

First successful perinatal management of pregnancy after ABO-incompatible liver transplantation

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Abstract

Many papers have reported on pregnancy and delivery after liver transplantation, but there have been no reports on pregnancy after ABO-incompatible liver transplantation. This paper reports the first successful pregnancy and delivery of a newborn after ABO-incompatible liver transplantation for fulminant hepatic failure. The patient was a 39-year-old female. She had an ABO-incompatible liver transplantation, donated from her husband, due to subacute fulminant hepatitis of unknown etiology. She was taking tacrolimus, methylprednisolone, and mizoribine orally for the maintenance of immunosuppression at the time of discharge. She was discharged uneventfully on postoperative day 38 without any rejection episodes. At 1 year and 6 mo after transplantation, she indicated a wish to become pregnant. Therefore, treatment with mycophenolate mofetil was interrupted at that time. After two miscarriages, she finally became pregnant and delivered transvaginally 3 years after the transplantation. All of the pregnancies were conceived naturally. The newborn was female with a birth weight of 3146 g; the Apgar scores were 9 and 10. Delivery was performed smoothly, and the newborn exhibited no malformations. The mother and the newborn were

discharged uneventfully. We suggest that pregnancy is possible for recipients after ABO-incompatible liver transplantation.

Key words: Pregnancy; Liver transplantation; Delivery; Fulminant hepatic failure; ABO-incompatible; Living donor

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Core tip: This report is on the first successful perinatal management of pregnancy after ABO-incompatible liver transplantation. We suggest that pregnancy should be allowed for those who previously received ABO-incompatible liver transplantation.

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INTRODUCTION

Liver transplantation has been established as a medical treatment for end-stage liver disease patients. In Japan, living-donor liver transplantation, including ABO-incompatible liver transplantation, is the most available procedure due to a chronic lack of deceased donor livers. We established a protocol for ABO-incompatible liver transplantation that uses immunosuppressants (*e.g.*, cyclosporin or tacrolimus), rituximab, steroids, mizoribine, and intraportal infusion therapy^[1,2]. Although there are extensive operative stresses involved and immunosuppressants are required, many papers have reported a successful pregnancy or delivery after liver transplantation^[3,4]. However, only two reports described pregnancy and delivery after ABO-incompatible kidney transplantation, and there have been no reports on pregnancy after ABO-incompatible liver transplantation^[5,6]. This paper reports the first successful pregnancy and delivery of a newborn after ABO-incompatible liver transplantation for fulminant hepatic failure.

CASE REPORT

A 39-year-old woman, gravida 1, para 1, received an ABO-incompatible liver transplantation, donated from her husband. The transplantation was due to subacute fulminant hepatitis that occurred two months after her first delivery; although the etiology was unknown, it was suspected to be drug-induced. She had no appreciable diseases, including hepatitis virus infections, or a past or family history of liver disease. She was allergic

to crab butter but not any medicines. Her blood type was O, Rh(+), and her HLA-A, B, DR was A2/A11, B35/B55, DR9/DR12. The donor's blood type was A, Rh(+), and his HLA-A, B, DR was A2/A24, B46/B48, DR8/DR16. Her anti-A and anti-B antibodies before hepatitis were uncertain due to a plasma exchange (PE).

She gave birth to her first baby by vaginal delivery at the age of 39 years old in February 2012. After delivery, she suffered from refractory periodontitis; she took the antibiotic cephem (cefdinir) for 6 d starting in April 2012 because of the periodontitis. Subsequently, she exhibited general malaise, general itching sensations, and chills. A dermatologist prescribed levocetirizine and prednisolone unguent, but the symptoms persisted with no improvement. She also had a problem with a second premolar tooth because she had exodontia and took the antibiotic cephem (cefdinir) to prevent infection. However, after taking this antibiotic, she experienced the sudden onset of jaundice and severe hepatic dysfunction [aspartate transaminase (AST)/alanine aminotransferase (ALT) = 948/1090 IU/L, T-Bil 138 μ mol/L, D/T = 0.71, prothrombin time-international normalized ratio (PT-INR) = 1.00]. She was admitted to the hospital with fulminant hepatitis of unknown etiology, and liver support therapy was performed. A liver biopsy revealed acute, drug-induced hepatitis. Her liver function continued to deteriorate (AST/ALT = 944/1114 IU/L, T-Bil 296 μ mol/L, D/T = 0.76, PT-INR = 1.23), and she developed hepatic encephalopathy two weeks later, when the first symptoms appeared. On the day hepatic encephalopathy appeared, she was transferred to our hospital. We performed PE five times and started continuous hemodiafiltration. The first PE was fresh frozen plasma of blood type O, and the others were blood type AB due to the possibility of ABO-incompatible liver transplantation. Although she was registered on the waiting list for deceased donor liver transplantation in Japan, the progression of liver dysfunction did not allow for much time to be spent waiting for a deceased liver donation [the model for end-stage liver disease (MELD) score increased from 28 to 36 in a week]. In addition, pancreatitis was suspected due to the PEs because of the elevation in serum amylase. An ABO-incompatible liver transplantation was performed 10 d after the first PE was performed; the liver was donated from her 33-year-old husband. Before transplantation, her anti-A antibodies were 64 \times (IgM) and 128 \times (IgG), and her anti-B antibodies were 32 \times (IgM) and 64 \times (IgG).

