American Journal of Transplantation 2005; 5: 1559–1561
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2005.00824.x

Case Report

Extended Survival by Urgent Liver Retransplantation after Using a First Graft with Metastasis from Initially Unrecognized Donor Sarcoma

Jorge A. Ortiz[a], Cosme Manzarbeitia[a], Khristian A. Noto[a], Kenneth D. Rothstein[b], Victor A. Araya[b], Santiago J. Munoz[b] and David J. Reich[a,*]

[a] *Liver Transplantation Program, Departments of Surgery and* [b] *Medicine, Albert Einstein Medical Center, Philadelphia, PA, USA*
* *Corresponding author: David J. Reich, reichd@einstein.edu*

A 58-year-old man underwent orthotopic liver transplantation for polycystic liver disease. Shortly after the procedure, it was discovered that the donor harbored a sarcoma of the aortic arch that had metastasized to the spleen, and bilateral renal cell carcinomas. The two sole organ recipients, our liver recipient and a lung recipient at another institution, were both listed for urgent retransplantation, which they received from the same second donor. The liver explant contained metastatic sarcoma. Twenty-four months survival following lung retransplantation has been previously reported. We report the 76-month disease-free survival in the liver recipient.

Key words: Donor malignancy, liver transplantation, sarcoma

Received 19 August 2004, revised 2 December 2004 and accepted for publication 20 December 2004

Introduction

Many reports have confirmed the safety of utilizing livers from donors with active or past non-melanoma skin cancer, small renal cell carcinomas (1) and certain central nervous system tumors (2). Reports of melanoma transmission resulting in disseminated disease in organ transplant recipients have been published (3). Other cancers known to be transmitted from donor to recipient include tumors of neuroendocrine origin, prostate carcinoma, choriocarcinoma, advanced renal carcinoma and lung cancer (4). Sarcoma, often highly malignant, is an uncommon cancer, and we found no other organ donor with sarcoma reported in the literature. In the face of organ transplantation from a donor with undetected malignancy, the options include maintaining the allograft or retransplantation.

We report the 76 months patient and graft survival of a liver transplant recipient who was urgently retransplanted after the first donor was found to have spindle cell sarcoma of the aortic arch and bilateral renal cell carcinomas. The first liver contained a metastatic focus of sarcoma. The lung recipient of the same two donors was previously reported to be free of disease after 24 months (5), and after 76 months continues to have normal graft function, without evidence of malignancy (RM Kotloff, MD, Hospital of the University of Pennsylvania, personal communication, December 2004).

Case Report

The recipient was a 58-year-old man with polycystic liver disease complicated by portal hypertension, esophageal varices and cachexia. The first donor was a 48-year-old woman with a history of hypertension who died from a cerebrovascular accident. The liver, left lung, pancreas and kidneys were all procured with standard techniques (6). The right lung was not procured because of excessive secretions at bronchoscopy. The heart was not used because of what was thought to be severe atherosclerosis of the ascending aorta. The viscera, including lung and liver, were otherwise grossly unremarkable.

Right and left kidney biopsies revealed 1.3 cm and 0.6 cm nodules, respectively. These had not been noted during the procurement but were found just prior to the planned renal transplants. Both were Fuhrman's grade 1 renal cell carcinomas. At autopsy, an intraluminal spindle cell sarcoma of the aortic arch involving the brachiocephalic, left common carotid and left subclavian arteries was discovered; this is the lesion that during the procurement had been mistaken to be atherosclerosis, based on gross appearance. The spleen, which was grossly normal, also contained multiple, microscopic, metastatic foci consistent with the sarcoma primary.

By this time, the liver and lung had already been transplanted. The patients were retransplanted 4 days later with organs from a 26-year-old head trauma victim. The liver transplant was uneventful. On pathologic examination, a 0.9-cm metastasis of sarcomatous origin was discovered deep in the first transplanted liver. The recipient was

discharged home without complication. Immunosuppression consisted of tacrolimus and prednisone. Tacrolimus doses were adjusted to maintain whole blood trough levels of 10–15 ng/mL initially and tapered to yield approximately 5 ng/mL by 6 months. Prednisone was begun at 20 mg/day and tapered off by 6 months. No post-transplant chemotherapy was employed. Full body CT scans obtained at 6 months and then yearly intervals, including 76 months after transplant, have not revealed any signs of cancer. At his last clinical examination 76 months after transplantation, the patient was free of disease without significant complaints.

Discussion

Transmission of donor malignancies has been reported since the beginning of clinical transplantation (7). As the donor population of the United States ages, it is more likely that malignancies will be found at the time of procurement (8). An incidence of up to 0.9% of renal cell carcinomas in cadaveric donors has been reported (9). The risk of having a donor with undetected malignancy may range between 1.3% and 5% (10, 11).

