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This is a pre print version of the following article:

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1610714> since 2016-11-19T12:23:14Z

Published version:

DOI:10.1111/ajt.13712

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(Article begins on next page)

Successful urgent liver retransplantation for donor-transmitted hepatocellular carcinoma

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Running title: Retransplantation for donor-transmitted HCC

Keywords: liver transplantation; donor management; donor-to-recipient tumor transmission; adverse event; post-transplant outcome

List of abbreviations:

CT, computed tomography; HCC, hepatocellular carcinoma; LT, liver transplantation;
US, ultrasound

Dear Editor,

on September 20, 2012, in Turin, Italy, the 2,372nd liver transplant (LT) was performed.

Donor was a 78-year old obese (120 kg, 180 cm) male who died of head trauma. He had arterial hypertension and type 2 diabetes, and no history of alcohol abuse. Hepatitis B and C serology were negative. Liver segments accessible to ultrasound (US) exploration appeared normoechoic and further computed tomography (CT) without contrast detected no abnormalities.

Recipient was a 59-year old male with HCV-related cirrhosis, genotype 2, MELD 17. The intraoperative course and immediate graft function were satisfactory, allowing an early extubation. Post-reperfusion biopsy showed mild macrovesicular steatosis (5-10%), without significant portal inflammation or fibrosis.

On day 1, US examination detected three hypoechoic areas (diameter 10, 12, 38 mm) in the right hemiliver and contrast-enhanced CT evidenced two nodules (10, 35 mm) in segments 5-8, both displaying slight arterial wash-in and partial venous wash-out (LI-RADS 4). US-guided percutaneous needle biopsy (Figure 1A) at histology showed Edmondson-Steiner grade 2 hepatocellular carcinoma (HCC) as definitive diagnosis.

This was notified to the National Transplant Center as an adverse event. After multidisciplinary consultation, an exceptional national appeal was made for an urgent retransplantation, performed on September 23 (Figure 1B). The postoperative course was uneventful, with discharge on day eight.

The explanted liver showed grossly normal aspect, but harbored three yellowish parenchymatous nodules, one larger (30 mm, grade 3 HCC) and two smaller ones (9 and 8 mm, grade 2) (Figure 1C); TNM stage II. Microvascular invasion was detected

peripherally to the largest nodule (Figure 1D). Cyclosporine and steroids were tapered, everolimus was added on day 30.

Follow-up included six-monthly chest-abdomen CT and humoral tumor markers (alpha-fetoprotein, cytokeratin-18 and albumin genes RNA transcripts). HCV recurrence was successfully treated with sofosbuvir+ribavirin from 9/2014 to 2/2015. At 3-year follow-up the patient is alive, with normal liver function and without biomolecular-radiological signs of HCC recurrence.

Kidneys from the same donor were also transplanted; after extensive information, one recipient decided to keep the graft, while the other asked for early explantation. Both kidney recipients are alive with no neoplastic disease.

This unique case raises two issues:

A How could this happen?

The risk of donor-to-recipient malignancy transmission is well-known (1,2), however, to our knowledge no case of HCC transmission has been reported, probably because cirrhotic livers are always discarded. In the current epidemic of HCC arising in subjects with metabolic syndrome, often without liver fibrosis/cirrhosis (HCC incidence 1/3,000-4,000 individuals) (3), extensive use of suboptimal grafts is bringing out this risk. Consequently, when US examination is not exhaustive, a liver contrast-enhanced CT would be needed to rule out HCC, especially in aged male obese donors.

A Was urgent re-LT justified?

Urgent retransplantation was proposed as the best available treatment because the malignancy was likely to be still confined to the liver and any alternative therapy would have been unfeasible immediately post-LT. By so doing, a 3-year disease-free survival has

been achieved, while in other cases suffering from different donor-transmitted tumors re-LT was unsuccessful (4,5).

Disclosure

The authors of this manuscript have no conflict of interest to disclose as described by the *American Journal of Transplantation*.

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Figure legend

Figure 1. Panel A. Liver ultrasound frame showing the procedure of percutaneous image-guided fine needle biopsy of the largest hypoechoic nodule detected in the graft on day 1 after liver transplantation.

Panel B. Intraoperative picture at urgent liver retransplantation: the right lobe of the graft (which is going to be explanted) shows no visible nor palpable abnormality on surgical exploration.

Panel C. Macroscopic pathological examination of the explanted liver graft harboring plurifocal hepatocellular carcinoma. A section in the right lobe shows a grossly normal liver and a 3-cm yellowish nodule located in segment 8. The cartouche depicts a further subcentimeter nodule found in another section in the right lobe. On palpation, the texture of the neoplastic nodules was similar to that of surrounding parenchyma.

Panel D. Light microscopy section showing the periphery of the largest nodule: Edmondson-Steiner grade 3 hepatocellular proliferation is present (on the left), with a neoplastic embolus within a vessel (arrow); the architecture of the non-neoplastic liver parenchyma is preserved without significant fibrosis (on the right) (hematoxylin-eosin staining, 100 x magnification).

