

Living Donor Liver Transplantation From Hepatitis C–Infected Donor to Hepatitis C–Infected Recipient

Henrik Junger,¹ Birgit Knoppke,² Kilian Weigand,³ Katja Evert,⁴ Frank W. Brennfleck,¹ Michael Melter,² Hans J. Schlitt,¹ and Stefan M. Brunner¹

Living donor liver transplantation (LDLT) from hepatitis C virus (HCV)–positive donors into HCV–positive recipients is not established yet.⁽¹⁾ We report a case of combining direct antiviral agent (DAA) therapy and living liver donation from a donor with chronic HCV infection (genotype 3a) to a recipient with congenital chronic HCV infection (genotype 3a).

omentectomy due to a pseudopapillary pancreas tumor (PPT) in 2015. Because of synchronous and diffuse hepatic metastases, three transarterial chemoembolizations were performed 2016, but with persistent liver metastases. After extended staging, no extrahepatic manifestation of the PPT was found. Because of irresectability of the liver metastases, liver transplantation was indicated for complete tumor clearance.

Case Report

RECIPIENT

The recipient, an 11-year-old female (body mass index [BMI] = 20.1 kg/m²), underwent subtotal left pancreas resection with splenectomy and partial

DONOR

Thirty-six-year-old female (mother) and daughter were noncitizens in the Eurotransplant region. Therefore, only LDLT was possible, and the mother was the only blood group match (BMI = 25.73 kg/m², AB0 group 0, Rh+). Both donor and recipient had a chronic HCV infection. At initial evaluation, the

Abbreviations: DAA, direct antiviral agent; HCV, hepatitis C virus; LDLT, living donor liver transplantation; PPT, pseudopapillary pancreas tumor; SVR, sustained virological response.

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ARTICLE INFORMATION:

From the ¹Department of Surgery, University Hospital Regensburg, Regensburg, Germany; ²University Children's Hospital Regensburg, University Hospital Regensburg, Regensburg, Germany; ³Department of Internal Medicine, University Hospital Regensburg, Regensburg, Germany; ⁴Department of Pathology, University of Regensburg, Regensburg, Germany.

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO:

Stefan M. Brunner, M.D.
Department of Surgery, University Hospital Regensburg
Franz-Josef-Strauss Allee 11

