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Living-related liver transplantation for fulminant hepatic failure in children

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Abstract Liver transplantation is increasingly accepted as a choice of treatment for fulminant hepatic failure (FHF) since it has been proved to significantly improve the survival rate in these patients compared with other therapeutic modalities. We have successfully performed a total of 76 living related liver transplantations (LRLT) three of which were for FHF. The first case was an 11-year-old boy with FHF due to an unidentified cause. He had required plasmapheresis a total of 24 times and haemofiltration to save his life before LRLT. He was transplanted with a left lobe (420 g) graft, calculated as 1.05% of his weight (40 kg). He recovered hepatic function uneventfully and was discharged from hospital after 7 weeks. The second case was a 13-year-old girl who developed FHF with grade III encephalopathy due to acute Wilson's disease, and was referred to us. She underwent LRLT with a left lobe graft (440 g), estimated as 0.95% of her weight (47 kg), which functioned well after surgery. The third case was a 13-year-old girl with grade II encephalopathy due to acute Wilson's disease. She was 27% obese with a body weight of 58 kg. She underwent LRLT with ABO blood group incompatibility with a left lobe (352 g), estimated as 0.80% of her weight (modified 44 kg). She was discharged with sensorimotor neuropathy due to vitamin B deficiency. The present results suggest that LRLT is feasible for FHF both clinically and ethically, and that a partial liver graft weighing around 1% of the recipient's weight can maintain the recipient's life. We limit the diagnostic indication for LRLT to chronic liver disease, since an urgent situation may affect a voluntary decision for the patient's parents to donate the partial liver. However, LRLT is thought to be an acceptable choice of treatment provided it is requested by the patient and family. Furthermore, it is a potential option for resolving the graft shortage in paediatric liver transplantation, being independent of cadaver donor availability.

Key words Living donors
Liver transplantation
Fulminant hepatic failure

Introduction

Fulminant hepatic failure (FHF) is a rare but serious clinical syndrome usually manifested by the acute onset of progressive jaundice, shrinking of the liver and hepatic coma [12]. The mortality rate from FHF in children has remained between 70 and 95%, depending on the cause of the disease and the age of the patient unless liver transplantation is performed [11]. Orthotopic liver transplantation has markedly decreased this mortality rate [1].

Living related liver transplantation (LRLT) has been introduced as an option among several therapeutic modalities to overcome the graft shortage in paediatric liver transplantation [2, 8].

Materials and methods

Between June 1990 and October 1993 a total of 76 LRLT were performed on children (ranging from 3 months to 17 years) of age, with end-stage liver disease (Table 1). Donors were selected solely from among parents of the recipients. Baseline immunosuppression consisted of tacrolimus and low-dose steroids. The patient survival was 90% (53/59) in elective cases and 7% (12/17) in emergency cases. Three of 17 emergency cases received three LRLTs for FHF. An 11-year-old boy (case 1)* without previous liver disease developed grade III encephalopathy with marked jaundice 16 days after the initial onset of symptoms. The cause of FHF was undetermined. Continuous venous haemofiltration, plasmapheresis (×24) and medical treatment prevented encephalopathy progression. LRLT was performed 2 months after the onset of encephalopathy.

A 13-year-old girl (case 2) with acute Wilson's disease developed grade III encephalopathy 8 days after the onset of jaundice. She was treated with plasmapheresis (×12) and underwent LRLT 4 months after the initial onset of encephalopathy. A 13-year-old girl (case 3) with acute Wilson's disease showed haemolysis and grade II encephalopathy 5 days after the initial onset of jaundice. LRLT was performed using an incompatible graft (B → A). Table 2 shows the clinical and biochemical data of all three cases. Table 3 shows the values of ceruloplasmin and serum and urinary copper for case 2 and case 3 with Wilson's disease.

