Table 1. Clinical characteristics of the first donors and the first and second recipients

Case no.	1st donor		1st recipient			2nd recipient			Body weight (kg)	Operation time	CIT (min)	WIT (min)	GRWR (%)	Follow-up (months)	Complication
	Donor	Graft	Indication	Age at LDLT	Gender	Indication	Age at DLT	Gender							
1	Father	LLS	MSUD	1 yr	F	PC deficiency	1 yr 11 months	F	9.5	7 h 21 min	237	33	2.57	16	None
2	Mother	LLS	MSUD	3 yr 7 months	M	BA	2 yr 4 months	M	11.3	12 hr 30 min	350	26	3.52	9	None
3	Mother	LLS	MSUD	1 yr 3 months	M	FH	2 yr 10 months	F	13	5 hr 3 min	252	23	1.64	8	None

postoperative course was uneventful except for acute cellular rejection. She was discharged on postoperative day 68 without any surgical complications. One yr and four months after the LD-Domino LT, the patient's PC activity was maintained at more than 80% and she has since remained symptom free.

Case 2

A two-yr and four-month-old boy presented with jaundice and white feces. At five months of age, he was diagnosed with BA and the Kasai procedure was performed. However, his clinical condition did not improve and he exhibited growth failure, repeated cholangitis, and progressive esophagus varix with a pediatric end-stage liver disease score of 17; therefore, the patient was listed for LT. Because his father had disk herniation and was under the treatment for a gastric ulcer and his mother had repeated episodes of pyelonephritis, he was on the DDLT waiting list. However, because he was considered to be a low priority on the waiting list, LD-Domino LT was taken into account as an option. The operative finding at LD-Domino LT revealed severe adhesion. The operation employed the removal of multiple intestinal adhesions, which was achieved with synechiotomy. The HVs were exteriorized as far as possible in the native liver parenchyma using a CUSA (Fig. 1a). The RHV, MHV, LHV, and superficial vein were sutured together by venoplasty at the back table, and the single cuff of the HVs was anastomosed to the IVC by joining the orifices (Fig. 1b). PV anastomosis was performed with the branch patch technique. A sufficient hepatopetal flow was obtained following the devascularization of the collateral vessels. Because the RHA of the first recipient was branched from the SMA, two arterial anastomoses were required in the second recipient. The first recipient's LHA and RHA were directly anastomosed to the second recipient's LHA and posterior RHA, respectively, because of a suitable orifice diameter. A new Roux-en-Y anastomosis was employed for biliary reconstruction. Immunosuppressive treatment was initiated with tacrolimus and low-dose steroids. The patient was discharged on postoperative day 31 without any surgical complications and was found to be doing well nine months after the LD-Domino LT.

Case 3

A two-yr and 10-month-old girl presented with cutaneous xanthomas on the wrists, elbows, and ankles (Fig. 2a). She suffered from high TC

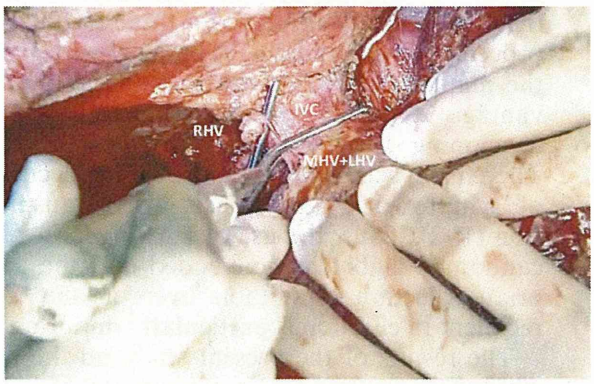
Table 2. Lipid profile in case 3 showing levels at baseline prior to any treatment; on maximal lipid-lowering drug and dietary therapy; and after liver transplantation without lipid-lowering drug therapy

			Postoperative day					
mg/dL	No treatment	On medication	Liver transplantation	1	7	30	90	180
TC (125–240)	1092	735	239	246	115	164	201	201
HDL-C	49	21	–	7	31	47	57	50
LDL-C (70–139)	975	732	–	230	68	100	129	135
TG (32–237)	129	60	–	19	87	223	70	52