It is well accepted that careful intraoperative inspection is crucial in order to minimize the chance of transplanting organs from cadaver donors with malignancy. It is unfortunate that in the case of this reported donor the procuring thoracic and abdominal surgical teams missed two separate malignancies. The aortic arch sarcoma was visualized but there was no appreciation that the completely intraluminal, atherosclerotic appearing lesion might be a malignancy—otherwise, frozen section biopsies would have been sent immediately. Although the spleen harbored microscopic metastases it was grossly normal. Even though the liver contained metastatic sarcoma there was only one very small focus, which was located deep inside the parenchyma and only noted after fine sectioning of the grossly normal organ. The renal cell cancers were missed during preliminary back table work at the donor hospital, which involved extensive but incomplete removal of perirenal fat. At the time, it was local common practice to leave complete removal of perirenal fat to be done at the various recipient centers. Since these small renal nodules were initially missed, the local transplant teams have agreed that more extensive back table dissection be performed by the donor team. Another factor that may have contributed to not recognizing cancer in this 48 years old, relatively young donor, is that there tends to be less concern regarding malignancy in younger, rather than in older donors, although vigilance is necessary with all age groups.

Sarcomas account for approximately 1% of all adult malignancies. Primary intimal sarcomas of the aorta are extraordinarily rare and highly malignant. As of November 2000, there were fewer than 25 cases reported in the literature. The presenting symptoms mimic more common aortic lesions (12). These tumors metastasize to the skin, bone, lung, brain and gastrointestinal tract (13). Survival is usually measured in months. Recipients of organs from these donors should be considered at very high risk for cancer transmission.

A management strategy for recipients of solid organs from donors harboring a malignancy has not been established. In kidney transplant recipients, cessation of immunosuppression and return to dialysis may be life saving. Given the shortage of donor organs, it is unclear whether retransplantation after discovery of a donor malignancy is a prudent use of a scarce resource. Retransplantation could remove an occult gross malignancy or microscopic focus of malignancy in the allograft. It is unclear how expeditiously such retransplantation needs to be performed to be effective. In our case, urgent retransplantation did remove tumor-bearing tissue and the recipient has achieved extended disease-free survival.

On the other hand, it has been hypothesized that stopping or substantially reducing immunosuppression and delaying retransplantation until there is graft rejection could facilitate immunologic attack on transmitted cancer cells, and rid the recipient of circulating micrometastases prior to retransplantation (14). Lipshutz et al. (14) reported the case of a liver recipient who was urgently retransplanted after the donor was found to harbor a pulmonary adenocarcinoma with metastatic mediastinal disease. This patient nevertheless succumbed to this donor transmitted malignancy 11 months after the procedure. It is unclear whether the 7-day wait before retransplantation played a role in cancer cell dissemination, or whether the type and stage of cancer were the more significant factors. Loren et al. (15) reported successful retransplantation of a heart transplant recipient performed 17 days after metastatic melanoma was discovered on the donor's autopsy, perhaps indicating that the interval is less important than the type and stage of cancer. Serralta et al. (16) reported six donors with early active genitourinary malignancies (four renal carcinomas and two prostate carcinomas) who produced six livers for transplantation. No retransplants were performed and no disease transmission was reported at an average of 51-month follow-up. This confirms recent experience that active early renal cell carcinoma in the donor has a low risk of transmission (17). Hence, retransplantation seems unnecessary if a small, low-grade renal neoplasm is discovered after procurement. On the other hand, large renal cell and prostate cancer transmissions have been reported (17,18).

Kaufman et al. (19) reviewed all donor related malignancies reported to the Organ Procurement and Transplantation Network database from 1 April 1994 to 1 July 2001. Fifteen tumors were transmitted. Patients with central nervous system tumors were excluded. Malignancies were transmitted to five liver, eight kidney and two heart recipients. Three of the five liver recipients were alive after

retransplantation. Of the two deaths, one succumbed to a donor-transmitted melanoma, the other to a tumor of neuroendocrine origin. The rate of transmission was calculated to be 0.025% or one tumor transmission for every 3881 donors.

In our case, the presence of a highly malignant sarcoma with splenic metastasis and bilateral nephromas made close surveillance a less attractive alternative. Based on consultation with the late Professor Israel Penn, MD, founder of the Israel Penn International Transplant Tumor Registry, the decisions to urgently retransplant the liver and lung recipients were made, given the potential high risk of sarcoma transmission. In fact, on evaluation of the explanted liver a metastatic focus of sarcoma was discovered.

Chan et al. (20) reported the development of a *de novo* spindle cell sarcoma of donor origin in a liver recipient. The patient has demonstrated 1.5-year disease-free survival after right hepatectomy. To our knowledge there are no prior reports of transplantation using organs from donors with active sarcoma.

