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First case report of domino living donor liver transplantation in Korea

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ABSTRACT

We report the first case of domino living donor liver transplantation in Korea; the first recipient was a 58-year-old woman with amyloidosis, and the second recipient was a 64-year-old man with downstaged hepatitis B virus related hepatocellular carcinoma. He had segmental portal vein tumor thrombosis initially, which disappeared by several locoregional therapies and radiation. We successfully performed domino living donor liver transplantation. A liver graft from a patient with amyloidosis is an effective and valuable source for patients without potential living liver donors.

1. Introduction

Amyloidosis is an autosomal dominant hereditary disease with neurologic, gastrointestinal, and cardiac symptoms from the irreversible extracellular deposition of misfolded amyloid resulting from a mutation of the transthyretin (TTR) gene [1]. More than 90% of circulating TTR is produced in the liver, thus, liver transplantation (LT) was initially proposed as a potential cure for preventing the progression of amyloidosis [2].

Because of the shortage in available liver grafts, many patients with hepatocellular carcinoma (HCC) or end-stage liver disease waited for several years before receiving a transplant or died from their liver diseases while awaiting transplantation. The liver of amyloidosis patient is essentially a normal liver except for the production of amyloid protein. Accumulation of this protein causes the symptoms of the disease, and the symptoms can take more than 20 years to manifest. Therefore, the liver in amyloidosis patient can be used as a liver graft from living liver donor for people who urgently need a LT.

The first recognized domino liver transplantation (DLT) using a liver from a patient with familial amyloid polyneuropathy (FAP) occurred in Portugal in 1995 [3]. Thereafter, many centers throughout the world also reported successful DLT using livers from patients with FAP [2]. Most of these transplants used a liver graft from a deceased donor as the source of the liver transplanted into the patient with FAP, but several centers in Japan have published their experience performing domino transplants in which a living donor was used as the source of the liver transplanted into the FAP domino donor [2].

DLT has never been reported in Korea, thus we introduce the first Korean case of domino living donor liver transplantation (LDLT) in amyloidosis patient.

2. Case description

The primary recipient of the LDLT was 58-year-old woman who, six years prior to transplantation, complained of sudden-onset palpitations. She had hepatitis B virus surface antigen (HBsAg), and her past history included hypothyroidism for which she received levothyroxine. A chest X-ray revealed cardiomegaly and pericardial effusion, and a cardiac MRI and heart biopsy proved amyloidosis. Nerve conduction study revealed mild sensorimotor polyneuropathy, but her motor and power were not impaired. A gene study showed a TTR gene mutation, but her other relatives did not have the TTR gene mutation. Preoperative echocardiogram showed increased left ventricle wall thickness, diastolic dysfunction grade 3 with left atrium enlargement, and a moderate amount of pericardial effusion. Her left ventricular ejection fraction was 56%. She continued to suffer from peripheral neuropathy, cardiomegaly, and pericardial effusion over a period of six years, and the natural course of her disease was expected to lead to a fatal outcome within a few years. Therefore, LT was indicated.

The living donor was the 24-year-old son of the first recipient. He did not have the TTR gene mutation and expressed his willingness to be the living donor for the patient. The second recipient was a 64-year-old man with downstaged hepatitis B virus (HBV)-related HCC. He had segmental portal vein tumor thrombosis (PVTT) initially, which viable tumors in the portal vein disappeared by several locoregional therapies and radiation. Because the patient did not have any potential living liver donors in his family and HCC recurrence can occur within a few months, he agreed to accept the domino liver graft from a patient with amyloidosis. He did not have an opportunity for deceased donor liver transplantation (DDLT) because his model for end-stage liver disorder (MELD) score was 6 points.

The living donor for the first recipient with amyloidosis underwent open extended right hepatectomy (630 mg). The macrosteatosis of the

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liver graft was 5%, and operation time was 299 min. His remnant liver volume was 34%, and the graft to recipient weight ratio (GRWR) was 1.15. We resected an extended right hepatectomy from the first recipient because we were concerned that her cardiac problems could cause an unstable hemodynamic state. Liver biopsy from 1st recipient reported 5% of macrosteatosis and fibrosis grade 2 or 3. The surgical procedure in the patient with FAP was essentially the same as that which occurs in regular LDLT. The common bile duct and hepatic artery were removed with the right lobe graft, and the right and left portal vein was divided just distal from the bifurcation of the portal trunk. The right lobe graft was removed first, and blood flow and hepatic flow of the left lobe was kept intact for preventing unstable hemodynamic changes. We did not use the left liver graft for implantation because of the HBV infection and small liver volume (330 mg). When the first recipient's left portal vein was clamped for portal vein anastomosis, her blood pressure was 70/40 mmHg despite usage of inotropics. Her hemodynamic state recovered after reperfusion. The first[t] recipient's blood loss was 1300 mL, and the operation time was 382 min.

