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Letter to the Editor

Emergency ABO-incompatible living donor liver transplant for patients with ultrahigh MELD scores

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To the Editor:

A 49-year-old Chinese man with treatment-naïve chronic hepatitis B presented with a one-week history of jaundice when admitted to our hospital. On admission, his bilirubin was 704 μmol/L, alanine aminotransferase 180 U/L, international normalized ratio 2.4, creatinine 140 μmol/L, and Model for End-stage Liver Disease (MELD) score 35. His serum HBV DNA was 64.7 IU/mL, and he was commenced on entecavir. Nonetheless, he developed acute-on-chronic liver failure on day 28 with grade 2 hepatic encephalopathy and a MELD score of 40 (bilirubin 709 μmol/L, international normalized ratio 3.3, creatinine 181 μmol/L). During his admission, he developed bacteremia and spontaneous bacterial peritonitis (SBP). His blood culture was positive of *enterococcus faecium* and *coagulase-negative staphylococcus* and his peritoneal fluid culture was positive of *coagulase-negative staphylococcus*. This was further complicated by the development of type 1 hepatorenal syndrome. His initial condition was so poor that intensive care with inotrope was needed. At the time of preconditioning, the sepsis due to SBP was barely controlled after optimization.

An emergency ABO-incompatible (ABOi) living donor liver transplant (LDLT) was planned, as there was no suitable liver donor compatible with his A positive blood group. His 29-year-old daughter with blood group AB positive was worked up as a living donor. The preoperative ABOi protocol was modified, as shown in Fig. 1. In brief, rituximab (375 mg/m^2) was given two weeks before liver transplant. Plasma exchange with fresh frozen plasma from donors with blood group AB positive was performed (totally 34 units of fresh frozen plasma). His anti-B immunoglobulin M and immunoglobulin G titers were brought down from 1:64 and 1:8 to 1:16 and 1:2, respectively. Mycophenolate mofetil (MMF) was given one week before LDLT. The dosage was adjusted according to the patient's preexisting infection and a total of 3 g was given preoperatively. Antimicrobial treatments including meropenem, vancomycin and anidulafungin were prescribed preoperatively as treatment for his SBP and sepsis, and postoperatively as prophylaxis.

Right lobe LDLT was performed at eight weeks after admission. The patient's body weight and height was 52.6 kg and 161.5 cm, respectively, with an estimated total liver volume of 1090 mL. His daughter, weighing 50.5 kg, donated the right liver lobe, and the volume of her liver remnant was 431.7 mL. The graft weighed 465 g, which translated into 43% of the patient's estimated standard liver mass, and contained the middle hepatic vein. In the recipient operation, total hepatectomy was performed with preservation of the inferior vena cava. The recipient's main portal vein was divided just below its bifurcation. Upon completion of total hepatectomy, the right hepatic vein and the common trunk of the middle and left hepatic veins were divided by vascular stapler. The native liver was severed and the inferior vena cava was cross clamped. No portal caval shunt was used. After flushing the graft with histidine–tryptophan–ketoglutarate solution at the back table, fusion venoplasty joining the right hepatic vein and middle hepatic vein with continuous 6–0 polypropylene suture was done. The graft was implanted to the recipient inferior vena cava by continuous 5–0 polypropylene suture. Portal vein anastomosis was completed with 6–0 polypropylene suture for both anterior and posterior walls in a continuous manner. The total warm and cold ischemic time was 32 and 81 min, respectively. Graft reperfusion was uneventful. The graft right hepatic artery was anastomosed to the recipient right hepatic artery. A duct-to-duct anastomosis was performed without any biliary stent.

In the immediate preoperative period, the patient's anti-B immunoglobulin M and immunoglobulin G titers were 1:16 and 1:2, respectively. We adopted the usual protocol of induction immunosuppression with 20 mg of basiliximab within 6 h of graft reperfusion and on postoperative day 4. Steroid injection was given intraoperatively with 1 g of hydrocortisone. On postoperative day 1 1500 mg of hydrocortisone was given. Immunosuppression was maintained with oral tacrolimus within 12 h of transplant at a dosage of 0.15 mg/kg body weight/d, and a trough level of 10–12 μg/L was maintained. MMF was administered at a dosage of 2 g/d and continued as maintenance, along with 10 mg of prednisolone twice a day.