Conclusion

Urgent liver retransplantation may be indicated for a patient who receives a liver from a donor found to harbor an occult malignancy with a high risk for transmission. Even if a donor organ with malignancy is transplanted, long-term survival may be possible following expeditious retransplantation. Diligent inspection of both younger and older donors prior to and at the time of procurement is necessary to minimize the potential morbidity and mortality associated with the development of donor transmitted post-transplant malignancy.

References

1. Carver BS, Zibari GB, Venable DD, Eastham JA. Renal cell carcinoma detected in a cadaveric donor after orthotopic liver and contralateral renal transplantation in two recipients: four-year follow-up. Transplantation 2001; 71: 1348–1349.
2. Kauffman HM, McBride MA, Delmonico FL. First report of the United Network for Organ Sharing Transplant Tumor Registry: donors with a history of cancer. Transplantation 2000; 70: 1747–1751.
3. Morris-Stiff G, Steel A, Savage P et al. Transmission of donor melanoma to multiple organ transplant recipients. Am J Transplant 2004; 4: 444–446.
4. Wilson RE, Penn I. Fate of tumors transplanted with a renal allograft. Transplant Proc 1975; 7: 327–331.
5. Kreisel D, Engels FH, Krupnick AS et al. Emergent lung retransplantation after discovery of two primary malignancies in the donor. Transplantation 2001; 71: 1859–1862.
6. Starzl TE, Miller C, Broznick B, Makowka L. An improved technique for multiple organ harvesting. Surg Gynecol Obstet 1987; 165: 343–348.
7. Martin DC, Rubini M, Rosen VJ. Cadaveric renal homotransplantation with inadvertent transplantation of carcinoma. JAMA 1965; 192: 752–754.
8. Harper AM, Rosendale JD, McBride MA, Cherikh WS, Ellison MD. The UNOS OPTN waiting list and donor registry. In: Cecka JM, Terasaki PI, eds. Clinical transplants. Los Angeles, CA: UCLA Tissue Typing Laboratory, 1998:73–90.
9. Carver BS, Zibari GB, McBride V, Venable DD, Eastham JA. The incidence and implications of renal cell carcinoma in cadaveric renal transplants at the time of organ recovery. Transplantation 1999; 67: 1438–1440.
10. Birkeland SA, Storm HH. Risk for tumor and other disease transmission by transplantation: a population-based study of unrecognized malignancies and other diseases in organ donors. Transplantation 2002; 74: 1409–1413.
11. Boggi U, Vistoli F, Del Chiaro M et al. A simplified technique for the en bloc procurement of abdominal organs that is suitable for pancreas and small-bowel transplantation. Surgery 2004; 135: 629–641.
12. Rudd RJ, Fair KP, Patterson JW. Aortic angiosarcoma presenting with cutaneous metastasis: case report and review of the literature. J Am Acad Dermatol 2000; 43: 930–933.
13. Santonja C, Martin-Hita AM, Dotor A, Costa-Subias J. Intimal angiosarcoma of the aorta with tumour embolisation causing mesenteric ischaemia. Report of a case diagnosed using CD31 immunohistochemistry in an intestinal resection specimen. Virchows Arch 2001; 438: 404–407.
14. Lipshutz GS, Baxter-Lowe LA, Nguyen T, Jones KD, Ascher NL, Feng S. Death from donor-transmitted malignancy despite emergency liver retransplantation. Liver Transpl 2003; 9: 1102–1107.
15. Loren AW, Desai S, Gorman RC, Schuchter LM. Retransplantation of a cardiac allograft inadvertently harvested from a donor with metastatic melanoma. Transplantation 2003; 76: 741–743.
16. Serralta AS, Orbis FC, Sanjuan FR et al. If the donor had an early-stage genitourinary carcinoma and the liver has already been implanted, should we perform the transplantectomy? Liver Transpl 2003; 9: 1281–1285.
17. Penn I. Transmission of cancer from organ donors. Ann Transplant 1997; 2: 7–12.
18. Loh E, Couch FJ, Hendricksen C et al. Development of donor-derived prostate cancer in a recipient following orthotopic heart transplantation. JAMA 1997; 277: 133–137.
19. Kauffman MH, McBride MA, Cherikh WS, Spain PC, Marks WH, Roza AM. Transplant tumor registry: donor related malignancies. Transplantation 2002; 74: 358–362.
20. Chan SC, Cheung ST, Leung SY, Liu CL, Fan ST, Lo CM. De novo sarcoma of donor origin in a liver allograft determined by microsatellite analysis: a short report. Liver Transpl 2004; 10: 320–323.