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CASE REPORT

Retrospective observation of therapeutic effects of adult auxiliary partial living donor liver transplantation on postpartum acute liver failure: A case report

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Abstract

We present a female patient with preterm labor, severe viral hepatitis B of acute phase, hepatic encephalopathy stage Ⅲ and coma. After delivery, the illness was exacerbated and the patient presented with clinical signs of vital organ dysfunctions such as acute respiratory distress syndrome, cerebral edema and hypoxemia that needed mechanical ventilation. Emergency liver transplantation was recommended after multidisciplinary panel consultations. The donor, her mother, consented to donate her right liver. Auxiliary partial orthotopic living donor liver transplantion (APOLDLT) was performed. After operation, the patient was on triple medication of tacrolimus plus mofetil mycophenolate and prednisone for immunosuppression. The combination of anti-hepatitis B virus (HBV) immunoglobulin and entecavir was initiated for anti-HBV therapy. Both the patient and the donor recovered well without any complications. The patient was followed up regularly. Her liver function, clinical signs and symptoms improved significantly. Until now, the recipient has been living for more than 78 mo free of any complications. The APOLDLT is a life-saving modality for rescuing patients with high-risk acute liver failure following HBV infection without available donor and hence is recommended under standardized antiviral therapy coverage as stated above.

Key words: Auxiliary partial orthotopic living donor liver transplant; Acute liver failure; Postpartum; Hepatitis B virus; Anti-hepatitis B virus immunoglobulin; Entecavir

Core tip: Auxiliary partial orthotopic living donor liver transplantation (APOLDLT) was performed on a female patient with preterm labor, severe viral hepatitis B of acute phase, hepatic encephalopathy and coma.

The patient was treated with triple medication for immunosuppression, and combination of anti-hepatitis B virus (HBV) immunoglobulin and Entecavir for anti-HBV therapy after operation. The patient has been living for more than 78 mo free of any complications. The APOLDLT is a life-saving modality for rescuing patients with high-risk acute liver failure following HBV infection without available donor.

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INTRODUCTION

Auxiliary partial orthotopic liver transplantation (APOLT) refers to the surgical procedure that preserves the partial liver of the recipient and the partial liver of the donor implanted orthotopically into the recipient. APOLT was first successfully performed by Gubernatis *et al*[1] in 1989. Up to date, not more than 100 cases of adult APOLT have been reported worldwide. The clinical indications for this procedure include acute hepatic failure and congenital metabolic hepatopathy[2-6]. In the late 1990s, living donor graft was used in APOLT and subsequently described as orthotopic living donor liver transplantation (APOLDLT)[7]. Currently, its indication has extended to living related liver transplantations for those with excessive small liver volume graft (ratio of implant to body weight of recipient, GRWR < 0.8) and ABO blood group incompatibility[8]. To the best of our knowledge, there has been no report of adult APOLDLT for rescuing patients with postpartum acute liver failure following severe hepatitis B virus (HBV) infection. We performed APOLDLT on a female patient with preterm labor, severe HBV infection of acute phase, hepatic encephalopathy and coma. The recipient has been living for more than 78 mo free of any complications.

CASE REPORT

A 26-year-old female patient diagnosed as HBV carrier for the past four years was admitted to the Obstetric Department of our hospital at 2 am on May 6, 2008. She had been experiencing menolipsis for more than eight mo and paroxysmal abdominal pain for one hour. Laboratory examinations showed the following results: blood group B, Rh positive; hepatitis B surface antigen (HBsAg) (+), hepatitis B e antigen (+), hepatitis B core antibody (+) with a HBV-DNA load of 2.06×10^7 copies/mL, hepatitis C virus (-); prothrombin time 26.3 s, prothrombin time activity percentage 29%, prothrombin international normalized ratio 2.05; alanine transaminase 3019.1 IU/L, aspartate aminotransferase 15.6 IU/L, total serum bilirubin 174.4 μmol/L, conjugated bilirubin 78.2 μmol/L and blood ammonia 154 μg/dL. The patient was diagnosed with $G_3P_1G_{33}^{+3}$ left occiput anterior preterm labor, severe viral hepatitis B of acute phase, hepatic encephalopathy stage Ⅲ and coma. She delivered a male infant weighing 1750 g at 3:30 am of May 6, 2008. But after 34 h of delivery, the liver function, coagulation function and model for end-stage liver disease score of the patient did not improve and she was transferred to the Surgical Intensive Care Unit at 1:00 pm of May 7, 2008. In spite of intensive care, the illness was exacerbated and the patient presented with clinical signs of vital organ dysfunctions such as acute respiratory distress syndrome, cerebral edema, and hypoxemia that needed mechanical ventilation. Emergency liver transplantation was recommended after multidisciplinary panel consultations. The patient was referred to the liver transplantation intensive-care unit at 10:00 pm of May 8, 2008 for preoperative preparation. The donor, her 52-year-old mother with blood group B, Rh positive, voluntarily consented to donate her right liver. She was evaluated physically and psychologically to be eligible for the donation procedure. The operation was approved by the Ethics Committee of our hospital. The surgery was performed from 8:40 am of May 9, 2008 to 1:00 am on May 10, 2008. Parameters on the donor and recipient are shown in Table 1.