Table 3. Amino acid levels before and after DLT

		Case 1						Case 2					Case 3			
Amino acids	Normal range (nmol/mL)	Before DLT	After 1M	After 3M	After 6M	After 9M	After 12M	Before DLT	After 1M	After 3M	After 6M	After 9M	Before DLT	After 1M	After 3M	After 6M
Leucine	80.9–154.3	96.8	113.8	107.3	87.3	86.9	81.1	139.0	102.2	76.3	71.7	90.7	120.5	132.7	154.7	143.8
Isoleucine	41.3–84.9	50.3	68.6	59.9	50.8	51.7	43.4	79.4	55.8	47.4	37.5	55.2	71.7	85.9	100.4	89.3
Valine	158.4–287.7	197.6	156.8	166.8	174.8	175.5	185.6	267.8	219.4	165.7	179.5	217.7	240.9	265.5	344.4	291.2
Alloisoleucine	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

a



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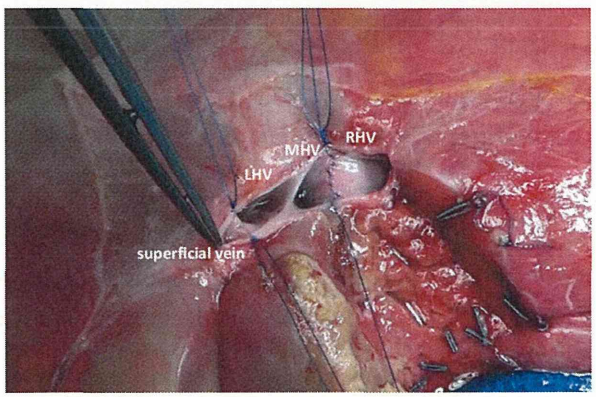
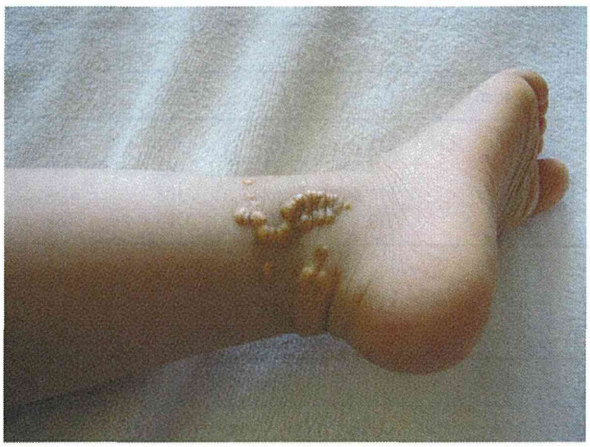


Fig. 1. (a) The HVs were exteriorized as far as possible using a CUSA. (b) The RHV, MHV, LHV, and superficial vein were sutured together to create a single cuff by venoplasty on the back table.

levels (>900 mg/dL) and was treated for hypercholesterolemia at one yr and four months of age. Sequencing of the LDL-R gene identified two mutations (c.418G>A and p.E119K/c.IVS12 + 2T>C). The LDL-R activity of the patient was 0%. Due to the patient's clinical history, she was diagnosed with compound heterozygous FH and was treated with a low-fat diet and medication. She had persistent severe hypercholesterolemia and her skin lesions enlarged. However, she showed no findings of coronary artery disease according to echocardiography and coronary vessel angiography. In addition to a cholesterol-restricted diet, medications including statins, cholesterol absorption inhibitors, and cholesterol dissimilation accelerators were administered. Despite the medications, her general condition was unresponsive and the TC level could not be controlled. Her parents had been evaluated as possible donors for LT, but were eventually excluded because they were heterozygous for FH and had low LDL-R activities (51% and 43%, respectively). For this reason, she was on the DDLT waiting list. The patient was selected to receive LD-Domino LT because of physical size matching to the first recipient on our waiting list. LD-Domino LT was performed at two yr and 10 months of age. The HVs were exteriorized as far as possible in the native liver parenchyma using a CUSA in order to create a longer vascular pedicle in the second recipient. The RHV, MHV, and LHV were sutured together by venoplasty at the back

a



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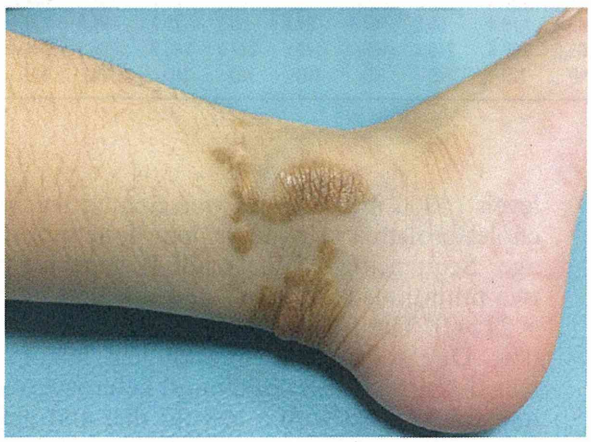