93053 Regensburg, Germany
E-mail: Stefan.Brunner@ukr.de
Tel.: +49 941 944 6801

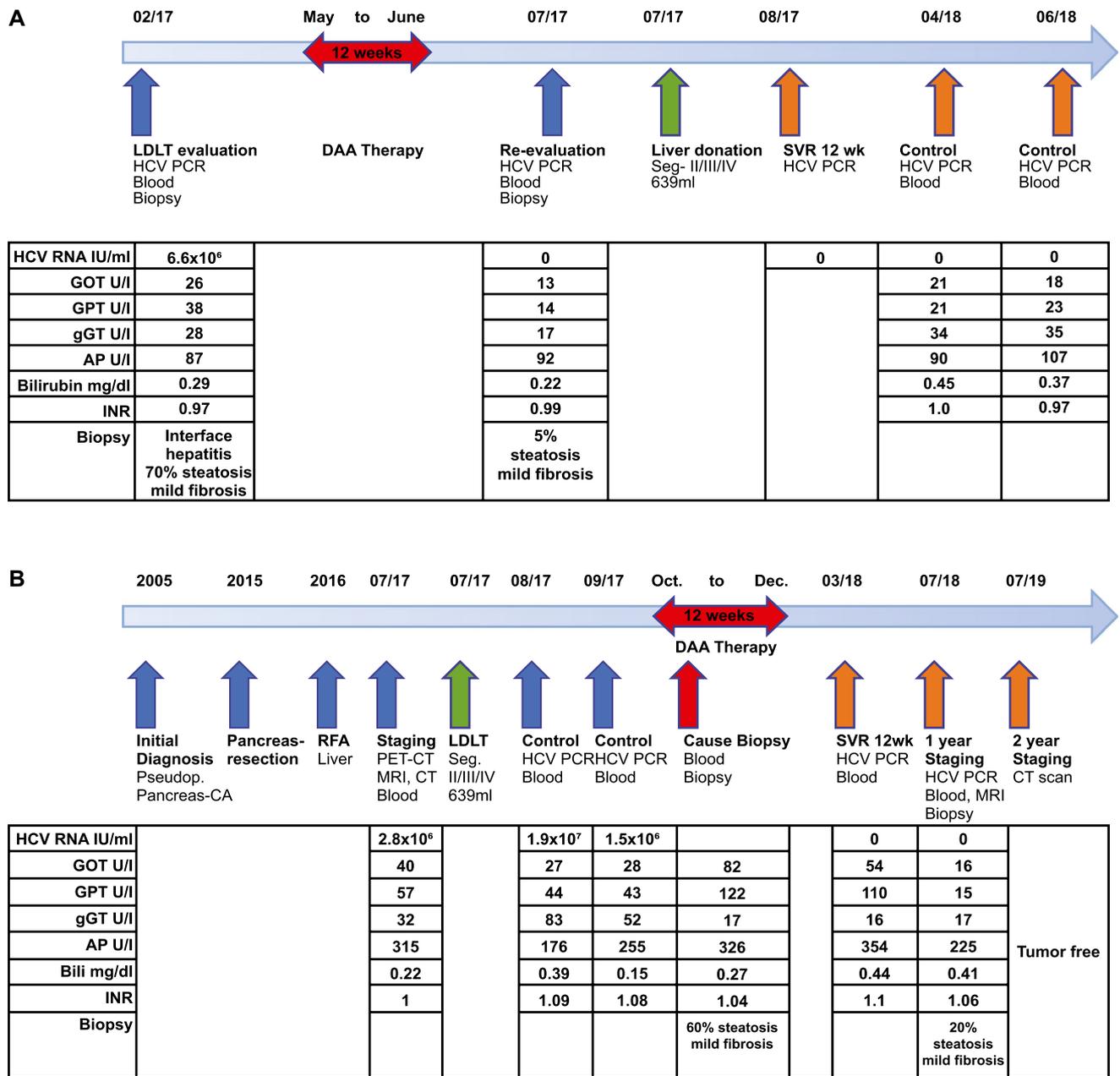


FIG. 1. (A) Therapy timeline of the donor with LDLT evaluation, DAA therapy, re-LDLT evaluation, liver donation, and 12-week SVR control, with laboratory results and histology results. (B) Disease history and therapy overview of the recipient with initial diagnosis, initial surgical resection, and transarterial chemoembolization therapy, staging, LDLT, DAA therapy, and 12-week SVR control followed by 1-year control with laboratory and histology results. Two-year computed tomography scan shows no tumor re-occurrence. Abbreviations: AP, alkaline phosphatase; Bili, bilirubin; CT, computed tomography; gGT, gamma-glutamyltransferase; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; INR, international normalized ratio; MRI, magnetic resonance imaging; PET, positron emission tomography; and RFA, radio frequency ablation.

mother had a serum viral load of 6.6×10^6 U/mL. and liver biopsy revealed an interface hepatitis with 70% steatosis hepatitis (Figs. 1A and 2A). DAA therapy with sofosbuvir 400 mg and velpatasvir 100 mg

was initiated for 3 months. At reevaluation, the HCV viremia was cleared, and HCV remained undetectable. Furthermore, liver enzymes were normal and the liver biopsy showed a marked reduction of the steatosis