Surgical procedure

APOLDLT was performed under general anesthesia. The right liver lobe of the recipient without the middle hepatic vein was routinely excised and the right hepatic portal vein was preserved to the best of our ability for the impending reconstruction of the portal. The right liver lobe of the donor without the middle hepatic vein was precisely obtained under ultrasound guidance. The dilated donor right hepatic vein was end-to-side anastomosed to recipient vena cava oval opening, which was longitudinally extended down from the right hepatic vein orifice. In the right liver lobe graft, the end-to-end anastomosis was performed for corresponding portal veins, right hepatic arteries and right hepatic ducts. The duration of the operation was 16 h. The warm and cold ischemia time of the right liver graft was 2 and 50 min, respectively. The time interval between donor liver implantation and reperfusion was 55 min. The blood loss of the recipient was 2000 mL.

Post-operative outcome

The patient was on mechanical ventilation for 178 h and regained consciousness 80 h later. She was on continuous renal replacement therapy for 72 h and treated with triple medication of tacrolimus plus mofetil mycophenolate and prednisone for immunosuppression. The combination of anti-HBV immunoglobulin (HBIG) and entecavir was initiated

Table 1 Important parameters of the donor and the recipient

	Height (cm)	Weight (kg)	Estimated standard liver volume (mL)	CT measured liver volume (mL)	Maximum donated liver volume (mL)	Minimum liver volume needed (mL)	Actual donated liver volume (mL)	GRWR	GW/ESLV[1]
Recipient	166	75.0	1306.05	-	-	750	-	0.80	49%
Donor	165	62.5	1277.55	1334.124	821.809	350	600	-	50%

[1]Estimated standard liver volume (ESLV) = 706.2 × body surface area (m^2) + 2.4, reference[9]; "-": Unmeasured; CT: Computed tomography; GW: Graft weight; GRWR: Graft-to-recipient body weight ratio.

Table 2 Changes of programmed liver biopsy and hepatitis B virus-M in both donor and recipient liver lobes

Time point	Serum HBV-M		Degree of hepatocyte necrosis		Hepatic tissue HBV-M	
	Donor	Recipient	Donor liver	Recipient residual liver	Donor liver	Recipient residual liver
Preoperation	(-)	HBV-DNA(+)[1], HBsAg(+), HBeAg(+), HBcAg(+)	0%	-	HBsAg(-) HBcAg(-)	HBsAg(+++) HBcAg(+++)
Intraoperation	(-)	HBsAg(+)	Few	90%	HBsAg(-) HBcAg(-)	HBsAg(+++) HBcAg(+++)
Postoperation 10 d	(-)	HBV-DNA(-)[2], HBsAg(+)	0%	10%	HBsAg(-) HBcAg(+)	HBsAg(+) HBcAg(-)
Postoperation 30 d	(-)	HBV-DNA(-)[2], HBsAg(+)	0%	0%	HBsAg(-) HBcAg(-)	HBsAg(-) HBcAg(-)
Postoperation 90 d	(-)	HBV-DNA(-)[2], HBsAg(+)	0%	0%	HBsAg(-) HBcAg(-)	HBsAg(+) HBcAg(-)
Postoperation 180 d	(-)	HBV-DNA(-)[2], HBsAg(+)	0%	0%	HBsAg(-) HBcAg(-)	Fail to sample
Postoperation 1 yr	(-)	HBV-DNA(-)[2], HBsAg(+)	0%	0%	HBsAg(-) HBcAg(-)	HBsAg(-) HBcAg(-)
Postoperation 2 yr	(-)	HBV-DNA(-)[2], HBsAg(+)	-	-	-	-
Postoperation 3 yr	(-)	HBV-DNA(-)[2], HBsAg(+)	-	-	-	-
Postoperation 4 yr	(-)	HBV-DNA(-)[2], HBsAg(+)	-	-	-	-
Postoperation 5 yr	(-)	HBV-DNA(-)[2], HBsAg(+)	-	-	-	-

