of a liver allograft from donors with early-stage (T1 to T2) renal cell carcinoma or early (T1) prostate carcinoma. (Liver Transpl 2003;9:1281-1285.)

Many studies have been published about the outcome of recipients of organs from donors with neoplasms of a different origin.1,2 The current recommendation is that organs from donors with malignancies not be used, with the exception of low-grade skin neoplasms, carcinoma in situ of such organs as the uterine cervix, or certain primary brain tumors.2

Because of the organ shortage, the percentage of elderly donors has increased continuously during the last years.3 Because the probability of malignancy increases with age, the possibility of an unsuspected tumor in the donor also increases proportionally. Despite preoperative screening for the presence of cancer, some donors may have an undiagnosed tumor at the time of organ donation. Because thoracic organs and the liver usually are procured before the kidneys, one of the most controversial situations is the detection of a small renal cell carcinoma or early-stage prostate neoplasm after procurement of donor organs for transplantation. Currently, no general agreement exists on how to manage these donor organs. Some investigators even proposed transplanting the kidney after resection of the renal tumor.4 Moreover, in some cases, the liver has already been implanted before the tumor is detected. What must we do then? Unfortunately, information in the literature regarding this question is scarce.

Our objective is to show results of our experience with liver allografts from donors with a genitourinary malignancy.

Patients and Methods

Between January 1996 and December 2001, we performed 684 liver procurements from cadaveric donors. Preoperative screening for cancer included review of clinical reports; clinical examination; biochemical analysis, with human chorionic gonadotrophin determination in all donors and prostate-specific antigen (PSA) determination in men older than 60 years; chest X-ray; abdominal ultrasonography; and review of the computed tomographic (CT) brain scan of donors who died of a cerebrovascular accident.

Differential surgical teams are involved in organ retrieval at our institution. First, thoracic and hepatic surgeons retrieve the heart, lungs, and liver. After these organs are procured, a urologist removes the kidneys. Kidneys are extracted at our institution within perirenal fat tissue, usually without opening Gerota’s fascia. The kidneys are used in our center or sent to another center, where backtable surgery and transplantation are performed. During the surgical procedure, hepatic surgeons carefully examine all accessible intra-abdominal
organs for evidence of neoplasms. This examination includes extensive palpation of the kidney within Gerota’s fascia. If a suspicious lesion is detected, a biopsy and prompt frozen section examination are performed. Following this approach, we detected an unexpected tumor in 11 of these donors (1.6%), with the result that organs from these donors were discarded (Table 1).

In the same period, we performed 582 liver transplantsations. In six cases (1.03%), a malignant genitourinary tumor was detected in the donor after implantation of the liver. There were four renal carcinomas and two prostatic neoplasies. In these six cases, only liver and renal grafts were procured.

Recipient age, sex, and indication for liver transplantation are listed in Table 2. Liver transplantation was performed using the cava preservation technique. We did not perform transplantectomy or modify routine treatment in any of these cases.

Posttransplantation immunosuppressive regimen included cyclosporine or tacrolimus in combination with corticosteroids (see Table 2 for each case). Doses and target ranges of immunosuppressive agents were as follows: methylprednisolone, 10 mg/kg, during the anhepatic phase, tapered to 20 mg/d on day 7; cyclosporine A, 15 mg/kg/d, divided into two doses adjusted accordingly to renal function to maintain levels between 250 and 350 ng/mL during the first month; and tacrolimus, 0.1 mg/kg/d, divided into two doses adjusted according to renal function, maintaining levels between 5 and 15 ng/mL during the first month. Our schedule of posttransplantation follow-up remained unchanged, including abdominal ultrasonography at 1, 3, and 12 months in the first year.

Table 1. Liver Donors Excluded for Neoplasm Detection During Surgery

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Donors</th>
<th>No. of Donors Discarded</th>
<th>No. of Donors Discarded for Malignancy (% of donors excluded)</th>
<th>Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>88</td>
<td>8 (9.1)</td>
<td>1 (11.1)</td>
<td>1 Renal cell carcinoma</td>
</tr>
<tr>
<td>1997</td>
<td>87</td>
<td>10 (11.5)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1998</td>
<td>125</td>
<td>15 (12.0)</td>
<td>4 (25.0)</td>
<td>2 Lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Astrocytoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Metastatic renal cell carcinoma</td>
</tr>
<tr>
<td>1999</td>
<td>123</td>
<td>17 (13.8)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2000</td>
<td>126</td>
<td>19 (15.1)</td>
<td>2 (10.5)</td>
<td>1 Renal cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Epidermoid pulmonary carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Prostatic carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Ovaric carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 Suprarenal tumor</td>
</tr>
</tbody>
</table>

NOTE. Values expressed as number (percent).

