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Living donor liver transplantation without the use of blood products

We report on two patients who presented with unresectable hepatocellular carcinoma complicating hepatitis B liver cirrhosis. After evaluation, both patients were accepted for liver transplantation. Being aware of the scarce availability of cadaveric liver grafts and the long waiting time, family members volunteered to be donors for the two patients. Living donor liver transplantation using right lobe liver grafts, including the middle hepatic vein, was subsequently performed without the use of blood products in both the donors and recipients. All involved recovered uneventfully from their respective operations.

Introduction

Orthotopic liver transplantation (OLT) is typically associated with a large volume of blood loss, although transfusion requirements have gradually decreased with refinements in surgical and anaesthetic techniques. There are even a few reports in the literature of successful liver transplantation without transfusion of red cells in Jehovah’s witnesses. In recent years, living donor liver transplantation (LDLT) using right lobe liver grafts has been frequently employed, especially in countries where there is scarce or no supply of cadaveric liver grafts. However, LDLT can be technically demanding in both the donor and recipient operations. We report two cases in which successful LDLT using right lobe liver grafts was performed without the use of blood products in both the donors and recipients.

Case reports

Case 1

A 51-year-old Chinese man had a history of chronic hepatitis B–related liver cirrhosis and splenectomy for thrombocytopenia in 1995. He also had a history of left lateral segmentectomy for a 2 cm hepatocellular carcinoma (HCC) in 1998. Histological examination of the resected specimen showed a 2 cm HCC with lymphovascular permeation (TNM stage II disease). The postoperative course was complicated by a single episode of gastrointestinal bleeding from oesophageal varices, which was controlled by injection sclerotherapy. Thereafter, he was maintained on oral propranolol.

Two years after hepatic resection, a 7 cm HCC recurrence was detected in the right lobe of the liver on computed tomography (CT). The patient’s clinical condition was explained in detail to his family members who, after discussing the effectiveness and limitations of various treatment options, including local ablative therapy, regional chemoembolisation, and liver transplantation, opted for the latter. After evaluation, the patient was put on the transplant recipient waiting list. Being aware of the scarce availability of cadaveric liver grafts and a long waiting time of more than 2 years, the patient’s wife, aged 44 years, volunteered...
to be a liver donor. The patient’s family members were not solicited for liver donation, and the decision to undertake LDLT was based entirely on the wife’s voluntary intent. An independent psychological assessment performed by a clinical psychologist confirmed that her decision to donate was made without coercion. Both the husband and wife were informed of the possible morbidity and mortality of the donor and recipient operations. Donor evaluations, including blood biochemistry, CT with volumetric measurement, and hepatic angiography, confirmed that the wife was indeed suitable to be a liver donor. At the time of the operation, laboratory studies of the recipient showed a platelet count of 67 x 10^9/L (normal range, 150-450 x 10^9/L), a haemoglobin level of 145 g/L (normal range, 140-175 g/L), an albumin level of 30 g/L (normal range, 35-50 g/L), a bilirubin level of 15 µmol/L (normal range, 5-21 µmol/L), an aspartate aminotransferase level of 128 U/L (normal range, 20-48 U/L), an alanine aminotransferase level of 105 U/L (normal range, 10-40 U/L), an alphafoetoprotein (AFP) level of 43 ng/mL (normal range, 0-20 ng/mL), and a prothrombin time of 12.8 seconds (normal range, 10-13 seconds).

The donor operation began with a bilateral subcostal incision with upward midline extension. Operative cholangiography was performed with fluoroscopy to outline the biliary anatomy. The right hepatic artery and right portal vein were isolated at the liver hilum. Parenchymal transection was performed to the left of the middle hepatic vein using an ultrasonic dissector without portal vascular inflow clamping. When the recipient’s total hepatectomy was complete, the donor’s right lobe liver graft, together with the middle hepatic vein, was harvested and back table perfusion with University of Wisconsin solution started. The intra-operative blood loss was 500 mL and the donor did not require any blood product transfusion. Her postoperative course was uneventful and she was discharged home on the seventh day after the operation.