Hepatitis B virus (HBV)-DNA was detected quantitatively: [1]2.06×10^7copies/mL, [2]$< 5 \times 10^2$ copies/ mL. -: Undetected; HBsAg: Hepatitis B surface antigen; HBeAg: Hepatitis B e antigen; HBcAg: Hepatitis B core antibody.

for anti-HBV treatment. The patient recovered well without any complications and was discharged on the 40th day after operation. The donor also recovered well without any complications and was discharged on the 15th day after operation.

The patient was followed up regularly according to the China Liver Transplant Registry hosted in Hong Kong University. Indices of blood flow hemodynamics of the left and right liver lobes, liver function, blood biochemistry, HBV-M, and serum drug concentration were detected and programmed liver biopsy was performed. The programmed liver biopsy enabled us to know the dynamic changes of hepatic regeneration and HBV status in both the donor's graft and the recipient's residual native liver lobe. The pathological and immunohistochemical staining results are shown in Table 2 and Figures 1-10. The donor liver graft presented a typical pathological change after implantation. The recipient residual liver regenerated rapidly after operation and more than 90% of the necrotized hepatocytes regenerated within two weeks. The liver function, clinical signs and symptoms improved significantly. Color Doppler flow image study revealed transient competing influence of the portal vein blood flow between the donor and the recipient portal vein branch, which were stabilized one month after the surgery, while the blood flow competing influence between the right and left hepatic arteries was unremarkable. CT scanning was performed one month, six months and 12 mo respectively after operation and revealed that the portal vein, hepatic artery as well as implanted liver lobe had fused well with recipient native hepatic lobe (Figure 11). Until now, the recipient has been living for more than 78 mo free of any complications.

DISCUSSION

Up to date, there has been no report of adult APOLDLT for rescuing patients with postpartum acute hepatic failure following severe HBV infection. In the treatment of acute hepatic failure by liver transplantation,

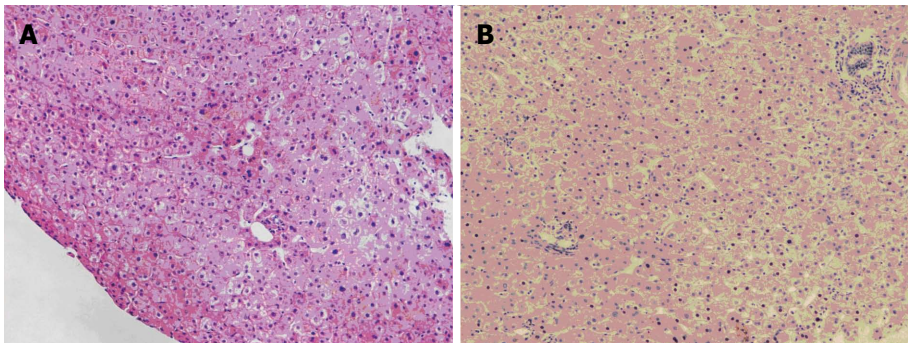

Figure 1 Liver biopsy prior to liver donation. A: Normal liver structure (HE, × 100); B: No hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 100).

