Case Report

Re-transplant with liver paired exchange donor

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Lifesaving re-transplantation with liver paired exchange donor

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Abstract

Liver re-transplantations (re-LTx) have been documented as high-risk operations considering technical and immunological challenges. However, improvements over the last two decades have increased success rates, bringing them closer to those of primary liver transplantations (LTx). At present, deceased organ shortage is a critical issue, and even potential live donors may not be suitable regarding vascular and biliary challenges, volume discrepancies, and ABO incompatibility for both primary and re-LTx. The hospital records of a patient who underwent two liver transplantations in our institution were evaluated retrospectively. A twelve-year-old girl with Progressive Familial Intrahepatic Cholestasis Type 3 underwent live-donor LTx with a graft from her mother. The patient required emergency re-LTx due to primary non-function of the graft, and there were no suitable deceased or live donors during that critical period. The patient was introduced to the liver paired exchange system and underwent a lifesaving re-LTx from an altruistic paired exchange donor. As a developing strategy, liver paired exchange transplantation is a reasonable solution to achieve the most suitable liver graft when it is most needed, especially in populations with very low deceased organ donation rates. There is a need for large studies to analyze the role and success of liver paired exchange transplantation in pediatric patients in urgent and elective situations.

Keywords: Children; liver paired exchange transplantation; liver re-transplantation.

Introduction

Liver transplantation (LTx) is a life-saving procedure for children with end-stage liver diseases and some inherited metabolic disorders. Outcomes of pediatric LTx have improved dramatically over the last two decades. However, 3–29% of the pediatric LTx population required re-transplantation (re-LTx) due to graft failure according to the literature. The major indications for re-LTx include vascular complications (especially hepatic artery thrombosis), primary graft non-function (PNF)/severe dysfunction, biliary complications, hyperacute, acute, and chronic rejection, and recurrence of the primary disease.[1–6]

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Liver re-transplantations have been documented as high-risk operations considering technical and immunological challenges. Ng et al. compared patient survival for primary transplants and re-transplants, revealing 88% and 67% one-year patient survival rates, respectively, in the Studies of Pediatric LTx (SPLIT) study among 246 pediatric re-LTx patients.[1] Moreover, patients who required early re-LTx showed 59% survival compared to 74% survival beyond 30 days, presenting the severity of early graft loss and the urgent requirement for a new graft to keep the patients alive. Vascular complications and PNF comprise more than 90% of early re-transplantation indications.[1–3]

Organ shortage becomes a critical issue when urgent transplantation is needed. Western studies reported that more than 90% of re-LTx cases were from deceased donors.[1,3] Unfortunately, countries on the eastern side of the world, including Turkiye, have very low organ donation rates and are mainly dependent on living donor LTx (LDLT). Additionally, some patients' potential live donors may not be suitable regarding vascular and biliary challenges, volume discrepancies, and ABO incompatibility. ABO-incompatible LTx and the use of technical variant grafts have been introduced with improving success rates, especially in Asian LTx centers. Furthermore, liver paired exchange transplantation (LPE-LTx) is an emerging approach to overcome difficulties in achieving the most suitable living liver allografts in the pediatric population.[7,8]

Materials and Methods

The hospital records of a patient who underwent emergency re-LTx from an LPE donor were evaluated retrospectively in terms of patient and graft characteristics and post-transplant outcomes. This study was approved by the Institutional Review Board of Inonu University (Approval no. 2025/8266).

Case Report

A twelve-year-old girl with Progressive Familial Intrahepatic Cholestasis Type 3 underwent left lobe LDLT with a graft from her mother. The patient's blood group was B Rh (−) and her mother's was B Rh (+). LTx was technically successful with normal reperfusion and Doppler ultrasonography (DUS) findings, and the patient was extubated within a couple of hours in the intensive care unit.

