

## Living-donor Sequential ABO-incompatible Kidney Transplantation after Liver Transplantation in a Patient with Alcoholic Liver Cirrhosis and End-stage Renal Disease

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A 47-year-old man developed chronic alcoholic liver cirrhosis and end-stage renal disease. He underwent blood-type-compatible liver transplantation with a graft from his daughter. After 8 months, sequential ABO-incompatible (ABOi) kidney transplantation was performed, with his brother as the donor (A to O). The patient had anti-A antibody titers (1:256). We performed pretransplant desensitization, including administration of rituximab, mycophenolate mofetil, tacrolimus, and prednisolone 2 weeks before the scheduled transplantation, and plasmapheresis (PP) and administered an intravenous immunoglobulin injection. The patient underwent PP before kidney transplantation until the anti-A antibody titer was <1:8. The patient achieved normal renal function within 4 posttransplantation days. Postoperative bleeding (diffuse hemorrhage) requiring additional blood transfusions and radiological intervention (drainage procedure) occurred 9 days after transplantation. The patient was discharged on day 20 of hospitalization. Nine months after the kidney transplantation, the recipient's and donor's liver and kidney functions were normal. ABOi renal transplantation after liver transplantation can be successfully performed in patients with high baseline anti-ABO antibody titers after preconditioning with rituximab and PP, and quadruple immunosuppressive therapy. However, caution is required regarding an increased risk of bleeding complications.

**Key Words:** Sequential ABO-incompatible kidney transplantation, Liver transplantation, Bleeding complication

**중심 단어:** ABO 부적합 신장이식, 간이식, 수술 후 출혈

### INTRODUCTION

Combined liver and kidney transplantation (CLKT) is an effective therapy for end-stage liver disease with chronic renal failure. However, it is a complex surgical procedure and difficult to manage perioperatively. Therefore, we performed sequential kidney transplantation (KT; ABO in-

compatible [ABOi]) after liver transplantation. We describe the case of a 47-year-old man who developed chronic alcoholic liver cirrhosis and end-stage renal disease (ESRD). He received a blood-type compatible liver transplant from his daughter. After 8 months, he received a sequential ABOi kidney transplant from his brother (A to O).

In the present case, several clinical obstacles were encountered, such as liver and kidney transplantation (LKT), ABO incompatibility, and bleeding complication after multiple plasmapheresis (PP). Herein, we discuss these issues in detail.

### CASE REPORT

A 47-year-old man had chronic alcoholic liver cirrhosis

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and unknown origin ESRD. His blood type was O Rh+. We performed blood type-compatible liver transplantation with a graft from his daughter. His Child-Turcotte-Pugh score was 5, model for end-stage liver disease score was 20, and graft-to-recipient weight ratio was 1.04. He had undergone living donor liver transplantation (LDLT) using by a modified right lobe graft and bile duct anastomosis was made by duct-to-duct. Immunosuppression consisted of prednisolone, tacrolimus, mycophenolate mofetil (500 mg/day). The target whole-blood trough level of tacrolimus was 8~10 ng/mL for the first 4 week and 7~9 ng/mL thereafter. The patient had ESRD, and he received hemodialysis 3 times per week via arteriovenous fistula (AVF) of left arm. He had no complication in hospital days after LDLT, discharged on postoperative 24th days. The immunosuppressive therapy remained with prednisolone/tacrolimus/mycophenolate

late mofetil. Prednisolone tapered gradually and stopped after 3 months. The function of the transplanted liver was normal.

After 8 months, we also performed sequential ABOi KT, with his brother (A to O) as the donor. The preoperative anti-A antibody titers were 1:256. As pretransplant desensitization, we administered rituximab, mycophenolate mofetil (1 g/day), tacrolimus, and prednisolone (10 mg/day) 2 weeks before the scheduled transplantation, performed seven PP sessions, and PP was performed every other day and immediately followed by intravenous administration of immunoglobulin at a dose of 100 mg/kg. In each PP session, one plasma volume was discarded and substituted at 100% volume with 5% albumin excluding the last session before transplantation; in the last session, we used fresh frozen plasma (FFP). The target whole-blood trough level of tacro-