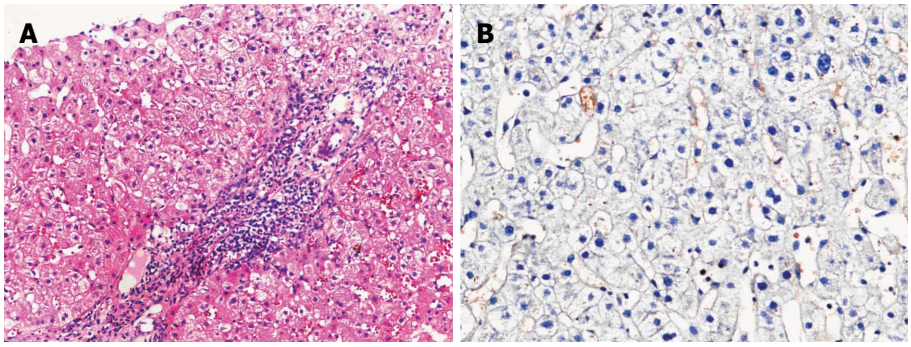

Figure 2 One month after liver transplantation. A: Mild hepatitis with portal inflammation (HE, × 100); B: Immunohistochemical staining of cytoplasms for hepatitis B core antibody (DAB, × 100).

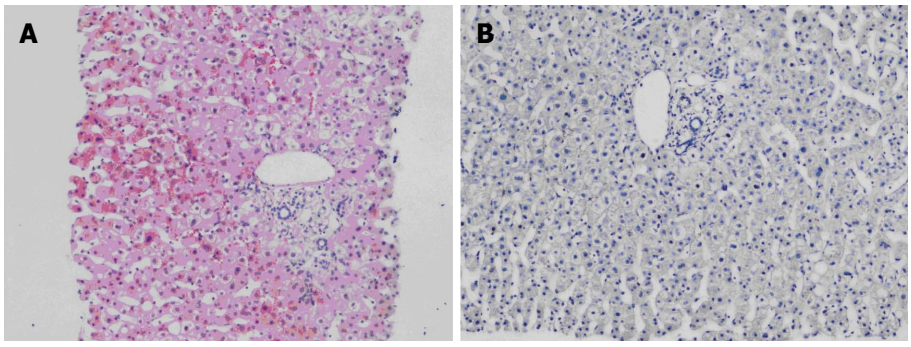

Figure 3 Three months after liver transplantation. A: Return to almost normal liver structure (HE, × 40); B: No hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 40).

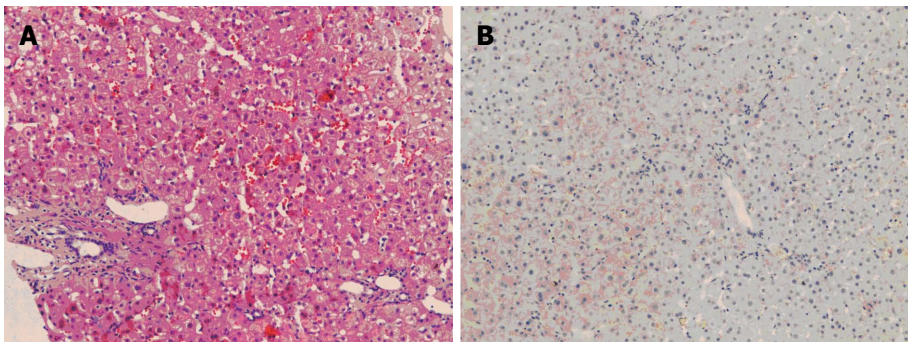

Figure 4 Six months after liver transplantation. A: Almost normal liver structure with a little matrix deposition in portals (HE, × 100); B: No hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 100).

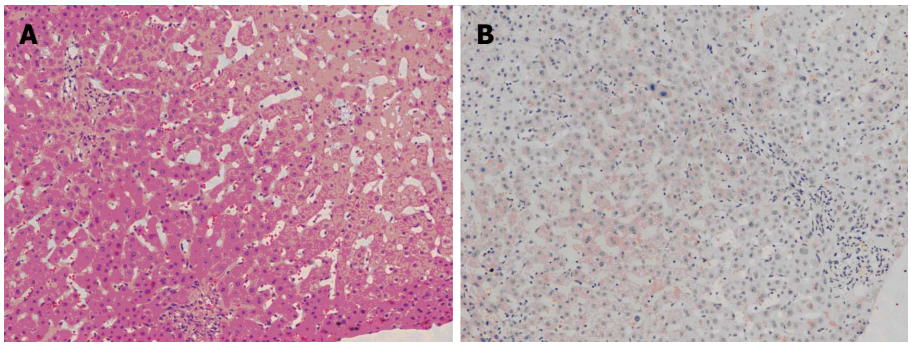

Figure 5 One year after liver transplantation. A: Almost normal liver structure (HE, × 100); B: No hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 100).

