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Transmission of clear cell tumor in a graft liver from cadaveric donor: Case report

Backes AN, Tannuri ACA, de Mello ES, Gibelli NEM, de Castro Andrade W, Tannuri U. Transmission of clear cell tumor in a graft liver from cadaveric donor: Case report.

Abstract: Neoplasms in children after organ transplantation are related to the type and intensity of immunosuppression and the donor–recipient serostatus, especially in relation to the Epstein–Barr virus. The patient was a two-yr-old female child with biliary atresia who underwent a liver transplantation from a female cadaver donor. Two adults received kidney transplants from the same donor. Nine months after transplantation, one of the adult recipients developed an urothelial tumor in the kidney graft. Imaging tests were repeated monthly in the liver-transplanted child and revealed no abnormalities. However, one yr and two months after the transplantation, the patient developed episodes of fever. At that time, imaging and liver biopsy showed a clear cell tumor of urothelial origin in the graft and the disease was limited to the liver. The patient underwent liver retransplantation, and she is currently free of tumor recurrence. Although rare, the occurrence of tumors in the post-transplant period from cadaver donors, without previously diagnosed tumors, is one of the many problems encountered in the complex world of organ transplantation.

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Key words: complications of liver transplantation – liver transplantation – malignancy – pediatric liver transplantation – children – pediatrics

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Neoplasms in children after organ transplantation are mainly related to the type and intensity of immunosuppression and to the donor–recipient serostatus, especially in relation to the Epstein–Barr virus. We report the occurrence of a rare renal tumor in the transplanted liver graft that was obtained from a cadaver donor who was not previously diagnosed with tumors; we describe the surgical procedures adopted and the clinical course.

Case report

The patient was a two-yr-old female child with biliary atresia who underwent a transplant of the left lateral segment of the liver from a 37-yr-old female donor cadaver, who died of a subarachnoid hemorrhage in December 2006. The child presented an excellent postoperative outcome. Two adults received kidney transplants from this donor and had good postoperative recovery.

Nine months after the transplant, we were notified that one of the kidney recipients developed an urothelial tumor in the graft. The evaluation of the child with abdominal ultrasound and chest and abdomen CT demonstrated no abnormalities. These tests were repeated monthly, with no abnormalities.

However, one yr and two months after transplantation, the patient developed episodes of fever and liver enzyme abnormalities. Ultrasound imaging was compatible with a five-centimeter "hematoma" in the graft. At that time, a CT revealed a hypodense lesion in the liver graft (Fig. 1). An open liver biopsy demonstrated that the lesion was a clear cell tumor of urothelial origin (Fig. 2). Tumor staging revealed that the disease was limited to the liver.

Because of the rarity of the situation, and the medical and legal aspects involved in the case, we requested priority for retransplantation, which was performed one wk later. During laparotomy, it was confirmed that the disease was confined to the liver. The patient underwent a reduced-size deceased donor liver transplantation utilizing the

Abbreviation: CT, computerized tomography.

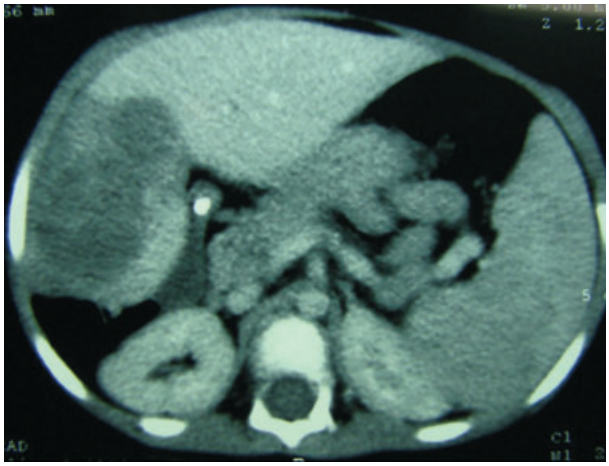

Fig. 1. CT imaging showing a hypodense lesion in the liver graft one yr and two months after the transplantation.

left lobe. The immunosuppression scheme was based on tacrolimus and low doses of prednisone. One month later, a permanently implanted catheter was installed for chemotherapy administration (gemcitabine and cisplatin). She presented two episodes of acute cellular rejection that were successfully treated with intravenous corticosteroids. Periodical thoracic and abdominal CT has been performed, and no tumor recurrence has been detected until now. The follow-up time is currently four yr.

Discussion

There are many reported cases of neoplasms following transplantation, most of which involve lymphoproliferative disorders. In addition, immunosuppression increases the risk of post-transplant malignancy, which may increase post-transplant mortality. Finally, other diseases, such as infectious diseases, can be transmitted by allograft transplantation (1).

Kidney and liver transplantations are frequently performed in children. The rates of most malignancies are higher after kidney transplantation compared with the general population (2). In renal transplantation, neoplasms have been reported after organ transplantation, but the risks and the histological features are poorly defined (3). The incidence of malignancy in kidney transplant recipients has been reported to be as high as 8.9%. De novo urothelial carcinoma is relatively rare among post-transplant malignancies and has never been reported in pediatric kidney transplant recipients. One study reported a high cumulative incidence of urinary tract urothelial carcinoma after kidney transplantation in adults (4). The elevated risk in this population may be explained by long periods of dialysis and the accompanying risk of acquired cystic renal disease, although renal carcinomas are also rare in pediatric recipients. Between 1968 and 1997, a total of 527 tumors were reported in 512 pediatric kidney recipients. Four cases of tumor after transplantation involved the patient's native kidneys, and three (0.56%) arose in the allograft. Post-transplant lymphoproliferative disease was the most frequently observed tumor (3, 4), constituting of 52.0% of all neoplasms; this trend is also observed in children who undergo liver transplantation (3).