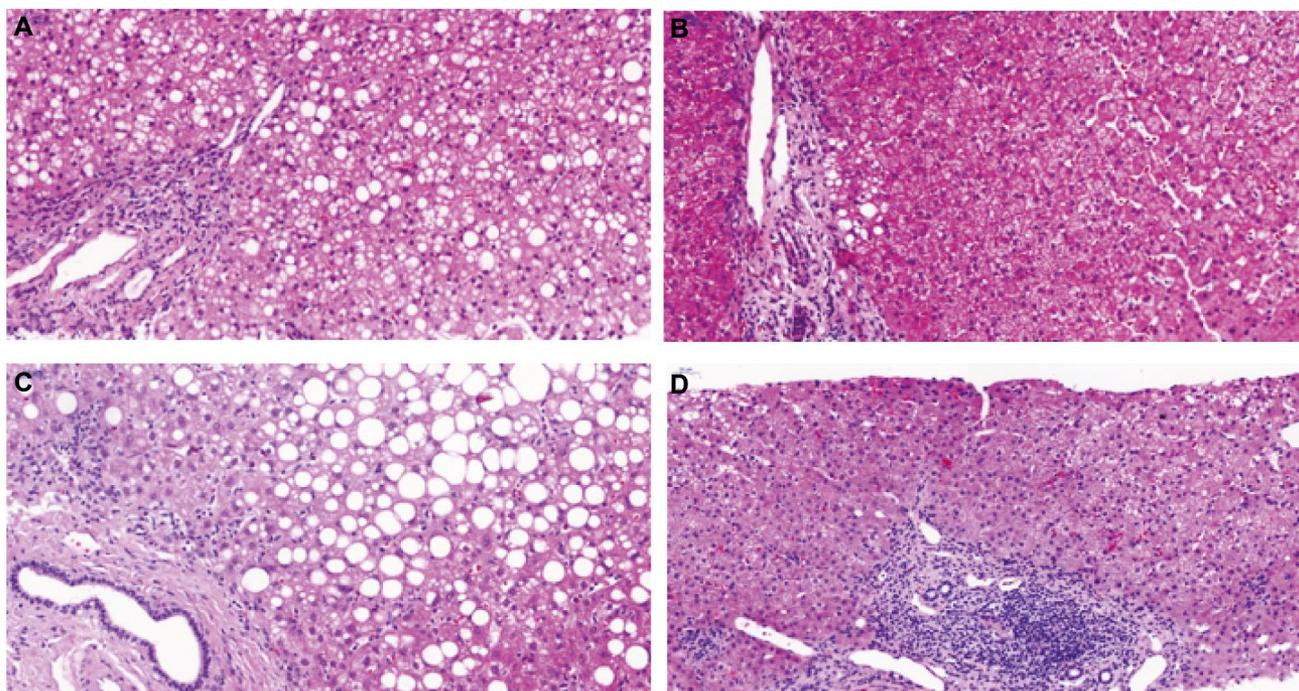


FIG. 2. Liver-biopsy hematoxylin and eosin staining. (A) Donor before DAA therapy with chronic, mostly portal, but discrete interface hepatitis with a severe steatosis hepatitis and mild fibrosis (1-2 Ishak score). (B) Donor after DAA therapy with only minimal steatosis hepatitis and stable mild periportal fibrosis. (C) Recipient under DAA therapy also shows severe steatosis hepatitis and mild fibrosis. (D) Recipient 1-year protocol biopsy with reduced steatosis hepatitis.

hepatitis to 5% (Figs. 1A and 2B). Consequently, no contraindications for living liver donation were seen. One year after donation, liver enzymes and cholestasis parameter in the donor were normal, as well as synthesis parameters, and HCV RNA was negative (Fig. 1A).

POSTOPERATIVE MANAGEMENT OF LDLT

LDLT was performed using the left lobe (segment II/III/IV, 693 mL) with a graft-to-bodyweight ratio of 1.6%. At transplantation, the recipient had an HCV viral load of 2.8×10^6 IU/mL. Seven weeks after transplantation, the volume of the graft increased to 1,221 mL or 91%. The HCV viral load reached its maximum of 180×10^6 IU/mL 1 month after transplantation. Two months later, the recipient had an HCV load of 1.5×10^6 IU/mL. DAA therapy was now initiated with sofosbuvir 400 mg and velpatavir 100 mg for 12 weeks. During the DAA therapy a liver biopsy was performed for elevated liver enzymes; it revealed no signs of rejection but a 60%

steatosis hepatitis (Figs. 1B and 2C). After the DAA therapy, HCV viremia was cleared with a sustained viral response by week 12, and HCV remained undetectable thereafter. The 1-year protocol biopsy showed a marked reduction of steatosis hepatitis to 20% and no signs of chronic liver injury (Fig. 2D). An abdominal magnetic resonance imaging scan 1 year after, and a computed tomography scan 2 years after, the transplantation showed no signs of tumor recurrence, neither in the bed of pancreatic resection nor in the transplanted liver.

Discussion

In the presented case, liver transplantation was indicated, as 85%-95% of patients with PPT are cured after complete tumor clearance, and successful liver transplantation for metastatic PPT has been reported.⁽²⁾ In the era of highly effective DAAs, graft survival among HCV-positive recipients has largely increased, with outcomes comparable to non-HCV-positive recipients.⁽³⁾

However, little is known about living donors with chronic HCV infection. Here, once HCV remains undetectable in the donor, the liver recovers quickly from the steatosis, and living liver donation could be performed without reoccurrence of HCV after donation. To monitor steatosis, we recommend an evaluation biopsy of the donor. LDLT was done before the donor sustained virological response 12 (SVR12), due to risk of extrahepatic tumor manifestation in the recipient. If the recipient is able to wait for the donor SVR12, we recommend this for donor risk reduction.

DAA therapy of the recipient was performed successfully after LDLT, due to unknown possible effects of the DAA therapy on the tumor biology and tumor growth of this rare tumor type. Nevertheless, now, 2 years after LDLT, HCV remains undetectable and the liver function of the recipient is normal and without signs of tumor recurrence.

Even if a single case does not allow definitive conclusion, the concept of antiviral DAA therapy in combination with LDLT in HCV-infected donors and recipients should be considered to increase the donor pool in this highly selective population. The optimal

timing for treatment of the pediatric recipient (before or after transplantation) remains to be clarified.

Author Contributions: H.J. conceptualized, drafted, and revised the manuscript. B.K. provided clinical data and reviewed the manuscript. K.E. provided pathological data and images. F.W.B. reviewed the manuscript. K.W., M.M., and H.J.S. reviewed and edited the manuscript. S.M.B. conceptualized, reviewed, and edited the manuscript.

REFERENCES

- 1) Tan HP, Patel-Tom K, Marcos A. Adult living donor liver transplantation: who is the ideal donor and recipient? *J Hepatol* 2005;43:13-17.
- 2) Wojciak M, Gozdowska J, Pacholczyk M, Lisik W, Kosieradzki M, Cichocki A, et al. Liver transplantation for a metastatic pancreatic solid-pseudopapillary tumor (Frantz Tumor): a case report. *Ann Transplant* 2018;23:520-523.
- 3) **Cotter TG, Paul S**, Sandikci B, Couri T, Bodzin AS, Little EC, et al. Improved graft survival after liver transplantation for recipients with hepatitis C virus in the direct-acting antiviral era. *Liver Transpl* 2019;25:598-609.

Author names in bold designate shared co-first authorship.