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Brief Communications

A Case of Donor-Transmitted Non-Small Cell Lung Cancer After Liver Transplantation: An Unwelcome Guest

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Disclosures of potential conflicts of interest may be found at the end of this article.

Abstract

Cancer transmission with organ donation has been previously reported with a variety of malignancies and organ transplants. The risk of transmission through organ transplantation from donors with a history of previously treated malignancies has been addressed by guidelines from transplant societies. Herein, we report a case of a patient who developed lung cancer confined to the liver after liver transplantation with no known history of malignancy in the donor. The suspicion of donor origin arose after positron emission tomography-computerized tomography scan showed metastatic lung cancer only involving the transplanted liver without a primary focus. Genetic analysis of the malignant cells confirmed donor origin of the cancer. ***The Oncologist*** 2019;24:e391–e393

Introduction

The incidence of malignancy transmission from donor to recipient after transplantation is extremely low. Although it poses a risk of cancer transmission to the recipient, transplantation from a donor with history of malignancy is not always considered a contraindication for organ donation. Guidelines define the minimum interval between cancer diagnosis, treatment, and transplantation in the donor based on the type of cancer, grade, and stage [1, 2]. In such cases, close observation with surveillance of the recipient is warranted. A rare, but more difficult, challenge arises when a suspected donor-derived malignancy is discovered after transplantation without a known history of malignancy in the donor. We report a case of donor-derived malignancy that occurred after liver transplantation.

Case

A 69-year-old man with prior history of smoking, alcoholic cirrhosis, and hepatocellular carcinoma (HCC) presented 6 months after deceased donor liver transplantation (DDLT). Six months before transplantation, he presented with HCC (4.2-cm mass in segment VII and a 2.3-cm mass in the gallbladder fossa) and cirrhosis. Computerized tomography (CT) scan of the chest, abdomen, and pelvis showed no metastasis. Chemoembolization and radiofrequency ablation were initially tried. However, because of worsening liver failure, DDLT was carried out 6 months after the diagnosis. The recipient's native liver showed micronodular cirrhosis and necrotic areas of hepatocellular carcinoma with greater than 90% tumor kill.

Four months after transplantation, a routine ultrasound showed two hypovascular but solid liver masses that were felt to be indeterminate but were not present on previous imaging. Abdominal CT scan confirmed the presence of three new hypovascular nodules (Fig. 1A). Six weeks later, liver magnetic resonance imaging showed innumerable liver masses (Fig. 1B). Positron emission tomography-computerized tomography showed abnormal uptake limited to the liver.

Liver biopsy showed poorly differentiated carcinoma with a positive immunohistochemistry for carcinoembryonic antigen and thyroid transcription factor 1 and negative immunohistochemistry for hepatocyte antigen and CDX2. The neoplasm had mixed histologic features of small-cell and non-small-cell carcinoma. The histologic and immunohistochemical features of the tumor were distinctly different from those of the prior HCC. These findings were suspicious for donor-transmitted malignancy. A polymerase chain reaction-based assay strongly suggested that the newly diagnosed metastatic carcinoma in the liver originated from the donor (Fig. 2). Interestingly, although the donor had a history of smoking, he did not have any known history of malignancy. He was 50 years old and had developed cardiac arrest with unknown down time, leading to subsequent anoxic brain injury. Chest x-ray and bronchoscopy did not reveal malignancy during the hospitalization, and he was pronounced brain dead. Lung examination at the time of organ procurement reportedly showed no signs of malignancy. Pathological examination of the donor liver showed minimal macrovascular fatty change and rare inflammatory cells.

