Transfusion-free Retransplantation for Post–liver Transplantation Hepatic Artery Thrombosis: How Much Augmentation Is Too Much?

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INTRODUCTION

Liver transplantation (LT) in Jehovah’s Witnesses and other patients who do not accept blood products remains a controversial issue, with only sporadic published case series in the current literature.1,2 We have previously described our experience with 19 cases of living donor liver transplantation (LDLT) in transfusion-free (TF) patients at our center and have now performed 27 total cases.3 This practice is achievable in these significantly coagulopathic individuals by using erythropoietin and ferric carboxymaltose to target a hemoglobin (Hgb) 13 mg/dL or greater, romiplostim for a platelet count (Plt) 125 × 10⁹/mL or greater, and vitamin K for an international normalized ratio (INR) below 1.7.4,5 Because of the high Model for End-Stage Liver Disease (MELD) score required to receive an offer for deceased donor allograft in United Network of Organ Sharing Region 5 and the controlled timing of recipient cell count augmentation, LDLT has become the near-exclusive option for TF LT recipients. This strategy, along with meticulous surgical techniques, allows us to minimize the risk of life-threatening blood loss. However, chemical augmentation of the patients’ coagulation system may increase the risk of vascular complications.6 Here, we present a case of TF LDLT that was postponed on 2 occasions because of a Plt count below our target goal. The patient was ultimately transplanted, with her postoperative course complicated by early hepatic artery thrombosis (HAT), which was determined to be, in part, due to medical augmentation of hematologic parameters before transplantation. Although it is our center’s experience that the thrombosis rate is comparable with the published rate in standard transfusion-eligible LDLT and this case demonstrates that HAT can be safely managed in this setting, further study on the risks and benefits of hematopoietic stimulants as pretransplant optimization is warranted.
CASE DESCRIPTION

O.Y. is a 56-y-old woman with a history of cirrhosis due to primary sclerosing cholangitis, complicated by hepatic encephalopathy, who was listed for deceased donor LT at a MELD score of 11. Before listing, she had no history of thrombotic events. Laboratory values at time of listing were significant for Hgb 12.0 mg/dL, Plt 53 × 10⁹/L, and INR 1.2. A few months later, she was initiated on romiplostim 4 µg/kg/wk with a Plt goal of 125 × 10⁹/L. Therapy continued for several months until her laboratory values were Hgb 11.8 mg/dL, Plt 150 × 10⁹/L, and INR 1.5. LDLT surgery was scheduled and canceled on 2 separate occasions because of inadequate Plts (Figure 1). The decision was made to continue romiplostim therapy at an increased dose (8.5 µg/kg/wk) until the date of surgery. Before LDLT, her laboratory values were Hgb 13.9 mg/dL, Plt 184 × 10⁹/L, and INR 1.6.

Six months after being listed, O.Y. underwent a TF LDLT using a right lobe allograft from her sister. Her sister had met all living donor requirements, including no prior history of thrombotic events and negative for Factor V Leiden mutation. Anastomoses were as follows: donor right hepatic vein to recipient right hepatic vein, donor right middle hepatic vein conduit to recipient left hepatic vein, donor right hepatic artery to recipient right hepatic artery with a Roux-en-Y hepaticojejunostomy. For all TF LTs performed at our center, we begin the case by carefully assessing for surgical challenges that may lead to excess blood loss. We also routinely reconstruct a portion of the middle hepatic vein to optimize the graft outflow and minimize the risk of graft dysfunction. We dissect the hepatic artery using the high hilar technique and do not excise the artery until the living donor organ is available. We use either the right or left hepatic artery, depending on the arterial quality and the size match. In this case, the right hepatic artery appeared healthy, and a right-to-right hepatic artery reconstruction using interrupted 8-0 Prolene was performed. Though a Roux reconstruction was used due to the patient's history of primary sclerosing cholangitis, both Roux and duct-to-duct reconstructions are used at our center. We also routinely measure portal venous pressures after hepatic artery reconstruction to ensure that there is a portal gradient of <10 mmHg. For all TF cases, we collect 2L of blood from the recipient in a closed circuit for acute normovolemic hemodilution (ANH), which is returned postoperatively. In this case, the estimated blood loss was 1.5L, and all ANH blood was returned. Cell Saver was used, but no blood was collected. Postoperatively, the patient's laboratory values were Hgb 13.0 mg/dL, Plt 200 × 10⁹/L, and INR 2.2.