Table 2. Donor and Recipient Characteristics

<table>
<thead>
<tr>
<th>Donor</th>
<th>Age (yr)/Gender</th>
<th>Tumor</th>
<th>Size (cm)</th>
<th>Stage</th>
<th>Age (yr)/Gender</th>
<th>Hepatopathy</th>
<th>Immunosuppression</th>
<th>Follow-Up (mos)</th>
<th>Status</th>
<th>Tumor Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>62/F</td>
<td>Renal cell carcinoma</td>
<td>2.5</td>
<td>1 (T1), grade I</td>
<td>63/F</td>
<td>Retransplant HCV</td>
<td>CyA + corticosteroids</td>
<td>55 Died (HCV recurrence)</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>63/M</td>
<td>Renal cell carcinoma</td>
<td>4.5</td>
<td>1 (T2), grade II</td>
<td>58/M</td>
<td>HCV + HCC</td>
<td>FK506 + corticosteroids</td>
<td>68 Live</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70/M</td>
<td>Renal cell carcinoma</td>
<td>3.0</td>
<td>1 (T2), grade I</td>
<td>54/F</td>
<td>PBC</td>
<td>CyA + corticosteroids</td>
<td>62 Live</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>57/F</td>
<td>Renal cell carcinoma</td>
<td>1.0</td>
<td>1 (T1), grade II</td>
<td>46/F</td>
<td>HCV</td>
<td>FK506 + corticosteroids</td>
<td>14 Died (HCV recurrence)</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65/M</td>
<td>Prostate carcinoma + glioblastoma</td>
<td>1.3</td>
<td>A1 T1a Gleason (2-3) 5</td>
<td>46/M</td>
<td>HCV + HCC</td>
<td>FK506 + corticosteroids</td>
<td>44 Live</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71/M</td>
<td>Prostate carcinoma</td>
<td>0.5</td>
<td>A1 T1a Gleason (1-2) 5</td>
<td>63/M</td>
<td>HCC</td>
<td>CyA + corticosteroids</td>
<td>62 Live</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HCV, hepatitis C virus; HCC, hepatocellular carcinoma; PBC, primary biliary cirrhosis; CyA, cyclosporine A.
between donor and recipient. In transplantation, enhances the risk for tumor transmission. However, immunosuppression, required in transplantation, between immunocompetent individuals is very low. The possibility of tumor transmission to the recipient after reperfusion of the donor organ. The dilemma becomes more complex when one deals with such life-saving organs as heart, lungs, or liver. After removal of these organs, the recipient can be saved only by another transplant. This may result in high morbidity and mortality. Moreover, retransplantation is dependent on availability of a new graft, and

Results

All six donors with unsuspected malignancy, from whom the liver had already been implanted, were elderly individuals (mean age, 64.6 ± 5.2 years), and all died of a cerebrovascular accident. Age, sex, and tumor characteristics are listed in Table 2.

The kidney tumors were detected at the time of backtable surgery by the urologist surgeons. Unfortunately, at that time, the donor liver was already implanted. The two prostate cancers and glioblastoma were detected at the time of donor autopsy. In both cases with prostate cancer, PSA values were normal. All tumors were early-stage cancers, without local or systemic spread (Table 2).

During the 5-year follow-up (mean, 50.8 ± 19.8 months), evidence of tumor transmission was not detected in any patient. Four patients are alive and free of malignancy, whereas the two other transplant recipients died of hepatitis C virus recurrence without evidence of tumor transmission at 14 and 55 months after transplantation.

All kidneys from donors with renal cell carcinoma were discarded before implantation. In the case of a solitary prostate carcinoma in the donor, the kidneys were not implanted. However, in the case of combined prostate carcinoma and glioblastoma in the donor, both kidneys were transplanted. The left kidney experienced arterial thrombosis in the recipient at the time of implantation; therefore, the procedure was not completed. The right kidney was implanted in a 50-year-old man. Despite adequate initial function, transplantectomy was performed 12 days after transplantation. The patient returned to hemodialysis therapy and the waiting list. Annual brain CT scan and regular PSA testing showed no evidence of tumor transmission during the 2 years of follow-up on the waiting list, until he was removed because of severe coronary artery disease.

Discussion

Discovery of a tumor in the donor after implantation of one of the organs results in a risk for tumor transmission to the recipient. The possibility of tumor transmission between immunocompetent individuals is very low. However, immunosuppression, required in transplantation, enhances the risk for tumor transmission between donor and recipient.

In transplantation, the risk for tumor transmission depends on the type and stage of tumor in the donor. Recently, to expand the donor pool, the use of donors with a past history of cancer has been proposed. In this review of the United Network for Organ Sharing, the investigators observed only a small risk for cancer transmission from donors with a past history of nonmelanoma skin cancer, selected cancer of the central nervous system, and selected cases of genitourinary carcinoma. Other investigators have studied the outcome of recipients of organs from donors with neoplasms of a different origin at the time of organ donation. The current recommendation is that organs from donors with malignancies not be used, with the exception of those from donors with low-grade skin neoplasms, carcinoma in situ of such organs as the uterine cervix, or certain primary brain tumors. Therefore, organs from donors with known genitourinary malignancy must not be used for transplantation, and these organs must not be offered to patients on the waiting list.