The second recipient received extended the right liver graft (605 mL) from the patient with amyloidosis. The operation of the secondary recipient was also performed in the same manner as regular LDLT. GRWR was 0.8, and the operation time was 519 min. Blood loss was 2000 mL.

3. Discussion

Liver graft in FAP patients with inborn errors of metabolism has been utilized for DLT because of structurally and functionally normal. Their explanted liver into a second recipient has offered another possible method of increasing liver graft availability. The recycling of these marginally- or metabolically-defective livers via DLT offers patients with end-stage liver disease (ESLD) who might not otherwise receive a liver graft through traditional means. Most importantly, given that most patients with FAP are relatively young at the time of their transplant, the domino liver grafts are harvested from young, hemodynamically stable patients without portal hypertension.

In Korea, patients with amyloidosis who have a normal liver function cannot receive a liver graft from a deceased donor because the allocation system is based on the MELD score. Therefore, potential transplant recipients, who do not have a living donor, may die while on the waiting list for a deceased donor liver. DLT using a liver graft from living donors for a recipient with amyloidosis has not been reported in Korea. Domino split-LT using a living donor can save the lives of patients with ESLD or with downstaged HCC.

In domino LDLT, the primary concern is to ensure the safety of both the amyloidosis patient and the living donor. Because the vessels of the LDLT from the first donor are not long enough for anastomosis, it is necessary to leave the hepatic vessels as long as possible when removing the liver from the amyloidosis patient to ensure safety for vascular reconstruction. This makes the vessels attached to the domino graft very short with multiple orifices, thus increasing the technical complexity of vascular reconstruction in the domino recipient. Careful decision-making during the procedure, such as where to divide the vessels in the amyloidosis patients, contributes towards successful domino LDLT and prevents surgical complications.

In the present case, we chose an elderly patient with advanced HCC who had a good response to locoregional therapies and radiation therapy. Initially, we recommended LDLT for curative therapy because of a low MELD score, but he did not have any potential living liver donors. In the United Network of Organ Sharing (UNOS) registry, recipients of a DLT were statistically significantly older, had a lower MELD score, were more often at home awaiting transplant, and experienced a waiting list time more than twice as long compared to recipients of a DDLT [4].

Geyer et al. showed that the outcome between DLT recipients and DDLT controls was comparable after propensity matching, and patients who underwent DLT had no increased risk of mortality or graft failure [4]. The central concern in recipients of DLT from amyloidosis patients is the risk of de novo amyloidosis. As predicted, circulating levels of variant TTR were soon detected in the blood of FAP domino liver recipients [1,5]. Despite the existence of variant TTR in these domino graft recipients, early reports were very encouraging and demonstrated little evidence of amyloid deposition in tissues or de novo disease in these patients [1,5]. Given that patients with amyloidosis almost never develop symptoms of polyneuropathy before the third decade of life, it was hoped that the natural history of the disease in the recipients of amyloidosis liver grafts would be similar. On the other hand, de novo amyloidosis in several recipients of domino liver grafts has been reported, and the onset of symptoms occurred 7–9 years post-transplant [2]. Patients born with FAP almost never become symptomatic before reaching the age of 20 years, thus the onset of symptomatic disease 7–9 years post-transplant seems to represent an acceleration of the natural course of the disease. Some possible explanations for the accelerated course of symptomatic FAP in domino liver recipients include the older age of transplant recipients and the influence of immunosuppressive drugs on amyloid deposition [6].

In conclusion, domino LDLT in a patient with amyloidosis proved to be successful, and as exemplified in the present case. A liver graft from a patient with amyloidosis is an effective and valuable source for patients without potential living liver donors.

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Conflicts of interest

The authors of this manuscript have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tpr.2019.100030.

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