Liver Transplantation Using Right Lobe Graft With Focal Nodular Hyperplasia: Report of 2 Cases

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ABSTRACT

We described 2 cases of adult-to-adult liver transplantation using right lobe grafts donated by 2 patients suffering from focal nodular hyperplasia, the volumes of which were 360 cm^3 and 220 cm^3. This study was performed in compliance with the Declaration of the Helsinki. For preparation of the graft, back-table hepatic venous outflow reconstruction, including replacement of the retrohepatic inferior vena cava and bridging of hepatic segment V5/V8, was performed by using prosthetic vessel grafts. The liver grafts after subtracting the weight of focal nodular hyperplasia functioned well without serious small-for-size syndrome or graft dysfunction in spite of graft-to-recipient weight ratio less than 0.8%. This suggested the functioning of hepatocyte within focal nodular hyperplasia, which avoided graft deficiency. These 2 recipients were given not only conventional immunosuppressants (tacrolimus and mycophenolate sodium) but also anticoagulants (low molecular weight heparin and warfarin). Thrombosis of the prosthetic inferior vena cava 1 month after transplant in recipient 1 was treated by placement of intravascular stent. Biliary duct anastomotic stricture 2 weeks after transplant in recipient 2 was treated by placement of biliary stent. These 2 recipients remain well at more than 2 years post-transplant. These successful explorative cases highlight the safe use of a graft containing focal nodular hyperplasia. The partial liver resection grafts with focal nodular hyperplasia could be applied to the patients on the waiting list for liver transplantation.

THE shortage of available donor organs is the main limitation on the development of liver transplantation. Despite the broadening of the selection criteria for liver donation, many potential suitable grafts are still not harvested because of inconformity to predefined criteria. Over the past decade, the use of marginal grafts in liver transplantation has been driven by the increased requirement of liver grafts and by a favorable outcome of their use [1,2]. The successful use of marginal grafts containing hepatic cavernous hemangioma in liver transplantation has been reported previously, which suggests safe use of such a marginal graft and good prognosis of patients [3,4]. In this case report, we present our preliminary experience of adult-to-adult liver transplantation using a right lobe graft containing focal nodular hyperplasia (FNH) and suggest the possible use of such a graft. Transplants in this marginal donor liver study were strictly implemented, and ethical approval was obtained from the Committee of Ethics at the First Affiliated Hospital of Nanjing Medical University. This study was performed in compliance with the Declaration of Helsinki.

The first 2 authors contributed equally to this work.

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CASE REPORTS

Case 1

In October 2016, a 43-year-old man with a 30-year history of hepatitis B virus (HBV) infection was admitted to the Department of Respiratory for pulmonary infection. The computed tomography (CT) scans of chest after admission revealed a 7 cm hepatocellular carcinoma in the right lobe of his liver. Given treatment for a hepatic tumor, the patient was transferred to the Liver Transplantation Center. By contrast-enhanced CT scans, the tumor was referred to as Barcelona Clinic Liver Cancer stage B. He had been treated with entecavir for 1 year, and the viral load of HBV was undetectable. Alpha-fetoprotein (AFP) was 23.9 ng/mL, which was a little higher than normal (< 20 ng/mL). Without metastases outside of the liver, he was listed for liver transplantation and included in the marginal donor liver study.

A 24-year-old woman presented to the hospital because of the discovery of a giant hepatic lesion that was 10 cm in diameter (Fig 1A). Through comprehensive examination, the hepatic lesion in the hepatic right lobe was likely to be diagnosed as FNH. The patients complained of right epigastric discomfort. Moreover, she expressed more concern about the progression of such a hepatic lesion and asked for the removal of the hepatic lesion. Written informed consent to donation and acceptance of such marginal liver graft was obtained from the potential transplant donors and recipients, respectively. All CT images of the donor were analyzed by using a quantitative imaging system (IQQA-Liver, EDDA Technology Inc., Princeton, NJ, USA) to evaluate the right lobe volume, FNH volume, and remnant liver volume as described previously [3]. The volumes of right lobe graft and FNH were calculated to be 700 cm^3 and 360 cm^3, respectively. Graft-to-recipient weight ratio (GRWR) was 0.92% for the recipient who weighed 76 kilograms, while GRWR was 0.45% with the exclusion of FNH. Intraoperative rapid biopsy confirmed the diagnosis of the hepatic lesions to be FNH. Ultrasonography was performed to reevaluate the location of the hepatic lesion and its relation with hepatic veins and to determine the dissection line. A right hepatectomy without inclusion of the middle hepatic vein was then performed. Hepatic venoplasty at the back table was performed to reconstruct the middle hepatic vein tributaries and retrohepatic inferior vena cava (IVC) in the graft (Fig 1B). Orthotopic liver transplantation was then performed on day 3 after admission. The postoperative course was uneventful in the donor, and she returned to her previous activity levels after the removal of the abdominal drain due to mild bile leakage on day 14 after surgery. After transplantation, immunosuppressive therapy consisting of tacrolimus and mycophenolate sodium was given to the recipient. Moreover, low-molecular-weight heparin sodium was also administered to prevent thrombosis if there was no risk of bleeding, and the anticoagulant was changed into warfarin. Warfarin would be taken for 1 year. The total bilirubin level was elevated to 141.3 μmol/L (8.3 mg/dL) and returned to normal 2 weeks after transplantation. The recipient experienced small-for-size syndrome (SFSS) but recovered 2 weeks after operation. AFP also declined to normal levels. The international normalized ratio was monitored and controlled in the range of 2.0 to 3.0. The CT scans were checked 1 month postoperatively and showed retrohepatic IVC thrombosis and pleural effusion. Implantation of a vascular stent in the retrohepatic IVC and thoracentesis was