The donor's left liver lobe (graft weight; 452 g, graft weight/recipient body weight = 0.93) was transplanted, and a splenectomy was also performed along with the insertion of an intraportal infusion catheter and immunosuppression, according to our protocol^[1] for ABO-incompatible liver transplantation. Rituximab was infused one time just after the liver transplantation. The operation time was 10 h and 18 min, and blood loss was 538 mL.

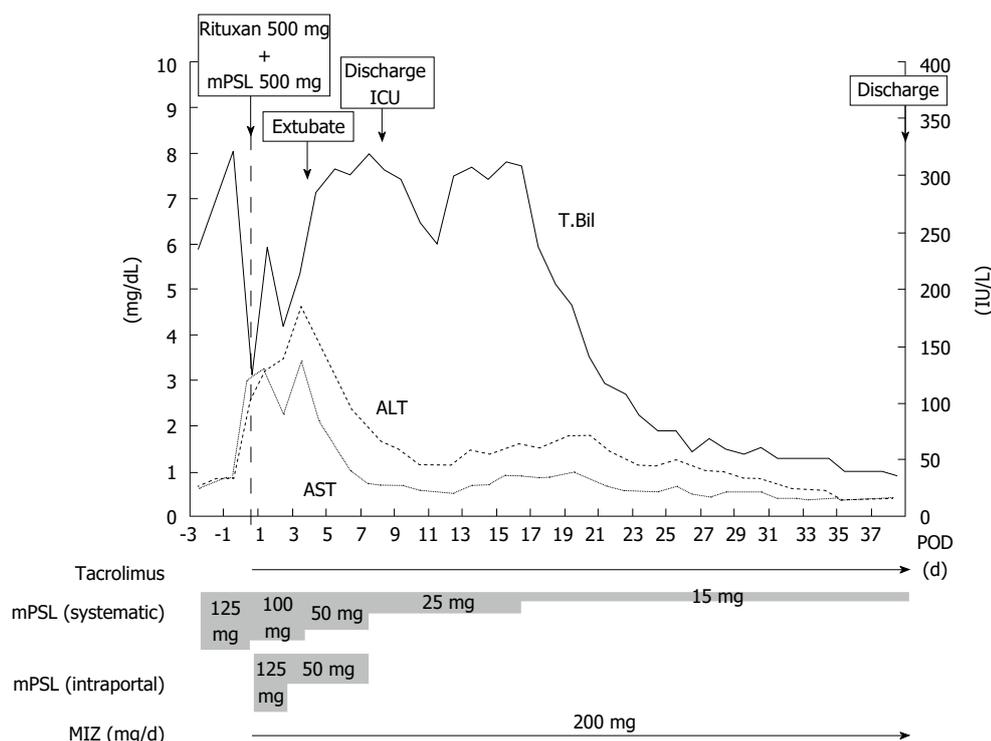


Figure 1 Perioperative laboratory data and immunosuppressive drugs. AST: Aspartate transaminase; ALT: Alanine transaminase; T.Bil: Total bilirubin; POD: Postoperative day.

Her encephalopathy improved promptly after the transplantation. She was extubated on postoperative day (POD) 3 and discharged from the intensive care unit on POD 7. Tacrolimus, steroids, and mizoribine were given, and intraportal infusion therapy was performed to prevent rejection (Figure 1). The jaundice and liver function gradually improved, and she was discharged from the hospital on POD 38 with no bacterial infections or rejection episodes (laboratory data at the time of discharge: AST/ALT = 18/16 IU/L, T-Bil 15 μ mol/L, D/T = 0.11, PT-INR = 1.08).

When she was discharged, she was taking tacrolimus (1.4 mg/d), methylprednisolone (mPSL; 15 mg/d), and mizoribine (200 mg/d) orally for the maintenance of immunosuppression, and her anti-A and anti-B antibodies were not increased; anti-A antibodies: 32 \times (IgM) and 256 \times (IgG), anti-B antibodies: 32 \times (IgM) and 64 \times (IgG). Although she developed steroidal diabetes, it was well controlled with insulin (HbA1c was within the range of 5.2%-6.1% during pregnancy).