The recipient operation also began with a bilateral subcostal incision with upward midline extension. Marked adhesion relating to two previous upper abdominal operations was encountered. Total hepatectomy was performed with preservation of the hepatic arterial branches, left and right portal veins, and stumps of the hepatic veins. However, intra-operative cell salvage was not employed because of the presence of malignancy. The liver graft was implanted to the orthotopic position, with hepatic venous anastomoses of the right hepatic and middle hepatic veins being followed by right portal vein anastomosis. The graft began functioning immediately on reperfusion, as evidenced by bile production, and was soft in consistency. Hepatic arterial anastomosis was performed using microvascular techniques. Doppler ultrasound showed patency and normal pulsatile waveforms in the hepatic venous anastomoses. Roux-en-Y hepatico-jejunostomy was constructed to the right hepatic duct. The intra-operative blood loss was 800 mL and the total fluid replacement was 3500 mL. The recipient remained haemodynamically stable throughout the operation and did not require any blood product transfusion. His postoperative immunosuppressive therapy consisted of steroids and tacrolimus. He was also put on oral lamivudine for hepatitis B prophylaxis. He was extubated on postoperative day 1, resumed a hospital diet on postoperative day 2, and was discharged home on postoperative day 17. Pathological examination of the liver explant confirmed the preoperative radiological diagnosis and showed macronodular cirrhosis of the liver, with a 7 cm moderately differentiated HCC.

Case 2

A 49-year-old Chinese man was attending the surgical clinic for the management of multifocal HCC complicating hepatitis B–related liver cirrhosis. He had been a known hepatitis B carrier since 1995 and had a slightly raised AFP level of 26 ng/mL. Computed tomography demonstrated three foci of HCC inside a cirrhotic liver; the largest one being 2.5 cm in diameter. Regional chemoembolisation was given once. However, unsatisfactory treatment was evident on subsequent CT, which demonstrated incomplete lipiodol staining and growing tumours. The patient’s clinical condition was explained in detail to his family members who, after discussing treatment options, which included continuation of regional chemoembolisation and liver transplantation, opted for transplantation. After evaluation, the patient was put on the transplant recipient waiting list. Being informed of the scarce availability of cadaveric liver grafts and a long waiting time of more than 2 years, the patient’s son, aged 22 years, volunteered to be a liver donor. The family members were not solicited for liver donation, and the decision to undertake LDLT was based solely on the son’s voluntary intent. An independent psychological assessment performed by a clinical psychologist confirmed that his decision to donate was made without coercion. Both the father and son were informed of the possible morbidity and mortality of the donor and recipient operations. Donor evaluations, including blood biochemistry, CT with volumetric measurement, and hepatic angiography, confirmed that the son was indeed suitable to be the liver donor. At the time of the operation, laboratory studies of the recipient father showed a platelet count of 234 x 10^9/L, a haemoglobin level of 132 g/L, an albumin level of 32 g/L, a bilirubin level of 13 µmol/L, an aspartate aminotransferase level of 34 U/L, an alanine aminotransferase level of 45 U/L, an AFP level of 7 ng/mL, and a prothrombin time of 12.3 seconds.

The donor operative procedure was essentially the same as that reported in the case 1 donor. The intra-operative blood loss was 250 mL and the donor did not require any blood product transfusion. His postoperative course was uneventful and he was discharged home on the sixth day after the operation.

The recipient operative procedure was also essentially the same as that reported in the case 1 recipient. Again,
immediate graft function was noted. The intra-operative
blood loss was 1300 mL and the total fluid replacement
was 7500 mL. The recipient remained haemodynamically
stable throughout the operation and did not require any blood
product transfusion. His postoperative immunosuppressive
therapy also consisted of steroids and tacrolimus. He was
also put on oral lamivudine for hepatitis B prophylaxis.
He too was extubated on postoperative day 1, resumed a
hospital diet on postoperative day 2, and was discharged
home on postoperative day 17. Pathological examination
of the liver explant confirmed the preoperative radiological
diagnosis and showed liver cirrhosis, with three foci of
moderately differentiated HCC.

Discussion

Following its introduction more than a decade ago, LDLT
has significantly eased the crisis of donor organ shortage
for liver transplantation. First performed successfully in
children,13 application of this innovative technique has recently been extended to adults through the use of a
right lobe graft.14 It is now the main source of liver grafts
in areas where there is scarce or no supply of cadaveric
grafts.

Donor safety is of prime importance during LDLT.9 In
particular, minimising blood loss during donor hepatectomy
minimises the risk of postoperative morbidity due to
hepatic dysfunction, as well as the risk of transmissible
disease due to contaminated blood product transfusion.
Since the establishment of the liver transplant programme
in our institute in 1991, hepatectomy has been performed
for 90 donors. To date, none has required any blood
product transfusion, with the exception of a single patient
who had anaemia from thalassaemia and received one unit
of homologous blood transfusion.