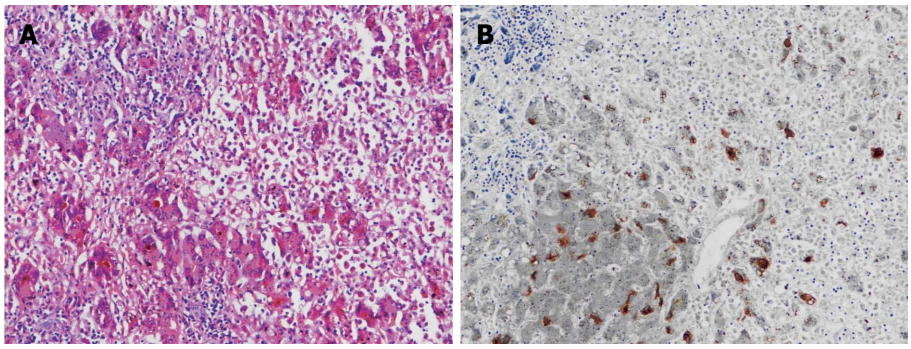

Figure 6 Histology of recipient liver. A: Acute severe hepatitis with massive necrosis (HE, × 100); B: Hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 100).

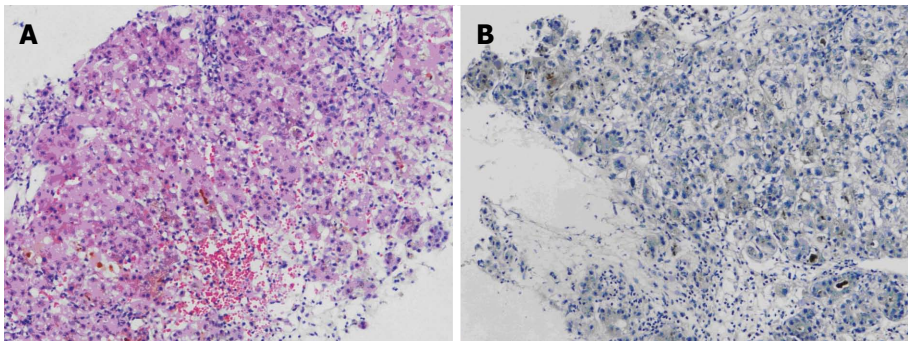

Figure 7 Histology of recipient residual left liver one week later. A: Acute hepatitis with less massive necrosis (HE, × 40); B: Hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 40).

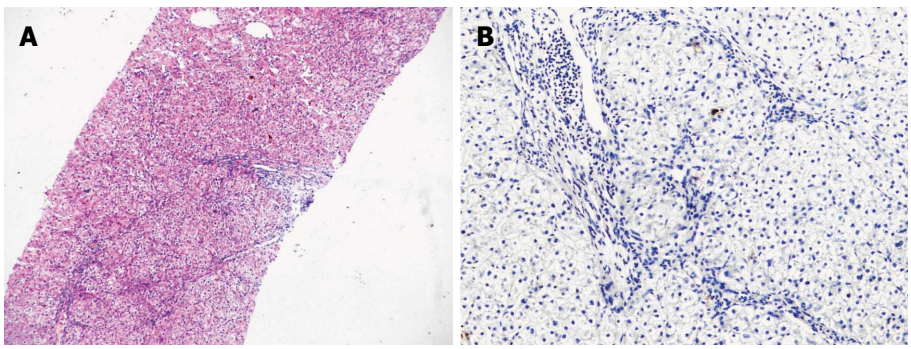

Figure 8 Histology of recipient residual left liver one month later. A: Restored hepatic structure with several fine fibrous septa (HE, × 40); B: No hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 100).