Her serum tacrolimus concentration was maintained between 3 ng/mL and 8 ng/mL as an outpatient. Her general condition improved gradually, and 1 year and 6 mo after transplantation, she expressed a desire to become pregnant. Thereafter, she conceived spontaneously but miscarried twice, 2 years and 2 years plus 6 mo after the transplantation. Three years after the transplantation, when she was 42 years old, she conceived spontaneously, and the perinatal clinical course was uneventful. At the 39th week of pregnancy, a female baby weighing 3146 g was delivered vaginally with Apgar scores of 9 and 10 at 1 and 5 min,

respectively. The intra- and postpartum courses were uneventful, and there was no postpartum hemorrhage. The baby exhibited no malformations and was healthy at the age of 6 mo. During the course of pregnancy, she took 4 mg/d of tacrolimus without reduction or suspension, and her levels of AST, ALT, and bilirubin remained within normal ranges. In addition, her anti-A and anti-B antibody levels were stable during the perinatal period: antenatal: anti-A antibodies: 2 \times (IgM) and 16 \times (IgG); anti-B antibodies: 32 \times (IgM) and 64 \times (IgG); postnatal: anti-A antibodies: 2 \times (IgM) and 8 \times (IgG), anti-B antibodies: 16 \times (IgM) and 64 \times (IgG). Although the blood type of the baby was uncertain, anti-A and anti-B antibodies did not increase during the pregnancy.

DISCUSSION

ABO-incompatible living-related liver transplantation is a procedure that is performed to resolve the lack of deceased donors. Due to the immunosuppression protocol for ABO-incompatibility comprising rituximab^[1], it has become a relatively straightforward procedure. Our protocol for ABO-incompatible liver transplantation has allowed patients to undergo transplantation with a prognosis similar to that of an ABO-compatible liver^[7]. This procedure greatly increases the likelihood of a successful transplantation in acute liver dysfunction patients who could not find an ABO-compatible donor. Indeed, in this case, the only donor available within the limited time was ABO incompatible. In the past, the survival rate of ABO-incompatible liver transplantation

was lower than that of ABO-compatible transplantation, but with improvements, there is currently no significant difference between ABO-compatible and ABO-incompatible transplantation in the Japanese registry^[8].

Many papers have reported obstetric complications during pregnancy after liver transplantation; liver dysfunction and preeclampsia are commonly reported according to systematic reviews^[9,10]. The rates of cesarean section and preterm delivery are also higher after liver transplantation than in the general population; accordingly, gestational age is shorter after liver transplantation than in the general population. Fortunately, the perinatal course in our patient was uneventful. In contrast to previous reports^[9,10], the patient delivered an appropriate-for-date newborn at full term.

Immunosuppression is an important point in pregnancy. The interruption of mizoribine use prevented teratosis, and no liver dysfunction was observed. Because mycophenolate mofetil was used, the patient needed a six-month interval before the pregnancy because of its teratogenic effects.

In conclusion, we experienced and reported the first successful management of a case of pregnancy after ABO-incompatible liver transplantation for fulminant hepatic failure.

COMMENTS

Case characteristics

The patient was a 39-year-old female. She had an ABO-incompatible liver transplantation, donated from her husband, due to subacute fulminant hepatitis of unknown etiology.

Clinical diagnosis

She was found to have jaundice, and hepatic encephalopathy was observed.

Differential diagnosis

Her differential diagnosis included drug-induced liver failure and viral infection.

Laboratory diagnosis

The laboratory evaluation showed significant hyperbilirubinemia, increased aspartate transaminase/alanine aminotransferase, hepatic dysfunction, and decreased prothrombin time-international normalized ratio.

Imaging diagnosis

Abdominal ultrasound and computed tomography revealed the atrophic change of the liver but no evidence of biliary obstruction.

Pathological diagnosis

She was diagnosed with drug-induced fulminant hepatitis upon liver biopsy.

Treatment

The initial treatment consisted of medical management comprising plasma exchange and continuous hemodiafiltration, followed by liver transplantation.

Related reports

There have been no reports on pregnancy and delivery after ABO-incompatible liver transplantation.

Term explanation

ABO-incompatible liver transplantation is a type of living-donor liver transplantation.

Experiences and lessons

This case suggests that the possibility of pregnancy for recipients of ABO-incompatible liver transplantation is equivalent to that for recipients of ABO-compatible liver transplantation.

Peer-review

This is a brief report of a successful pregnancy after ABO incompatible liver transplantation. The manuscript is well written and would be of interest to the readers of this journal, the references are up to date.

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