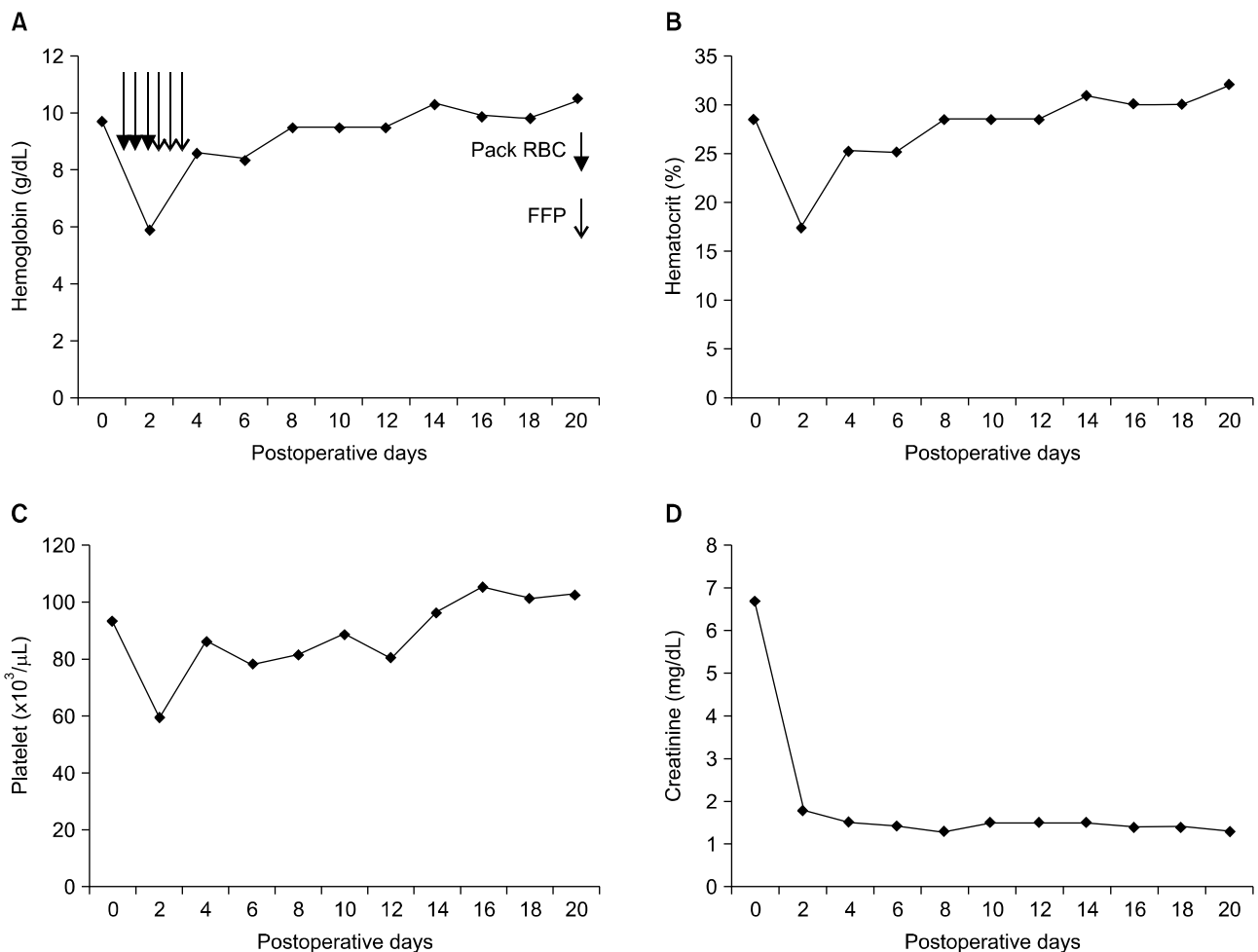


Fig. 1. (A) Hemoglobin, (B) hematocrit, (C) platelet, and (D) creatinine levels after kidney transplantation.

limus was maintained at 8~10 ng/mL. We also injected 200 mg of rituximab intravenously 2 weeks before surgery. After the PP, his laboratory findings were hemoglobin 8.8 g/dL, platelet 88,000/uL, prothrombin time 75% (INR, 1.25), activated partial thromboplastin time (aPTT) 35.4 sec, aspartate transaminase 13 IU/L, alanine transaminase 10 IU/L, total bilirubin 0.3 mg/dL, blood urea nitrogen (BUN) 52.9 mg/dL, and creatinine 7.0 mg/dL, the anti-A antibody titers of the patient were <1:8. Anti-ABO antibody (immunoglobulin G/immunoglobulin M) was checked daily from the

initiation of PP/intravenous immunoglobulin (IVIG) until the 2nd week after transplantation. At first, the target titer at transplantation and during the first 2 weeks after transplantation was 1:4. During the surgery, diffuse bloody oozing was observed. At postoperative day 2, the patient needed transfusion of several packed red blood cells and FFP (Fig. 1). There was perinephric hematoma in the radiologic study (Fig. 2). At postoperative day 9, we performed percutaneous drainage of the perinephric hematoma (Fig. 3). The patient was discharged with good graft function on postoperative day 20. Three year after the procedure, the liver and renal allograft function was normal.