Fig. 2. Cutaneous xanthomas. Appearance at diagnosis time (a) and after six months from liver transplantation (b).

table, and the single cuff of the HVs was anastomosed to the IVC by joining the orifices. PV anastomosis was performed with the branch patch technique. Because the RHA of the first donor was branched from the SMA, along with a sufficient length, the GDA was ligated and the CHA was dissected in the first recipient. The first recipient's CHA was anastomosed to the second recipient's CHA. A new Roux-en-Y anastomosis was employed for biliary reconstruction. Within one day of LT, the plasma LDL-C level significantly decreased to 239 mg/dL and the lipid profile promptly normalized (Table 2). Her immunosuppressive protocol was the same as that of cases 1 and 2. A histological examination of the explanted liver showed low lipid content with oil red O staining. The patient's postoperative course was uneventful, and on postoperative day 19, she was discharged. Over time, the patient improved and the cutaneous xanthomas gradually decreased within six months with average LDL-C levels of 120 mg/dL (Fig. 2b). Subsequent liver ultrasounds were normal with no visible steatosis.

Discussion

This case series highlighted two important clinical issues: (i) LD-Domino LT is technically complicated compared with deceased donor Domino LT; however, LD-Domino LT is a safe and feasible therapeutic option for expanding the donor pool through the use of technical refinement in the reconstruction of the second recipient and 3D-CT to determine the dividing site of the vessels of both recipients preoperatively between two institutions. Using a living donor offers advantages for making a satisfactory image assessment and preparing for operation. (ii) DLT using the whole liver from a pediatric patient with MSUD can be effective in a pediatric patient with proper physical size matching.

DLT was first performed in 1995 in Portugal as a strategy for addressing the disproportionate supply of deceased organ donors and the rising waiting list for DDLT (2). The latest update of the DLT registry displayed a total of 1085 DLT procedures performed with patients with FAP as the main donors (2). However, the main disadvantage of using a FAP donor is the risk of developing amyloidosis in the DLT recipient. There have been several reports of the occurrence of symptomatic amyloidosis after transplantation (1, 2). Thus, the use of FAP livers for DLT cannot be highly recommended and the appropriate selection of suitable livers as the second recipient in children is particularly important.

The results of the present study on the use of whole liver graft obtained from pediatric patients with MSUD who had undergone LDLT rendered the procedure technically complex, but excellent postoperative functional recovery was achieved in the second recipient. This benefit may be related to the larger size of the graft and by not performing resection or reduction. Our findings demonstrated that whole liver graft could be safely used.

Potential candidates for LD-Domino LT are patients on DDLT waiting lists with good physical size matching to a donor. In this case series, all second recipients were unable to undergo LDLT for various reasons. In case 2, the parents had medical problems which made them ineligible as donors for LDLT, and in cases 1 and 3, the parents were excluded due to heterozygous disease mutations.

LD-Domino LT recipients generally have a longer CIT, ranging from 237 to 350 min

(Table 1), compared with our usual LDLT series; the reason for this is most likely because LD-Domino LT was performed between two institutions. The surgical procedure of LD-Domino LT was technically demanding due to the second recipient's original disease, and the case with a previous surgical history had a longer operation time than the other two metabolic disorder cases. However, the continued success of LD-Domino LT may help to determine which disease is suitable for the second recipient.

FH is an autosomal dominant disorder characterized by markedly increased plasma LDL-C and can progress rapidly to premature cardiovascular risk (6). Homozygous and compound heterozygous FH patients exhibit the rapid development of atherosclerosis with death due to coronary artery disease even in childhood. Because LDL apheresis delays, but does not prevent the development of atherosclerosis, heart and heart–LT have been applied in these patients (6). According to previous evidence, 75% of the LDL-R concentration is located in the liver, and LT becomes the treatment of choice for FH. LT provides a source of normal LDL-R, which may clear cholesterol from the plasma so effectively that the disease would be completely cured without additional medication (7). Therefore, LT before the onset of coronary artery disease offers the best chance for a potential cure for patients with compound heterozygous FH.

To date, 18 previous cases of successful LT for FH have been reported (7); however, there have been no such reports of LD-Domino LT for FH. A few studies have reported the use of a heterozygous donor graft, but the patients required additional medications to control their cholesterol levels after LT (8). Therefore, LDLT from a heterozygous donor for FH is not recommended.