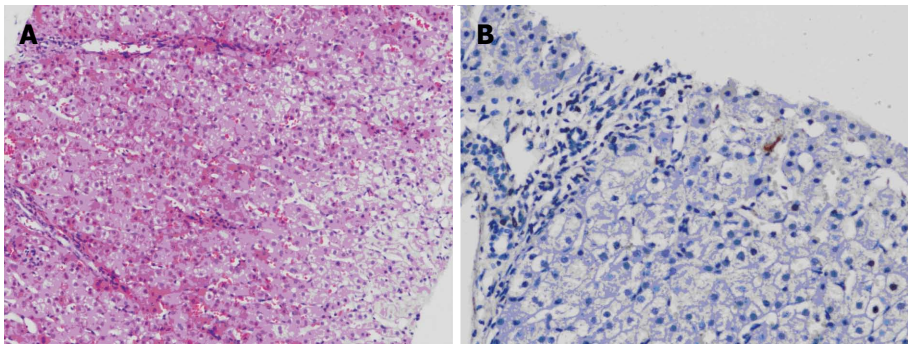

Figure 9 Histology of recipient residual left liver three months later. A: Almost normal liver structure (HE, × 40); B: Hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 40).

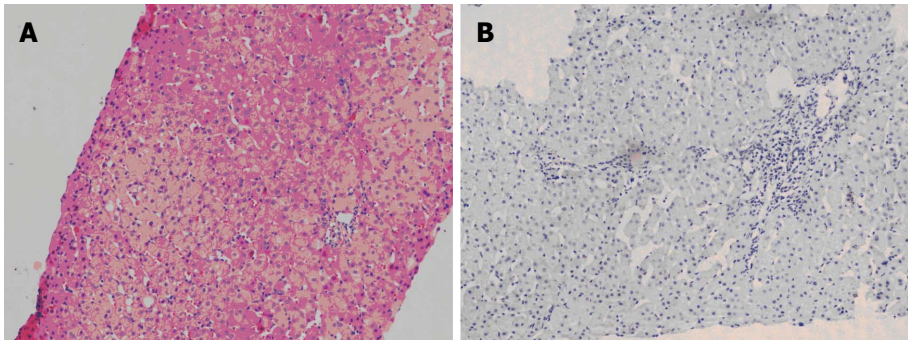

Figure 10 Histology of recipient residual left liver one year later. A: Normal liver structure (HE, × 40); B: No hepatocyte immunohistochemical staining for hepatitis B surface antigen (DAB, × 40).

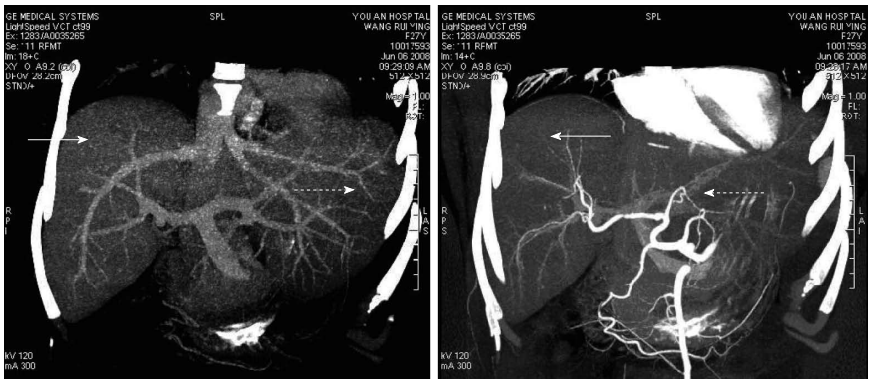

Figure 11 Computed tomography scan of fused liver one month after operation and 3-D reconstruction of hepatic vessels. Donated right liver graft (solid arrows); Residual native left liver lobe (dotted arrows).

compared with the conventional living related and cadaver liver transplantations, APOLDLT makes not only the regeneration of the residual liver, but also the feasibility of discontinuation of immunosuppressors possible[7]. Moreover, due to the timeliness of living related donor liver, the procedure can be performed in the treatment of acute liver failure[10]. The graft-to-recipient weight ratio (GRWR) in this case was 0.8, lower than the criteria of GWRW $\geqslant$ 1.0. Therefore, we selected the APOLDLT procedure in order to avoid the small-for-size syndrome. It consequently proved that the implanted donor liver graft promoted the rapid regeneration potential of the residual necrotized liver, and the regenerated residual native liver supported mutually the implanted liver graft to resume its functions. Postoperative CT scan findings and biochemical indices revealed the anatomically well fused donor and recipient liver lobes with coordinated functions (Figure 11).