The graft function was normal on postoperative day 18, with anti-B immunoglobulin M and immunoglobulin G titers of 1:64 and 1:16, respectively (Fig. 2). He was discharged on day 20,

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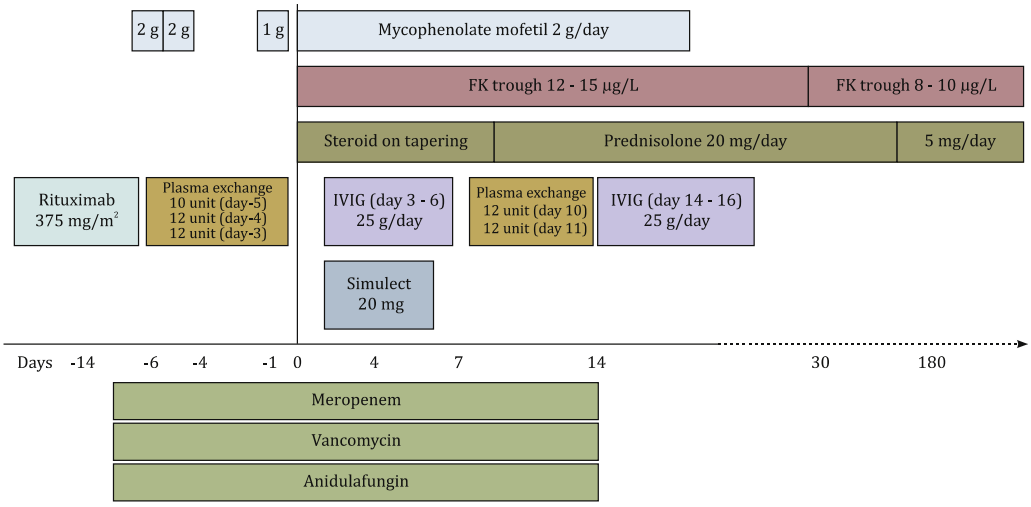

Fig. 1. Modified perioperative ABO-incompatible protocol. FK: Tacrolimus; IVIG: intravenous immunoglobulin.

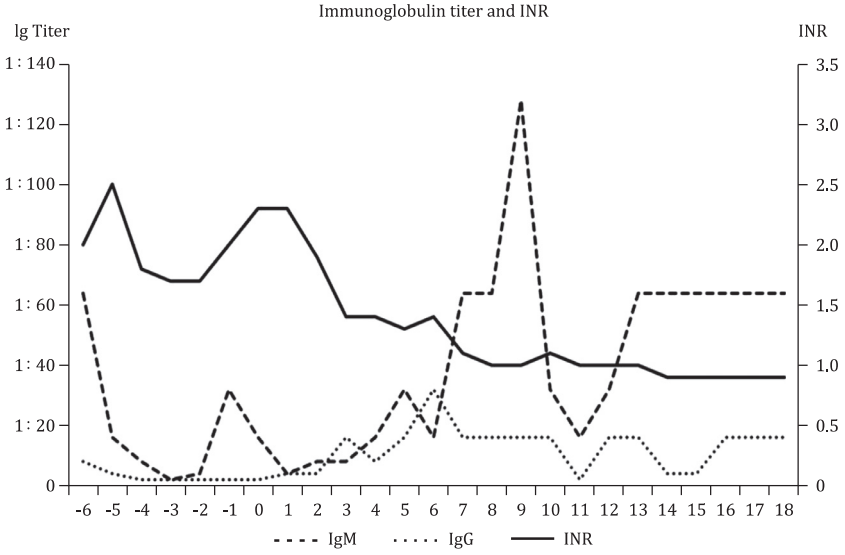

Fig. 2. Perioperative trend of immunoglobulin and international normalized ratio.

and the titers were 1:64 and 1:4, respectively. At 1 year after transplant, his graft function and immunoglobulin titers remained stable. He resumed work and no complication has been observed. His daughter recovered smoothly and was discharged on day 7 after the donation.

The rate of organ donation by the deceased in Hong Kong is low when compared with the Western world, but the demand for liver transplant is high due to the high prevalence (~8%) of hepatitis B virus infection in the city. Therefore, LDLT is often the only option. From 2009 to 2016, our center worked up 828 potential donors, and 82 (10%) of them were ABOi. A similar situation was observed at a Korean center, where an increase of 15% in the total number of LDLT was achieved with performing ABOi LDLT [1]. To circumvent the ABOi barrier, our center has performed donor interchange liver transplant previously [2], but this strategy is more likely to be implemented for chronic recipients only. In emergency cases like the one described herein, the patients are just too ill to wait for a suitable donor-recipient pair for donor interchange. Furthermore, the donor in the current case has AB blood type; this virtually means that no other donor-recipient pair would have the incentive to interchange with this family. The experience of this patient shows that the blood group barrier can be overcome in patients with ultrahigh MELD scores, as long as the underlying infection is adequately controlled.