Table 1 Number and diagnosis of patients receiving LRLT (June 1990 to October 1993)

Biliary atresia	62 (1*)
Alagille syndrome	1
Intrahepatic cholestasis	2
Liver cirrhosis	3
Wilson's disease	2
Protoporphyria	1
Budd-Chiari syndrome	2
Fulminant liver failure	1
Glycogen storage (IV)	1
Thyrosinaemia	1
Total	76

* Case 1, see above

Table 3 Cerulosplasmin, and serum and urinary copper

	Patient 2	Patient 3
Serum copper (μg/dl)	71	143
Urinary copper (μg/day)	1000–5000	4000–8000
Ceruloplasmin (mg/dl)	33	10.0
Haemolysis	+	+ + +
Kayser-Fleischer ring	+	+

Results

The ratio of the graft weight (440, 440, 320 g) to the recipient body weight (GRBWR) was 1.05%, 0.94% and 0.61%, respectively. The patients were discharged 47, 27 and 62 days, postoperatively, respectively, with a primary functioning graft. The postoperative course was uneventful in case 1 and case 2, but case 3 developed sensorimotor neuropathy due to a marked decrease in vitamin B. Follow-up after 1 year showed normal liver function and no recurrence of original disease.

Discussion

Liver transplantation is a well-established procedure for FHF. The timing of liver transplantation in FHF is critical. If the decision is too early, some livers whose lesions are reversible may be replaced unnecessarily. On the other hand, the decision has to be taken before the development of major complications, particularly cerebral oedema and sepsis. However, no guarantee can be given that a donor will be available when required.

LRLT has developed as an option among several therapeutic modalities to overcome the graft shortage [2, 8]. The use of the living donor graft can make the

Table 2 Clinical and biochemical data

Patient	Age (years)	Cause	Bilirubin (mg/dl)	AST (U/l)	Creatinine (mg/dl)	Prothrombin time (s)
1	11	Unknown	24.5	89	1.0	20.0
2	13	Wilson	17.8	128	0.5	21.7
3	13	Wilson	27.0	88	0.6	27.8

timing of liver transplantation independent upon the patient's condition with FHF.

Essential factors in LRLT are volunteer spirit, donor safety and the advantages of the procedures [2, 8, 9]. To confirm the volunteer spirit, we obtain two informed consents at intervals after explaining the risks and benifits of LRLT. And finally, a member of the Ethics Comittee of Kyoto University approves the informed consent.

The time to obtain informed consent in urgent transplantation is limited owing to the emergency nature of the procedure. Many procedures such as blood exchange, plasmapheresis, haemofiltration and dialysis have been performed as interium measures in liver transplantation to prevent disease progression and stabilize the patient's condition. These treatments provide valuable time to obtain informed consent and to make surgical preparations.

It is important to estimate the lower limit of liver graft volume that will tolerate the transplantation procedures and meet the recipient's metabolic needs [7]. In liver transplantation from a cadaveric donor the minimum small-for-size liver successfully transplanted in a large host is, to the present author's knowledge, 41% of the normal liver weight of a healthy individual of the same size, age and sex as the recipient [13].

A left lobe graft was used in 7 of 76 recipients (the body weight ranged from 36.4 kg to 58.0 kg) who included three patients with FHF. The ratio of graft weight to the recipient body weight was from 0.61 to 0.94% (average 0.83%) in seven patients using a left lobe. The 13-year-old girl with acute Wilson's disease showed the smallest ratio of 0.6%, but the patient's ideal body weight should be considered to evaluate the size matching between the graft weight and recipient body weight [5]. The modified ratio was 0.80% taking into account the obesity. The minimum small-for-size graft required in a large host for successful LRLT is not known.

An ABO-incompatible graft was used in three patients with FHF; such grafts have been associated with an increased incidence of severe rejection, arterial thrombosis and cholangitis [4, 10]. Our protocol to deal with ABO-incompatible LRLT is that blood exchange or plasmapheresis is performed to decrease the preformed ABO antibody titer and after operation. In our ten ABO-incompatible cases, the incidence of rejection was 10% and no such association was found.

LRLT has definite advantages with respect to graft viability, histocompatibility, evaluation of size matching and selection of timing of LRLT, and was successfully performed for FHF in children [3, 6].

It is concluded that LRLT allows great flexibility in the management of transplantation in children with FHF and is an option for overcoming the graft shortage in urgent cases.

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