However, in some cases, the graft has already been implanted when the tumor is detected. Detection of a small renal cell carcinoma during procurement of the donor kidneys is an infrequent, but not exceptional, situation. An incidence of up to 0.9% of renal carcinomas in cadaveric donors has been reported. First, our series shows that it is necessary to perform an exhaustive examination during extraction surgery in the donor to identify tumors. Extraction of kidneys within perirenal fat tissue could result in delayed discovery of a donor’s renal tumor. It could be necessary to remove perirenal fat tissue, especially in elderly donors. Autopsy of the donor is not always performed, which could result in an underestimated incidence of other tumors, such as prostate carcinoma. In a Danish study, risk for having a donor with undetected malignancy was found to be 1.3%. The approach to this situation is controversial, and general guidelines in these cases have not been defined.

Transplantectomy is the first option when a tumor is detected in the donor after implantation of one of the organs. Theoretically, transplantectomy removes a possible tumor in the recipient. However, there is no evidence to support transplantectomy as a method to avoid circulating malignant cells transmitted from the donor to the recipient after reperfusion of the donor organ. The dilemma becomes more complex when one deals with such life-saving organs as heart, lungs, or liver. After removal of these organs, the recipient can be saved only by another transplant. This may result in high morbidity and mortality. Moreover, retransplantation is dependent on availability of a new graft, and
immunosuppression cannot be discontinued. What must we do then?

Again, therapeutic options should be considered in the context of type and stage of tumor. In at least nine instances, a kidney with a small primary renal carcinoma has been transplanted after excision of the lesion. No evidence of tumor transmission has been reported in these cases after a follow-up ranging from 1 to 259 months (average, 79 months). However, in two other cases, tumor was found in the transplanted kidney. In one case, the kidney from a donor with renal carcinoma in the contralateral kidney, which was removed because of rejection 3 months after transplantation, showed a small carcinoma, and in the second case, a small papillary carcinoma (17 mm) in the contralateral kidney resulted in massively infiltrating undifferentiated renal carcinoma in the graft 4 months after transplantation. This case was treated with graft removal and immunosuppression discontinuation, with satisfactory outcome.

The situation becomes increasingly complicated if the graft is a life-saving organ, as in our case. These patients need retransplantation and maintenance of immunosuppression for graft removal.

Review of cases of cardiothoracic transplant recipients of an organ from a donor with renal malignancy showed that renal cell carcinomas without capsular invasion did not result in tumor transmission. However, in the case of vascular invasion of the tumor in the donor, tumor transmission appears to be early. Moreover, on at least one occasion, tumor transmission of a small renal papillary carcinoma of 17 mm to a heart recipient resulted in bone metastases and patient death. One case of a heart transplant from a donor with prostate cancer resulted in metastatic prostate cancer in the recipient 10 months after transplantation and death of the patient 36 months after transplantation. It must be noted that in this donor, spread of the prostate adenocarcinoma to the pelvic lymph nodes was detected.

We found four cases in the literature in which an unsuspected early renal carcinoma was detected after the liver had already been implanted that were managed without transplantectomy. In one case, a liver from a donor with a T1 renal carcinoma had been transplanted. The patient was alive and free of disease after a 4-year follow-up. Two recipients of a split-liver transplant from a donor with a 2-mm renal cell carcinoma both remained free of transmission after 1 year. Another recipient of a liver from a donor with an 8-mm renal cell carcinoma died 7 months after the procedure of graft-versus-host disease without evidence of tumor transmission at autopsy.

Experience in transplantectomy as a method to avoid tumor transmission in the case of liver transplantation is limited. We found four cases reported in the literature of liver removal after transplantation, but all had a tumor-bearing graft at the time of transplantectomy; therefore, the procedure was not performed to avoid tumor transmission, but to treat it. These tumors were metastatic pancreas carcinoma, metastatic adenocarcinoma, undifferentiated squamous cell carcinoma, and sarcoma. In all cases, outcome after transplantectomy and retransplantation appeared to be satisfactory.

No agreement exists concerning how to manage patients who receive a liver graft from a donor with early-stage genitourinary tumors. We decided not to perform transplantectomy and retransplantation. This decision was based on the risks of retransplantation, limitation of organ availability, and limited evidence to support retransplantation as a suitable strategy to help prevent tumor transmission. Adequate information of risks must be provided to recipients, although asymmetry of information must be avoided. Patients were informed of the risks of retransplantation, absence of general guidelines for these cases, and the limited experience in retransplantation as a method to avoid tumor transmission after the graft was reperfused. Transparency must be one of the objectives in the management of transplant recipients. In this way, it is possible that the risk for tumor transmission be included in all consents for transplantation, especially in the era of graft shortage and marginal elderly donor use.

Our series showed the absence of tumor transmission in six liver recipients from donors with early-stage renal carcinoma (T1 to T2) and early prostate carcinoma (T1) after an average follow-up of 49 months. Our results suggest it is not always necessary to perform transplantectomy or use special treatment modalities in these cases.

References