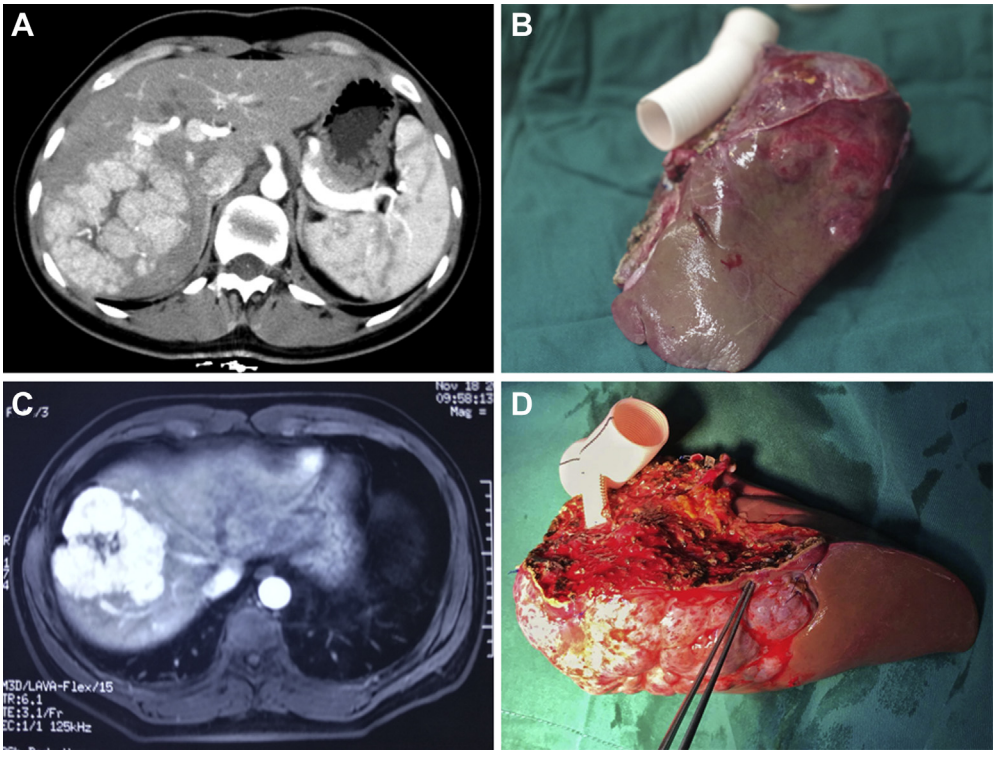

Fig 1. Case 1. **(A)** CT scans demonstrating a large liver lesion in the right lobe; **(B)** Right lobe grafts reconstructed with prosthetic vessel grafts. Case 2. **(C)** Magnetic resonance imaging showing a large liver lesion in right lobe; **(D)** Right lobe grafts reconstructed with prosthetic vessel grafts.

performed. The recipient was discharged home and remained well at 26 months postsurgery.

Case 2

On October 26th, a 43-year-old woman who had a 20-year history of HBV infection and had symptoms of epigastric distention and fatigue was admitted to the Liver Transplantation Center. An abdominal contrast-enhanced CT showed a 10 cm liver tumor and several satellite foci with invasion of the right hepatic portal vein, which is located in the right liver. The tumor was Barcelona Clinic Liver Cancer stage C, and AFP was above 1210 ng/mL. She was administered entecavir after admission despite a low level of HBV replication. Considering no metastases outside of the liver, she was also listed for liver transplantation and included in the marginal donor liver study. In addition, she underwent transhepatic arterial chemotherapy and embolization (TACE) to control tumor progression within duration of waiting time.