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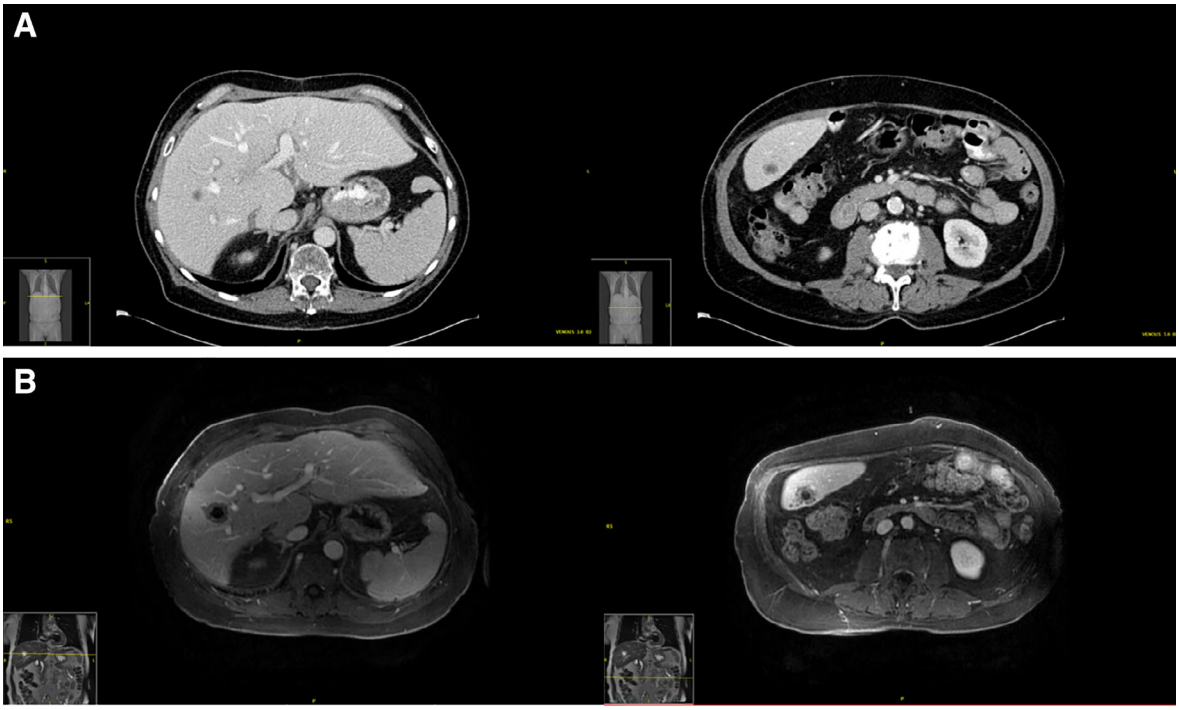

Figure 1. Imaging showing progression of the lesions over time. **(A):** Computerized tomography scan of the abdomen showing two of the three liver lesions found on follow-up scans 4 months after transplantation. **(B):** Magnetic resonance imaging of abdomen showing the progression of the two liver lesions seen before with progression after a period of 6 weeks of observation.

A discussion about retransplantation was initiated as the recipient's malignancy was confined to the liver; however, he was deemed ineligible because of the diagnosis of metastatic lung cancer. Immunosuppression was reduced. Carboplatin and etoposide were begun because of the small-cell component, and the liver metastases stabilized after two cycles. However, further imaging after cycle 4 showed progression in the liver without other metastasic sites. Progression of hepatic metastases and reduced immunosuppressive agents led to liver failure and the patient's death.

Discussion

Donor-derived malignancy has been reported with a variety of malignancies and organ transplants [1]. Herein, we report a case of a patient who developed lung cancer confined to the liver after liver transplantation. We were able to confirm donor origin of the cancer by genetic analysis.

To our knowledge, donor-derived lung cancer in a liver graft has only been reported once before. Lipshutz et al. reported a 41-year-old man whose donor was found to have a metastatic pulmonary adenocarcinoma a few days after liver transplantation, which led to retransplantation [3]. Although the pathology from the extracted liver from the first donor did not show any signs of malignancy, the recipient developed metastatic lung cancer 11 months after transplantation and died shortly thereafter. In our patient, the malignancy was pathologically confirmed 6 months after transplantation, with no known malignancy in the donor by history, imaging, bronchoscopy, or lung examination during procurement. Pretransplant imaging was done with chest x-ray, which is a suboptimal method for excluding malignancy compared with CT scan, and it is unknown whether there was a cytology examination on the bronchoalveolar lavage as it was done for infectious evaluation rather than a suspicion of malignancy.

After confirming the donor as the source of the lung cancer, the challenge in our case was whether to explant the affected organ. A renal transplant recipient can resume dialysis if a cancer develops in the graft, but our patient would not survive without a second liver transplant for which he was deemed ineligible because of the presence of metastatic lung cancer. Although this was confined to the graft by imaging, concern was raised over likely microscopic spread which would result in further progression of disease at retransplantation.

Decreasing immunosuppressive medications and administering systemic chemotherapy were ineffective, and liver failure developed, most likely because of a combination of progression of cancer and decreased immunosuppression. Even today, with the availability of broader treatment options, it is unlikely that a better outcome could have been achieved without removal of the graft and retransplantation.

The risk of cancer transmission through organ transplantation from donors with previously treated malignancies has been addressed by guidelines from different societies [4]. For donors with no known history of malignancies, current recommendations are to perform malignancy screening as indicated by age and/or sex. In contrast, a more stringent interpretation of the Italian national guidelines that incorporated histopathological examination led to higher detection rate for donor malignancy [5]. Whether novel screening tests, such as circulating tumor DNA, would be helpful in early detection of malignancy in the future is still unclear but should be studied.