As the concept of LD-Domino LT is generally well established with the priority being the safety of the first recipient, limitations and technical difficulties often occur in the second recipient (9). The biggest challenge of LD-Domino LT using a whole MSUD liver without a sufficient length of HVs pedicle and multiple HAs is the reconstruction of the vessels. For the reconstruction of the HVs, native HVs that are hidden under the liver parenchyma were exteriorized as far as possible in the native liver parenchyma using a CUSA because longer, extensive HVs were essential to facilitate the reconstruction in the second recipient. By venoplasty at the back table, the RHV, MHV, and LHV were sutured together to create a single cuff. Few reports have discussed the optimal techniques of outflow reconstruction (10–15). In this case series, we employed the

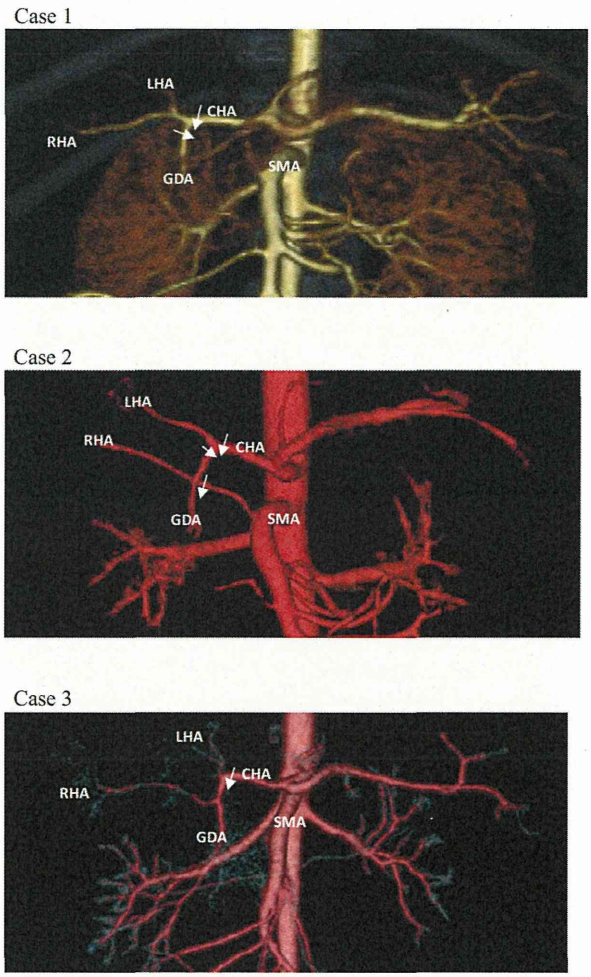

Fig. 3. Three cases of HAs according to the 3D-CT findings in the first recipient. Arrows denote the sites of dissecting.

technique described by Chan et al. (12), which was venoplasty of the RHV, MHV, and LHV stumps and the single cuff of the HVs anastomosed to the IVC without an interpositional graft or patch. The successful outcomes reassure us of the usefulness of this technique.

The vessels of the living donor graft from the first donor were not sufficiently long to allow anastomosis. Therefore, it was necessary to leave the HAs as long as possible when removing the liver from the patient with MSUD to ensure safety for vascular construction. This led to the presence of multiple vessels with insufficient length in the whole MSUD liver graft, which added to the difficulty of the HAs reconstruction. Notably, the success of LD-Domino LT largely depends on the reconstruction of the HAs. To that end, we determined the dividing sites of the vessels according to the preoperative 3D-CT findings (Fig. 3) between two institutions. During implantation of the graft in the second

recipient, we ligated the GDA to gain mobility and to obtain sufficient length for the anastomosis. The anastomosis was end-to-end and performed using 9-0 nylon under the operating microscope maintaining careful alignment. Patency and satisfactory pulsatility of the hepatic arterial flow was confirmed by intraoperative Doppler ultrasonography.

For the reconstruction of the PV, PV anastomosis was performed with the branch patch technique in all the cases. There were no surgical complications, and all recipients had good postoperative functional recovery. In addition, all second recipients maintained normal plasma BCAA levels on an unrestricted protein diet after LD-Domino LT (Table 3). These findings are supported by our previous report (5).

In conclusion, according to the early results from this case series, LD-Domino LT was effective and safe for patients who are on the DDLT waiting list and are likely to die without an LT. In Japan, the number of deceased donors remains extremely low, and the use of LD-Domino LT may relieve some of the challenges of organ shortage. In general, most patients with MSUD requiring LT are pediatric patients, and thus, LD-Domino LT may offer a valuable and potential opportunity for physical size matching in such patients. Further studies with a greater accumulation of patients and a longer follow-up will be necessary to establish LD-Domino LT using an MSUD donor.

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Conflict of interest

The authors of this manuscript have no conflict of interest.

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