Orthotopic liver transplantation is typically associated
with a large volume of blood loss. Bontempo et al16 reported
a median red cell transfusion requirement of 10 units in an
unselected liver transplant population. Fortunately, increased
understanding of coagulopathy and fibrinolysis,11 together
with improvements in surgical haemostasis using argon
beam coagulation and the introduction of intra-operative
cell salvage, have led to a reduced demand for blood prod-
uct transfusion.12 However, cell salvage is expensive and
requires relatively sophisticated equipment and trained
personnel to perform. Theoretically, disseminated intra-
vascular coagulation, adult respiratory distress syndrome,
and renal failure can arise from the reintroduction of fat
microemboli, denatured protein, free haemoglobin, cell
fragments, and platelet-leukocyte microaggregates into
the blood stream, although better designed studies have so
far failed to show a significant increase in these compli-
cations.15 Unfortunately, both our transplant recipients had
HCC and hence were not considered suitable candidates
for cell salvage because of fears of retransfusing exfoliated
cancer cells.

The timing of the procedure is particularly crucial. Be-
cause of the infrequent supply of cadaveric grafts at our
centre, patients put on the waiting list have to wait at least 2
years before they can have a transplant. It is our experience
that more than half of these candidates succumb to major
complications before a timely graft is available. In addition,
even if a transplant does eventually take place, the opera-
tion can be difficult because of extensive vascular adhesions
that have arisen as a result of repeated episodes of spontan-
eous bacterial peritonitis occurring in the interim. Both our
patients had HCC and, given their clinical conditions, it did
not seem appropriate to wait for cadaveric grafts to become
available. Living donor liver transplantation, however,
enabled early transplantation to take place, before decom-
pensation of liver function and associated coagulopathy
had occurred, thus allowing the operations to be done
successfully without the use of blood products.

In a recent meta-analysis of prospective, randomised,
controlled studies of pharmacological strategies designed
to decrease bleeding associated with cardiac surgery, ad-
ministration of aprotinin decreased the risk of allogenic
blood transfusion.17 The use of aprotinin to decrease trans-
fusion requirements in patients undergoing OLT is
supported by the results of a recent multicentre, randomised
study, although the effectiveness of this approach has
been challenged.16 Aprotinin is not routinely given to
patients undergoing liver transplantation at our centre, and
was not given to either of the two recipients reported here.

Meticulous surgical technique and haemostasis with
electrocautery and argon beam coagulation contributed
significantly to the avoidance of blood transfusion in the
two recipients described here. Maintaining haemostasis was
particularly important, since both patients had HCC and one
had a history of two previous upper abdominal surgeries.
Another major contributory factor was our increasing
experience with, and refinement of, the LDLT technique
using right lobe liver grafts.17 We placed great emphasis on
careful reconstruction of the right and middle hepatic vein
anastomoses, so that liver graft dysfunction and congestion
would not occur. Liver graft congestion increases bleeding
from the cut surface of liver and the hepatoduodenal area
due to unresolved portal hypertension. Excessive blood loss
during liver transplantation can result in unfavourable
outcomes, including cerebrovascular complications.18
Furthermore, perioperative transfusion has been found to
promote recurrence of HCC after hepatic resection and
result in shorter disease-free and overall survival.19,20 Avoid-
ance of blood product transfusion will thus be one of our
aims in future liver transplant operations.

Liver transplantation is a recognised treatment for HCC
in selected patients, and the survival results of those chosen
to undergo OLT for HCC are not inferior to those undergo-
ing OLT for non-malignant disease. Mazzaferro et al21
reported excellent disease-free and overall survival rates
of 92% and 85%, respectively, 4 years after OLT in 35
patients with a solitary HCC not exceeding 5 cm in diameter or no more than three tumours, with none greater than 3 cm in diameter. To justify the use of scarce cadaveric liver grafts in this population, many transplant centres have employed the Mazzaferrera criteria to select candidates for OLT. However, the same selection criteria should not be strictly applied to patients undergoing LDLT, as the grafts are ‘dedicated to the beloved’ of the donors. Moreover, because the recipients of LDLT are not competing with other recipients for cadaveric grafts, the survival results of LDLT for HCC should be compared to those in the absence of transplantation in any attempt to justify the technique. In fact, the Mazzaferrera criteria have been questioned in recent studies, and expanding the tumour size limits does not seem to have adversely affected survival rates. Yao et al., for example, reported excellent survival results of 90% and 75.2% at 1 and 5 years, respectively, in patients undergoing OLT for HCC ≤ 8 cm in size.

Although LDLT can be performed without the use of blood products in selected patients, this does not imply that it can or should be recommended for all patients with HCC. The efficacies and drawbacks of treatment options available should be discussed with potential donors and recipients, and ethical issues should be adequately addressed. Of paramount importance is a proper psychological assessment of the donor to assure appropriate voluntarism on their part. This informed consent must be gained before establishing the suitability of their liver for transplantation through the usual functional and radiological tests.

**Conclusion**

Living donor liver transplantation without the use of blood products still poses a major challenge, but can be achieved in selected patients, including those with HCC, provided the surgical technique and perioperative care are of a sufficiently high standard, and a timely graft is available.

**References**