On postoperative day (POD) 1, the abdominal ultrasound with Doppler demonstrated increased velocity in the portal veins (right 170 cm/s) with normal arterial flow indicated by good Doppler waveforms and resistance indices of 1.0 (which is expected POD 1). Abdominal ultrasound on POD 2 indicated resistance indices of 0.69–0.72 (normal, 0.5–0.8). Laboratory evaluation on POD 4 demonstrated a slight increase in liver enzymes that prompted further anatomical evaluation. Though cholescintography showed no biliary pathology, abdominal ultrasound revealed an absence of flow in the right hepatic artery. Abdominal angiogram confirmed occlusion of the hepatic artery immediately distal to a patent hepatic artery anastomosis (Figure 2). On POD 5, interventional radiology attempted to traverse the occlusion but was unsuccessful. The patient was subsequently relisted with a MELD exception score of 40 for early HAT without evidence of severe graft dysfunction.

Before retransplantation, additional romiplostim was administered to augment Plt to >125 × 10⁹/L. On POD 13, the

**FIGURE 1.** Graph of hemoglobin and platelet values throughout O.Y.’s course in relation to initially scheduled transplant dates, actual LDLT date, and DDLT retransplantation date. Initially, romiplostim 4 µg/kg was given every 4 wk. Because of persistent thrombocytopenia, the dose was increased to romiplostim 8.5 µg/kg every 4 wk. Epogen 30,000 units every 4 wk was also given for 3 mo. DDLT, deceased donor liver transplantation; Hgb, hemoglobin; LDLT, living donor liver transplantation; Plt, platelet count.
The hepatic artery to the graft is not opacified with contrast, consistent postoperative changes consistent with right lobe liver transplantation.

To this day, she has had no further vascular or thrombotic complications. Most recently, her laboratory values were Hgb 13.9 mg/dL, Plt 158 × 10^9/L, aspartate aminotransferase 16 U/L, alanine aminotransferase 15 U/L, and alkaline phosphatase 83 U/L suggesting ongoing excellent graft function.

Patient underwent deceased liver retransplantation with cava-plasty, infrarenal aortic jump graft, and Roux-en-Y hepaticojejunostomy. ANH was again used before surgery and returned at the end of the case. Estimated blood loss was 500 mL. The Cell Saver was used, but no blood was collected. Postoperative laboratory values were Hgb 9.5 mg/dL, Plt 148 × 10^9/L, and INR 1.6. Over the following several days, her liver enzymes improved. Her second postoperative course was complicated by 2 episodes of acute cellular rejection successfully treated with steroids and titration of immunosuppression.

O.Y. continues to follow in our transplant hepatology clinic routinely, with most recent visit being 3 y from her second transplant. Most recently, her laboratory values were Hgb 13.9 mg/dL, Plt 158 × 10^9/L, aspartate aminotransferase 16 U/L, alanine aminotransferase 15 U/L, and alkaline phosphatase 83 U/L suggesting ongoing excellent graft function. To this day, she has had no further vascular or thrombotic complications.

DISCUSSION

To our knowledge, this represents the first published case of retransplantation in a TF patient. As we have developed our TF program, we have addressed the technical complications that have occurred in a similar manner to transfusion-eligible LDLT patients. HAT is an established complication of LDLT and must be planned for if a program is to pursue TF LT. This case demonstrates that salvage operations can be safely performed using TF techniques. At our center, 2 of the total 27 TF LDLTs (7.5%) have been complicated by HAT, a rate similar to the complication rate reported by the Adult-to-Adult Living Donor Liver Transplant Cohort Study in 2002 (6.5%). Fortunately, we have suffered no patient losses related to these procedures. We continue to believe that our approach offers acceptable outcomes to a patient population who would otherwise be denied the opportunity to receive a life-saving transplantation procedure.

Besides the technical difficulty of the LDLT operation, TF LDLT poses significant medical challenges. One medical strategy used by our center includes preoperative augmentation of blood counts and correction of coagulopathy to buffer and limit expected intraoperative blood loss. Augmentation agents do not come without risk. The use of erythropoietin and romiplostim has been associated with increased incidents of venous and arterial thromboembolic events. This case suggests that although aggressive blood count augmentation mitigates risks associated with intraoperative bleeding, an unintended consequence may be an increased risk of thrombotic complications when administered to TF living donors preoperatively. This is an area of study that requires further investigation, particularly as to whether our center’s augmentation goals are higher than necessary to safely proceed with TF LT.

Overall, this case provides a unique insight into complications related to the treatment of TF LDLT patients. O.Y. had no previous history of clotting disorders and—in consultation with Hematology—it was decided that a pretransplant hypercoagulable evaluation was not indicated. As her postoperative ultrasound demonstrated no evidence of hepatic artery stenosis, it is more likely that the subsequent development of HAT was due to the prothrombotic state associated with medical augmentation rather than a technical complication. Ongoing studies are needed to optimize our medical management of TF patients and any patients where hematologic augmentation is used to reduce the need for blood transfusions. This case also demonstrates that even in the most dramatic complications of LDLT, retransplantation remains feasible in a TF setting.

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