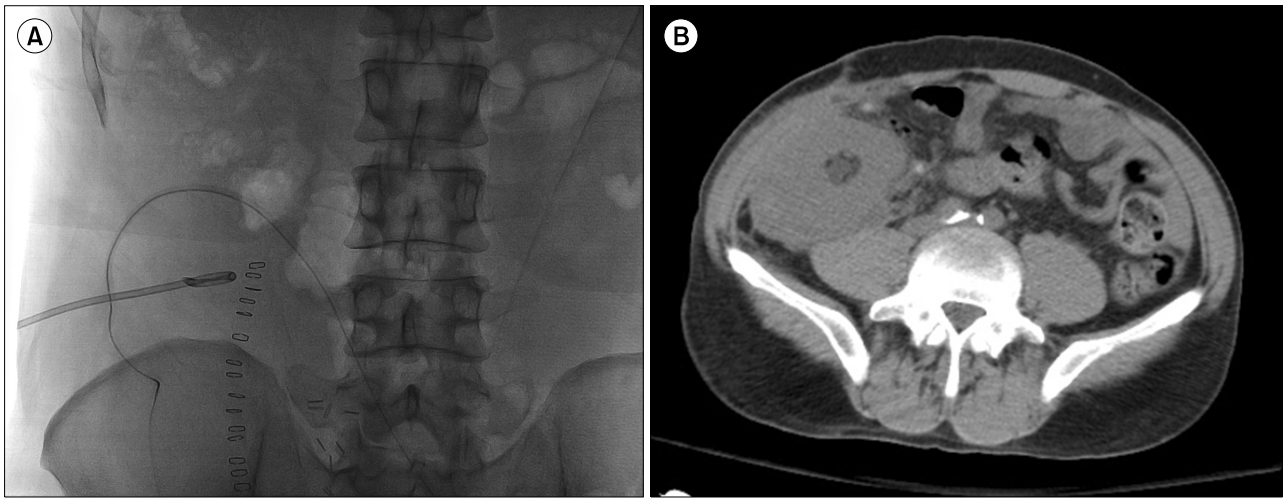


**Fig. 2.** Computed tomographic images showing a perinephric hematoma. An approximately 8×9 cm phlegmonous change with an approximate 5×2 cm fluid collection seen in the right side of the transplanted kidney.

### DISCUSSION

Since the first case of simultaneous LKTs by Margreiter in 1983, it has become the only treatment modality for certain patients with irreversible end-stage liver and kidney diseases(1). In our patient who had alcoholic liver cirrhosis and ESRD, living-related sequential liver ABO compatibility and kidney ABO incompatibility transplantations were performed with grafts from different donors. In our literature search, we did not find any report of a case similar to the present case.

The superiority between CLKLT and sequential liver and kidney transplantation (SeqLKT) is controversial. CLKLT and SeqLKT may be considered equal(2). The severity of



**Fig. 3.** (A) Plain film showing pigtail drainage in the hematoma location. (B) Computed tomographic image showing the improvement after the drainage procedure: decreased fluid collection around the transplanted kidney in the right iliac fossa.

surgical stress and the shortage of organs in CLKT make SeqLKT more preferable among surgeons. SeqLKT has the advantage of allowing for a sequential renal transplantation in normal liver function after liver transplantation. Therefore, the coagulation function is normal. In terms of organ shortage, the use of a living-related donor is a good alternative. However, liver and kidney transplant donors are exposed to high risks. In our case, the patient received the liver graft from his daughter and the kidney graft from his brother. More prospective randomized studies are required to compare the operative methods of CLKT and SeqLKT because of the many factors that affect the results, such as original disease and donor characteristics.