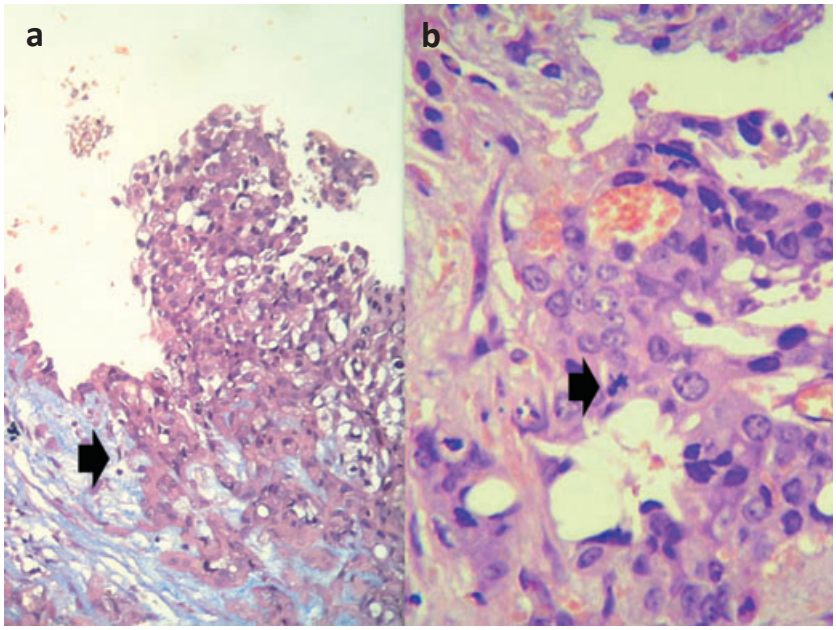

Fig. 2. (a) Hematoxylin–eosin-stained sections of the tumor biopsy. Note the epithelial neoplasia formed by multiple layers of growing cells along the cystic cavity. Observe the stroma infiltration (arrow). (b) Note the atypical nuclei and mytosis (arrow).

De novo renal cell carcinoma was described in two pediatric recipients of living parental donor kidney transplants, and this tumor had not been previously described in renal allografts transplanted from a living donor, until these cases. In these cases, both children had received growth hormone to stimulate post-transplantation somatic growth (3). In another case report, Schmidt et al. (5) described a child who received a small cell renal carcinoma that was transplanted from a living related donor. Some authors recommend that an annual ultrasound examination of the allograft should be performed in the pediatric population, but others have recommended periodic examinations to allow the early diagnosis of malignancy, although this is not routine practice in all pediatric transplant units (3, 5). Cancer should continue to be a major focus of prevention in kidney transplantation (2).

Inadvertent transmission of primary cancers from organ donor to recipient is an uncommon but recognized complication of solid organ transplantation. The incidence of tumor transmission is reported to be 0.02–0.2%, with a mean time to diagnosis of 14.2 months (6). Birkeland et al. (7) calculated that the risk of having a donor with undetected malignancy is eight in 626 patients (1.3%) and the risk of transmitting cancer is one in 626 (0.2%), using the population-based cancer registry. Penn et al. reported on 164 recipients of allografts from 96 cadaveric donors and 19 living related donors with proven malignancy. Seventy-two of the 164 patients developed a cancer that was usually identical to that found in the donor. Only six recipients of liver allografts transplanted from donors with established malignancy were reported. The nature of the tumors and clinical outcomes of these six recipients were not stated (8). Finally, we conclude that a close monitoring of all liver transplanted children is quite important, with periodical physical examinations and imaging studies in order to perform early detection of neoplasms.

Once a post-transplant malignancy is identified, determining whether or not the malignancy is of recipient or donor origin significantly influences the treatment algorithm. In cases of malignant lymphoproliferative disorders, which are typical examples of non-transmitted malignancy from the donor, treatment consists of stopping immunosuppression and starting intravenous ganciclovir and anti-CD20 monoclonal antibody therapy (9). For donor-transmitted malignancies, in addition to the withdrawal of immunosuppression, explanation and/or retransplantation may be utilized as part of the treatment protocol.

The most common transmitted tumors include melanomas, non-small cell lung cancer, renal cell carcinoma, choriocarcinoma, high-grade primary brain tumors, hematologic malignancies, and neuroendocrine carcinomas (10–17). However, this is the first reported case in the literature of urothelial clear cell tumor of donor origin transmitted to a pediatric liver recipient.

In conclusion, although rare, the occurrence of tumors after transplantation from cadaveric donors without previously diagnosed tumors is one of the many problems in the complex world of organ transplantation. Cooperation between teams allowed workup with serial evaluations that led to the discovery of cancer and the possibility of retransplantation in a timely manner, with no recurrence to date.

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