ABOi LDLT for acute liver failure associated with hepatic encephalopathy has been reported by a Japanese group [3]. Our patient was in an even poorer condition; he presented to us as emergency admission with continuous deterioration, with multiple complications including hepatic encephalopathy, type 1 hepatorenal syndrome, and SBP. The decision on ABOi LDLT was consensual after multidisciplinary meetings between the transplant surgeons, hepatologist, hematologist, microbiologist and anesthetist, together with his very supportive family. It was agreed that further delay while waiting for a deceased donor graft would very likely result in progressive deterioration with worsening hepatic encephalopathy and cerebral edema. This was balanced against the risk of uncontrolled sepsis with the preexisting infection, which might be aggravated by plasma exchange, rituximab, and MMF.

ABOi LDLT has been reported in large series from Asian centers [1,4,5]. Most of the patients included had chronic cirrhosis.

In general, most patients with fulminant hepatic failure or acute-on-chronic liver failure are excluded from ABOi LDLT because of high urgency conditions. Infective complications and inadequate preparation in these patients are the main concerns. Take our patient as an example, his presenting status was immunosuppression with SBP. We adopted a protocol similar to the Japanese group's [5], with the use of rituximab and plasma exchange. We used a much lower preoperative dose of MMF, given that the patient was already immunosuppressed with liver failure, which was made evident by the recent SBP and bacteremia. With this approach, the anti-B immunoglobulin M titer was reduced rapidly from 1:64 to 1:2. The recovery after transplant was uneventful, without any evidence of infective complications or antibody-mediated rejection. As ABOi LDLT is associated with a higher rate of biliary complications, close monitoring and stringent follow-up are necessary.

The protocol for ABOi LDLT is evolving. Minimized protocols have been advocated recently [4,6], and complicated protocols with splenectomy, local graft infusion, intravenous immunoglobulin, plasmapheresis and rituximab have been reported [7]. Egawa et al. [8] reported that antibody-mediated rejection was significantly reduced after the use of rituximab. On the other hand, minimal antibody-mediated rejection was seen with the abandonment of plasmapheresis in a study by Lee et al. [6]. Although we adopted a more traditional protocol, we do not rule out that a minimized protocol [4,6] would also succeed. Further studies are needed for clarifying case selection criteria for immunomodulation protocols.

In conclusion, ABOi LDLT should be considered as a feasible option for high urgency patients, even those with ultrahigh MELD scores, provided that the underlying infection is adequately treated.

Contributors

CKSH proposed the study. FJYY, CACY and DWC collected the data. CKKW performed the research, analyzed the data and wrote up the manuscript. LCM oversaw the study. All authors approved the final manuscript. CKSH is the guarantor.

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Ethical approval

Not needed.

Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

[1] Song GW, Lee SG, Hwang S, Kim KH, Ahn CS, Moon DB, et al. ABO-incompatible adult living donor liver transplantation under the desensitization protocol with rituximab. Am J Transpl 2016;16:157–170.
[2] Chan SC, KSh Chok, Sharr WW, Chan AC, Tsang SH, Dai WC, et al. Samaritan donor interchange in living donor liver transplantation. Hepatobiliary Pancreat Dis Int 2014;13:105–109.
[3] Yasuda M, Ikegami T, Imai D, Wang H, Bekki Y, Itoh S, et al. The changes in treatment strategies in ABOi living donor liver transplantation for acute liver failure. J Med Invest 2015;62:184–187.
[4] Lee CF, Cheng CH, Wang YC, Soong RS, Wu TH, Chou HS, et al. Adult living donor liver transplantation across ABO-incompatibility. Med (Baltimore) 2015;94:e1796.
[5] Ikegami T, Yoshizumi T, Soejima Y, Uchiyama H, Shirabe K, Maehara Y. Feasible usage of ABO incompatible grafts in living donor liver transplantation. Hepatobiliary Surg Nutr 2016;5:91–97.
[6] Lee EC, Kim SH, Shim JR, Park SJ. A comparison of desensitization methods: Rituximab with/without plasmapheresis in ABO-incompatible living donor liver transplantation. Hepatobiliary Pancreat Dis Int 2018;17:119–125.
[7] Rummler S, Bauschke A, Bärthel E, Jütte H, Maier K, Ziehm P, et al. Current techniques for AB0-incompatible living donor liver transplantation. World J Transpl 2016;6:548–555.
[8] Egawa H, Teramukai S, Haga H, Tanabe M, Mori A, Ikegami T, et al. Impact of rituximab desensitization on blood-type-incompatible adult living donor liver transplantation: a Japanese multicenter study. Am J Transpl 2014;14:102–114.

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