However, starting from the first post-transplant hours, transaminases, INR, bilirubin levels, and ammonia were observed at high levels, with profound acidosis. There was no thrombosis, and arterial, portal, and hepatic flows were normal as proven by DUS and triphasic computed tomography. Peak values were: ALT 3447 U/L, AST 3976 U/L, INR 7.59, lactate 7.5 mmol/L, total and direct bilirubin 30 and 12 mg/dL, and ammonia 1401 µg/dL. Continuous renal replacement therapy and plasmapheresis were started, and the patient was intubated with grade 3 encephalopathy.

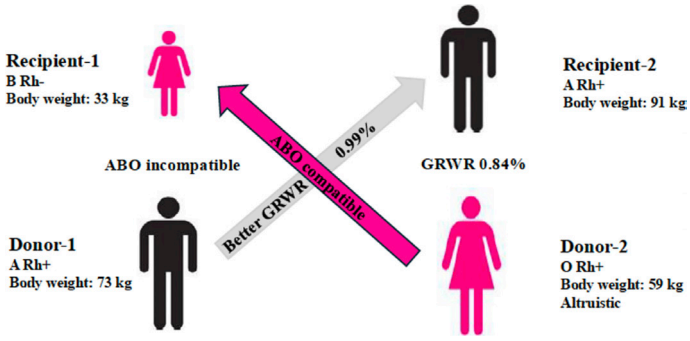

Figure 1. The 2-way LPE transplantation scheme with recipient and donor characteristics.

She was listed nationwide for emergency re-transplantation due to PNF with deceased donor allograft need. None of her family members nor volunteers were appropriate donors due to ABO incompatibility. Unfortunately, there was no available deceased donation at that time, and she was included in the LPE Program in the Liver Transplantation Institute at Inonu University. A suitable donor was designated by the system within 24 hours.

A forty-year-old female (Donor-2), who was originally accepted to be a right lobe liver donor for her father (Recipient-2), agreed to be an altruistic donor for our pediatric patient (Recipient-1) with the exchange of the child's older brother (Donor-1) as her father's donor. Donor-2 with a blood group O Rh (+) was an ABO-compatible fit for Recipient-1. Besides altruism as being the starter for this two-way LPE transplantation, Donor-1 with A Rh (+) blood group was a superior donor for Recipient-2 with identical blood group and a better graft-to-recipient weight ratio (GRWR) of 0.99% compared to his daughter's graft with a 0.84% GRWR value (Fig. 1).

Donor and recipient operations were all successful with no major complications. The re-transplanted patient was extubated on the first postoperative day and was fully recovered following two liver transplantations two days apart. Histopathological examination of the explanted graft revealed PNF (Fig. 2).

Discussion

Pediatric LTx outcomes have been improving over the decades as a result of advances in surgical techniques, immunotherapy modalities, and perioperative management. More than 90% patient and graft survival ratios have been reported in the current era for pediatric LTx. Graft failure and re-LTx rates have varied from 3% to 29% in both Eastern and Western pediatric LTx centers in the last 10 years.

Re-LTx has been recognized as a riskier operation than primary LTx because of technical and immunological challenges. However, many articles have shown improvements in re-LTx outcomes, proving that it is stringent but commendable for long-term survival of pediatric patients.[1–6] Dreyzin et al.[3] reported better success rates for re-LTx cases at 86% one-year patient survival after 2002 compared to 73% prior to 2002. Two landmark pediatric re-LTx studies from the SPLIT registry and Vock et al.[7] with Scientific Registry of Transplant Recipients (SRTR) data presented 43% and 49% early re-LTx ratios, which occurred in emergency settings due to graft vascular complications and PNF.

Additionally, chronic biliary strictures, chronic rejection, and recurrence of the primary disease were the main indications for late re-LTx cases. Unfortunately, early graft loss has been associated with worse