With the advancement of immunosuppressive agents and PP, graft survival in ABO-incompatible KT has highly improved(3). However, in a previous case of baseline anti-ABO antibody titer ( $>1:256$ ), the patient needed additional sessions of pretransplant PP/IVIG(4). In our case, the preoperative anti-A antibody titer was 1:256. We performed seven PP sessions and administered an IVIG injection (100 mg/kg) until the anti-A antibody titer of the patient was  $<1:8$ . Posttransplant PP is controversial. To deplete the B-cell population in a patient with a high titer, previous reports suggested splenectomy or rituximab administration with splenectomy(5). A B-cell-depleting antibody was recently discovered that can replace splenectomy in patients with high titers(6). Two weeks before the surgery, we did not perform splenectomy but administered a 200-mg rituximab injection intravenously.

Our search of the relevant medical literature yielded 10 reported cases of sequential living donor LKT seven of the 10 patients were infants or small children, two adolescences. Adult SeqLKT including our experience reported only two cases. SeqLKTs were performed with a mean interval of 3.6 months (22 days~8 months) between the two procedures in infants and children(7). Adult SeqLKT including our experience were performed with an interval of 8, 10 months between the procedures. More studies are required to compare the two procedures interval of SeqLKT because of the many factors that affect the results, such as original disease and donor characteristics.

Recent study reported that pre-emptive transplantation, a high pretransplant BUN level, A high anti-ABO antibody

titer after PP, a low platelet count of  $\leq 100,000/\text{mm}^3$  after PP, and a prolonged aPTT were associated with an increased risk of bleeding after ABOi KT, and the type of substitution fluid used during PP did not result in statistically significant differences between PP and PP using high portion of FFP group(8).

The risk of hemorrhage after PP is increased. After PP, postoperative bleeding is not uncommon. Plasma exchange itself produces a decrease in clotting factors. However, an increase in these factors is noted in a few hours. When multiple PP sessions are performed in a short period, coagulopathy is prolonged(9). ABOi KT usually needs several PP sessions, as in our case.

In conclusion, CLKT is an effective therapy for end-stage liver disease with chronic renal failure. However, it is a complex surgical procedure and perioperative management is difficult. Therefore, we performed SeqLKT. ABO-incompatible renal transplantation after liver transplantation can be performed successfully in patient after preconditioning with rituximab and PP, and quadruple immunosuppressive therapy. However, the intensified desensitization in patients might be associated with an increased risk of bleeding complications.

## REFERENCES

- 1) Bertelli R, Nardo B, Cavallari G, Ercolani G, Lauro A, Neri F, et al. Kidney transplantation combined with other organs in Bologna: an update. *Transplant Proc* 2008;40:1867-8.
- 2) Nakamura M, Fuchinoue S, Nakajima I, Kitajima K, Tojimbara T, Takasaki K, et al. Three cases of sequential liver-kidney transplantation from living-related donors. *Nephrol Dial Transplant* 2001;16:166-8.
- 3) Rahman T, Harper L. Plasmapheresis in nephrology: an update. *Curr Opin Nephrol Hypertens* 2006;15:603-9.
- 4) Tobian AA, Shirey RS, Montgomery RA, Tisch DJ, Ness PM, King KE. Therapeutic plasma exchange reduces ABO titers to permit ABO-incompatible renal transplantation. *Transfusion* 2009;49:1248-54.
- 5) Shimmura H, Tanabe K, Ishida H, Tokumoto T, Ishikawa N, Miyamoto N, et al. Lack of correlation between results of ABO-incompatible living kidney transplantation and anti-ABO blood type antibody titers under our current immunosuppression. *Transplantation* 2005;80:985-8.
- 6) Sonnenday CJ, Warren DS, Cooper M, Samaniego M, Haas

- M, King KE, et al. Plasmapheresis, CMV hyperimmune globulin, and anti-CD20 allow ABO-incompatible renal transplantation without splenectomy. *Am J Transplant* 2004;4:1315-22.
- 7) Mor E, Nesher E, Ben-Ari Z, Weissman I, Shaharabani E, Eizner S, et al. Sequential liver and kidney transplantation from a single living donor in two young adults with primary hyperoxaluria type 1. *Liver Transpl* 2013;19:646-8.
- 8) Kim MH, Jun KW, Hwang JK, Kim JI, Chung BH, Choi BS, et al. Risk Factors for Postoperative Bleeding in ABO-Incompatible Kidney Transplantation. *Clin Transplant*. Epub 2015 Feb 3. DOI: <http://dx.doi.org/10.1111/ctr.12525>.
- 9) Gelabert A, Puig L, Maragall S. Coagulation alterations during massive plasmapheresis. In: Sieberth HG, ed, *Plasma exchange*. Stuttgart: Schattauer Verlag; 1980:71.