HBV markers in the serum of the recipient and in the hepatic tissues of both liver lobes changed rapidly under combined entecavir and HBIG prophylactic protocol, with the features as follows: (1) HBV virus load in recipient serum decreased rapidly from 2.06 × 10^7 copies/mL to < 5 × 10^2 copies/mL within nearly two weeks; (2) the donor liver graft presented with detectable HBcAg

positive transiently, which was eliminated in a short time (< 30 d); (3) HBV-M in the recipient residual native left liver lobe was eliminated rapidly; and (4) HBsAg was persistently present in the recipient serum with the HBV DNA concentration of less than 5×10^2 copies/mL. The latest programmed liver biopsy showed that HBV markers by immunohistochemical stainning in both the donor liver graft and recipient residual native left liver lobe were all negative. These protective mechanisms against HBV are still unclear, and were postulated to be related to the protective period of the newly implanted liver as reported by Lu *et al*[11] and Dai *et al*[12]. Although HBV markers in recipient serum decreased by a magnitude of 10^5 and disappeared in native residual liver, demonstrating that the HBV elimination may be achieved under short-term effective antiviral therapy protocol in this case, its long-term progression remains to be determined. We must admit, from a long-term perspective, the viral carrier status of the recipient would significantly influence the fate of the recipient and the donor liver graft implanted as well as the native residual liver. Therefore, in contrast to the acute liver failure not caused by HBV, HBV carrier status of native residual liver and HBV allograft re-infection are not only the major concerns of immunosuppressive agent weaning as mentioned previously, but also the key factors deciding long-term survival of both living allograft and recipient, which remain a great challenge to clinicians and need to be further clarified by future follow-up studies. However, despite the concerns mentioned above, APOLDLT is still a life-saving modality for rescuing patients with high-risk acute liver failure following HBV infection without available donor and hence is recommended under standardized antiviral therapy protocol.

COMMENTS

Case characteristics

A 26-year old female patient diagnosed as hepatitis B virus (HBV) carrier for the past four years had been experiencing menolipsis for more than eight months and paroxysmal abdominal pain for one hour.

Clinical diagnosis

The patient was diagnosed with $G_3P_1G_{33}^{+3}$ left occiput anterior preterm labor, acute severe HBV infection, hepatic encephalopathy and coma.

Differential diagnosis

Alcoholic liver disease, hepatic cirrhosis, primary carcinoma of liver and hepatic abscess.

Laboratory diagnosis

Hepatitis B surface antigen (HBsAg)(+), hepatitis B e antigen (+), hepatitis B core antibody (+) with a HBV-DNA load of 2.06×10^7 copies/mL, hepatitis C virus (-); prothrombin time 26.3 s, prothrombin time activity percentage 29%, prothrombin international normalized ratio 2.05; alanine transaminase 3019.1 IU/L, aspartate aminotransferase 15.6 IU/L, total serum bilirubin 174.4 μmol/L, conjugated bilirubin 78.2 μmol/L and blood ammonia 154 μg/dL.

Imaging diagnosis

Computed tomography showed liver augmentation.

Pathological diagnosis

Acute severe hepatitis with massive necrosis, and hepatocyte immunohistochemical staining for HBsAg positive.

Treatment

Auxiliary partial orthotopic living donor liver transplantion (APOLDLT) was performed under general anesthesia.

Related reports

There have been less than 100 cases of adult APOLDLT reported worldwide; but no report of adult APOLDLT for rescuing patients with postpartum acute hepatic failure following severe HBV infection.

Term explanation

Orthotopic living donor liver transplantion refers to the surgical procedure that preserves the partial liver of the recipient and the partial liver of the donor implanted orthotopically into the recipient.

Experiences and lessons

APOLDLT is a life-saving modality for rescuing patients with high-risk acute live failure following HBV infection without available donor and hence is recommended under standardized antiviral therapy.

Peer-review

The authors have described adult auxiliary partial living donor liver transplantation on a case of postpartum acute liver failure following HBV infection, and showed that APOLDLT is a life-saving modality for rescuing patients with high-risk acute liver failure following HBV infection without available donor and hence is recommended under standardized antiviral therapy protocol.

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