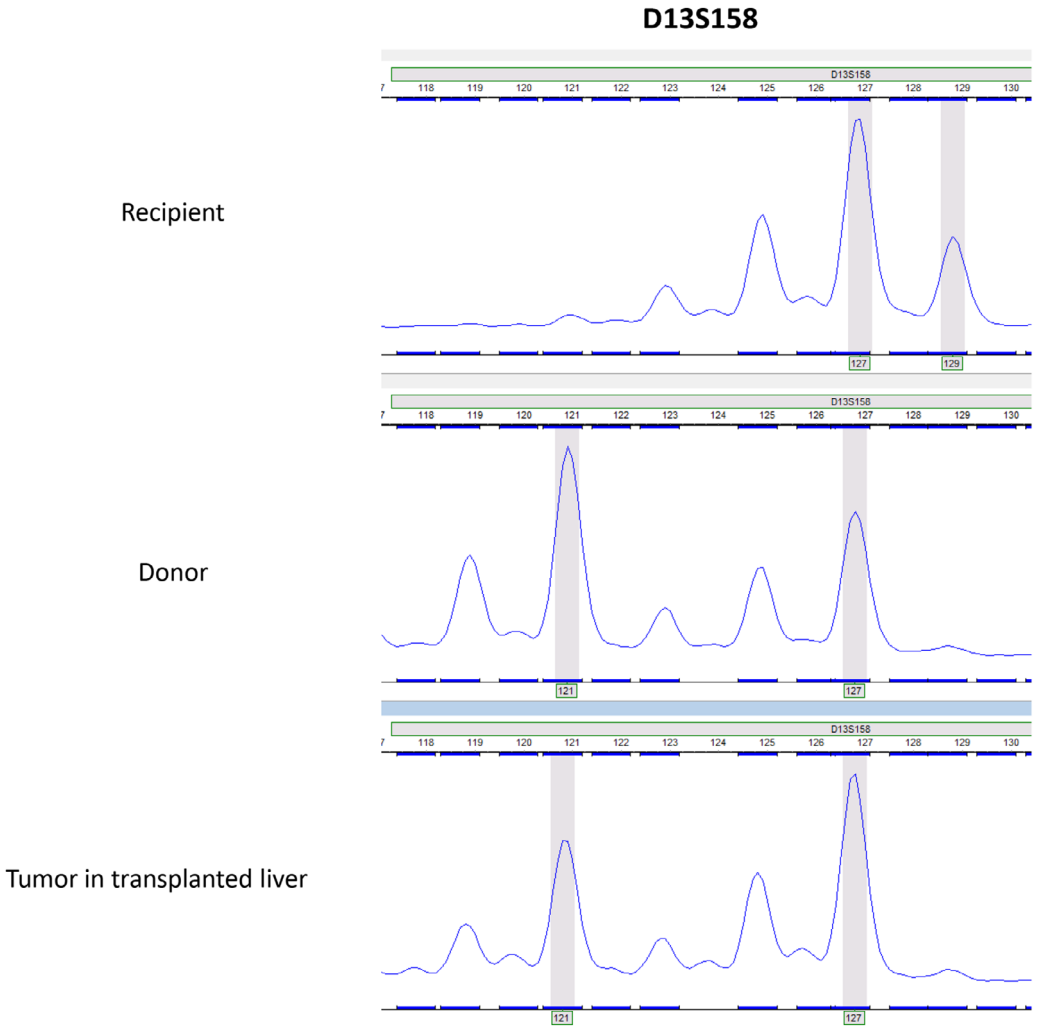

Figure 2. Representative genotyping results for 1 of the 8 informative markers (D13S158) demonstrating that the genotype of the tumor in the transplanted liver is the same as that of the donor. A panel of DNA markers that recognize highly variable regions of human DNA was used in a polymerase chain reaction-based assay to compare DNA isolated from the liver tissue of the donor with the tumor and liver tissue of the recipient. The 12 markers tested were *D7S484*, *D13S158*, *D10S197*, *D14S70*, *MYC1*, *D21S1252*, *D8S262*, *D17S250*, *D15S1002*, *D16S520*, *D2S2368*, and *DS6441*. Eight of the 12 markers gave satisfactory results, and for those markers, 8 of the 8 genotypes of the newly diagnosed carcinoma matched those of the donor allograft tissue, whereas only 1 of the 8 genotypes of the carcinoma matched those of the patient's native liver.

To our knowledge, this is the only case in literature describing donor-derived lung cancer in a liver graft without known malignancy in the donor. Although there are current recommendations on donor eligibility after a cancer diagnosis, disease-free intervals before consideration of donor suitability, screening methods, and mandatory reporting of donor-derived malignancy, the prognosis for patients who develop donor-derived malignancy remains poor, and optimal screening practices as well as best treatment options for affected patients remain unclear and should be further addressed.

Disclosures

The authors indicated no financial relationships.

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