A 35-year-old man was admitted to the hospital because of the discovery of a giant hepatic lesion that was about 8 cm in diameter (Fig 1C). Like the former donor, this patient also had abdominal symptoms and expressed more anxiety. After written informed consent was obtained from the donor and recipient, the recipient was determined to be ready to receive a right lobe graft with FNH for liver transplantation. Volumes of right lobe graft and FNH were calculated to be 650 cm^3 and 220 cm^3. GRWR was 1.08% for this recipient with body weight of 60 kilograms, while GRWR was 0.72% with the exclusion of FNH. Intraoperative assessment was also performed as in case 1. A right hepatectomy without inclusion of the middle hepatic vein was then performed. Hepatic venoplasty at the back table was done as did in case 1 (Fig 1D). Orthotopic liver transplantation was then performed in this recipient on day 28 after admission. The postoperative course was uneventful in the donor. After transplantation, the same immunosuppressive therapy and anticoagulant were administered. In recipient 2, the total bilirubin level was elevated up to 166.8 μmol/L (9.8 mg/dL) on postoperative day 7. After steroid-pulsed therapy, the total bilirubin level declined to 85 μmol/L (5.0 mg/dL) but elevated up to 171.5 μmol/L (10.0 mg/dL) 3 days later. In addition, she complained of acholic stool. Considering the possibility of biliary obstruction, endoscopic retrograde cholangiopancreatography was performed on postoperative day 15, which showed biliary anastomotic stricture and dilated intrahepatic bile duct. The patient was then treated with the placement of a biliary stent, and the total bilirubin level declined to normal within 1 week. A postoperative CT scan 7 months after surgery did not show any abnormality and tumor recurrence. One metastatic nodule was found by CT 11 months after transplantation. Sorafenib was then administered, and radiotherapy was performed. The metastatic nodule did not progress, and no tumor recurrence in the liver was found by CT 22 months after transplantation. This patient remained well 26 months after surgery at the last follow-up.

DISCUSSION

The main limitation of liver transplantation all over the world remains access to an allograft. Marginal donors are a widely accepted source of organs to supply the growing demand for livers from patients on transplant waiting lists as liver donor acceptance criteria are relaxed, which was shown to have an outcome similar to ideal grafts [5]. For example, the successful use of marginal donor liver graft containing cavernous hemangioma for liver transplantation has been reported previously. Focal nodular hyperplasia (FNH) is the second most common hepatic benign tumor whose etiology is still poorly understood [6]. FNH is thought to represent a proliferative cell response resulting from arterial malformation. Most of the patients are asymptomatic, and the tumor is discovered incidentally; others are difficult to distinguish from hepatocellular adenoma, for which resection or curative treatment is recommended due to its potential for hemorrhage and malignant transformation [6]. Unlike hepatocellular adenoma, pregnancy and oral contraceptives have not been demonstrated to play a role in the development or progression of FNH [6]. Identification of classic FNH by way of its spoke-wheel central scar on contrast-enhanced magnetic resonance imaging or triphasic and multisection spiral CT is relatively straightforward. In the absence of symptoms and with a firm establishment of diagnosis, a conservative approach should be recommended. For our cases, FNH is more than 5 cm and located close to the liver capsule, which resulted in symptoms. Given the patients' will, surgical resection is the treatment of choice. Until now, liver transplantation using such a graft containing FNH was rarely reported [7,8]. To the best of our knowledge, ours are the first 2 cases of successful adult-to-adult liver transplantation using right lobe grafts containing FNH.

It is well known that FNH is a polyclonal hepatocellular proliferation, in other words, which is composed of benign-appear hepatocytes, otherwise arranged in nodule. Whether hepatocytes in FNH can function well or not is still poorly understood. In our cases, GRWR was 0.92% and 1.08% for these 2 recipients, respectively. In case of exclusion of FNH, graft-to-recipient weight ratio was 0.45% and 0.72% for these 2 recipients [9]. SFSS is a clinical syndrome defined following liver transplantation (especially in split liver transplantation or adult-to-adult living donor liver transplantation) or extended hepatectomy, in which the remnant liver is insufficient to maintain normal liver function. It is mainly characterized by postoperative abnormal liver function such as long-term cholestasis, elevated transferases and blood ammonia, portal hypertension, and severe ascites. While developed in the first recipient, SFSS was avoided with GRWR below 0.8% in the second recipient, which, expectedly, is attributable to the powerful growth potential of the liver. In addition, the functioning of hepatocytes in FNH also plays a role. Follow-up CT scans did not show much change in the size and shape of FNH but showed an increase in liver parenchyma volume of the graft. Therefore, for liver transplantation using the allograft with FNH, GRWR could be lowered to 0.8% without SFSS. However, the long-term follow-up and well-designed experiments are required to confirm this hypothesis.

In conclusion, we report 2 cases of successful liver transplantations by using right lobe grafts with FNH in patients with hepatocellular carcinoma beyond Milan criteria. While progression of FNH in the right lobe graft is not clearly known, these 2 cases highlight that the partial

liver graft with FNH could be used for liver transplantation. More cases are necessary to confirm the use of such a graft.

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