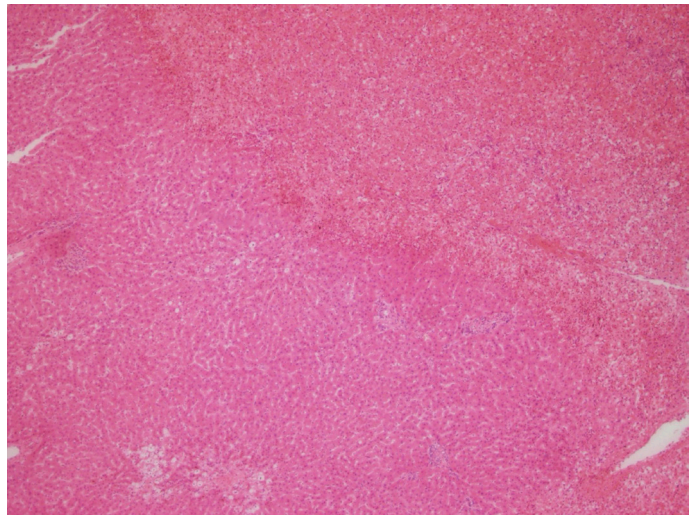

Figure 2. A well-demarcated zone of extensive hepatocyte necrosis in the upper right and liver parenchyma with viable hepatocytes below (HE, 40X).

patient survival due to factors including preoperative critical condition, ventilator support, intensive care unit stay, and long waiting times to find a proper graft, which may result in the patient being too sick to transplant.[1,4] However, Vock et al.[7] reported better survival for early re-LTx patients, contrary to most of the literature, stating that an early enough re-LTx before the patients became too sick and before they developed sepsis explained the improved outcomes.

PNF is one of the most challenging indications for urgent liver re-LTx in pediatric patients. PNF is defined as a transplanted graft with inadequate function in the absence of surgical problems, including vascular thrombosis. Patients rapidly develop liver failure with coagulopathy, profound acidosis, and multiorgan dysfunction, which is almost fatal without immediate intervention. PNF is relatively uncommon in the pediatric population and in live donor grafts due to careful young and healthy donor selection and advances in organ preservation. However, it still occurs in approximately 20% of cases. Survival chance for a pediatric PNF patient has been reported as up to 70% with a well-timed re-LTx.[1–7]

Living or deceased donor allografts with variations have been utilized for re-LTx depending on regional organ donation rates. North American and European countries have the opportunity to use more than 80% deceased donor grafts, in contrast to most Asian transplant centers that must rely mainly on LDLT.[1–10]

Identification of a suitable live donor can be challenging in urgent re-LTx even with many volunteers from the family circle. Unfortunately, only 30–55% of potential live donors can donate to their intended recipients, and alternative strategies are needed to overcome ABO incompatibility, disproportionate graft-residual volumes, and technical challenges involving vascular and biliary structures. ABO-incompatible LDLT has been introduced in this context, but especially in Western populations there is reluctance regarding results of antibody-mediated rejection and lack of consensus on pre- and post-transplant treatment modalities globally.[8–10]

LPE transplantation has been developed to overcome barriers to achieving the best allograft for the benefit of all participants in the exchange group. A milestone study by Yılmaz et al. from the Inonu LTx Institute recently reported the largest LPE experience with 85 adult and pediatric

cases consisting of 2–6-way exchanges as of 2024. The authors stated that none of the patients received a "less favorable" graft than a direct donation. The series included 45 incompatible pairs and 19 altruistic compatible pairs, which led to a 24.2% increase in LDLT volume of the center in 2023. Altruistic donors enabled patients with incompatible donors to achieve lifesaving LTx with the benefit of their original recipients (better GRWR, ABO-identical graft).[8–10]

Our patient was one of the survivors in Inonu University LTx Institute with an altruistic LPE donor in an emergency re-LTx, despite having a family member who wanted to donate but was not compatible.

Conclusion

Liver re-LTx is a complex but improving intervention that provides hope for pediatric patients with graft failure. Availability of a proper allograft remains the most critical problem when urgent liver re-LTx is required. As a developing strategy, LPE transplantation is a reasonable solution to achieve the most suitable live donor liver allograft when it is most needed, with good ethical practices. Large studies are needed to analyze the importance and success of LPE transplantation in pediatric patients in both urgent and elective situations.

Ethics Committee Approval: This study was approved by the Institutional Review Board of Inonu University with approval (date: 12.08.2025, number: 2025/8266).

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