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Case Report

Pediatric Living Donor Liver Transplantation from Adult Allograft Liver After Resection of Focal Nodular Hyperplasia: The Report Three Cases

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Abstract Three pediatric living donor liver transplants were performed at Ramathibodi Hospital in Thailand. The recipients were two children with biliary atresia and one child with neonatal cholestasis jaundice with suspected biliary atresia. All three donors had a single liver lesion, which was suspected to be focal nodular hyperplasia (FNH) on preoperative imaging.

Because no other living donor candidates were available for the recipients, living donor liver transplants were performed. First, a wedge resection of the liver mass was performed. The liver mass was sent for a frozen section intraoperatively to confirm the diagnosis of a benign lesion and to ensure free-margin resection. Then, the transplantation was performed using a standard technique. The liver masses were 1.4-2.3 cm in diameter.

The liver donor hepatectomy was performed simultaneously with the recipient's total hepatectomy. The estimated liver graft volume was 176.5-336.5 cm3. The estimated graft-recipient weight ratio (GRWR) was 1.4-3.7%. The actual graft weight was 168-371 grams, and the actual GRWR was 1.6-3.5%. The liver graft was implanted in the recipient using a standard piggyback technique.

The donor and recipient were discharged after the operation without any complications. Follow-up ultrasound of the upper abdomen at six months showed no disease recurrence.

Keywords: Living liver donor, Pediatric liver transplantation, Focal nodular hyperplasia

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Introduction

Most Asian countries perform liver transplants from living donors because of the low rate of deceased donor donation. Especially, a pediatric liver transplant has a low chance of getting a liver from a deceased donor because the splitting of the liver to a pediatric patient needs a high-quality liver from a deceased donor.[1,2] Focal nodular hyperplasia (FNH) is the second most common benign liver tumor. The usual incidental finding is from investigations in mostly premenopausal women and asymptomatic.[3] A liver allograft with mass is a marginal organ for liver transplantation, but FNH is a benign liver tumor without the potential for malignant transformation. The treatment of choice for FNH is expectant management and follow-up of the imaging. So, it probably expanded the organ donation pool.

There are 3 previous reports of the successful outcome of liver transplantation from liver allograft with FNH. The follow-up showed no clinical difference.[4-6]

The success of living donor liver transplantation (LDLT) is donor safety with adequate functional liver for the recipient. There are few published reports about liver allografts with FNH. One report using deceased donor liver allograft with FNH.[4] Two reports using living donor liver allograft with FNH from adult-to-adult LDLT.[5,6] We report on adult to pediatric LDLT from liver allograft with FNH.

Presentation of Cases

Case 1

A Thai boy, 2 years and five months old, presented with recurrent cholangitis. His comorbid disease was biliary atresia with post-operative portoenterostomy (Kasai's operation), cirrhosis, portal hypertension, and hepatorenal syndrome. After Kasai's operation was performed, he was admitted to several episodes due to recurrent cholangitis or upper gastroesophageal bleeding (UGIH). Physical examination findings: body weight 13.5 kilograms, marked ascites, no melena. Laboratory findings: hematocrit 14%, platelet 55,000 per microliter, prothrombin time international normalized ratio 2.39, total bilirubin 3.8 mg/dl, albumin 1.83 g/dl, serum creatinine 0.55 mg/dl. Our workup found cirrhosis from liver biopsy and esophageal varices from Esophagogastroduodenoscopy (EGD). Pediatric end-stage liver disease (PELD) score of 24.3 points. He was admitted for nutritional improvement and treatment of recurrent cholangitis. Reevaluation PELD score of 19.8 points before liver transplantation. This recipient has an indication for liver transplant by the failure of Kasai's operation with recurrent cholangitis.

The living liver donor was his mother, a 32-year-old woman. She has the thalassemia trait but no other underlying disease. Physical examination was unremarkable. Her laboratory was within normal limits. Computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a solid mass of 1.5 cm at segment III, which is suspected to be focal nodular hyperplasia (FNH) by correlation with her history and imaging characteristics (Figure 1a, 1b). The estimated left lateral liver volume was 230.49 cm3, and the estimated graft-recipient weight ratio (GRWR) was 1.7% – no contraindication by liver anatomy.

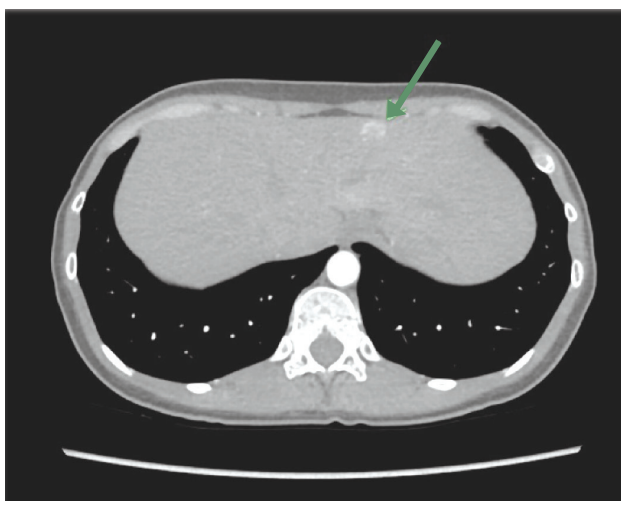

Figure 1a Contrast CT scan shows the mass size 1.5 cm. at segment 3 (S3) in the arterial phase.

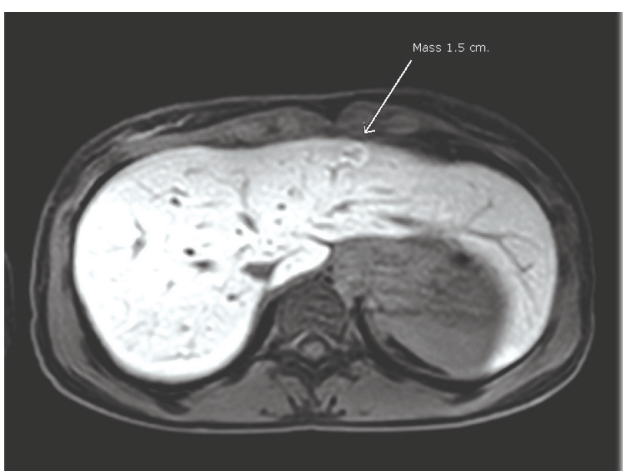

Figure 1b MRI scan shows the mass size 1.5 cm. at segment 3.

The recipient and donor operations were performed as standard procedures. The donor procedure was performed first to evaluate liver mass and intraabdominal organs. The wedge resection of the liver mass at segment III was performed using an intraoperative ultrasound guide and a cavitron ultrasonic surgical aspirator (CUSA) without the Pringle maneuver (Figure 1c). The specimen was sent for pathologic examination intraoperatively. After the pathologist was reported to confirm FNH with a free margin of 4 mm., the operation of the recipient was started for an explant liver, and then the donor's left lateral hepatectomy was proceeded at the same time. The donor's total operative time was 450 mins, and total blood loss was 600 ml. The actual left lateral segment weight was 250 grams, and the actual GRWR was 1.8%.

Implant liver grafting was performed with the standard procedure – no massive bleeding at the cutting surface and wedge resection area after reperfusion. The total recipient operation was 760 minutes, and total blood loss was 7,250 ml. due to severe adhesion from the previous recipient's procedure.

The donor's ultrasound of the upper abdomen at seven months after surgery showed no recurrence of the FNH.

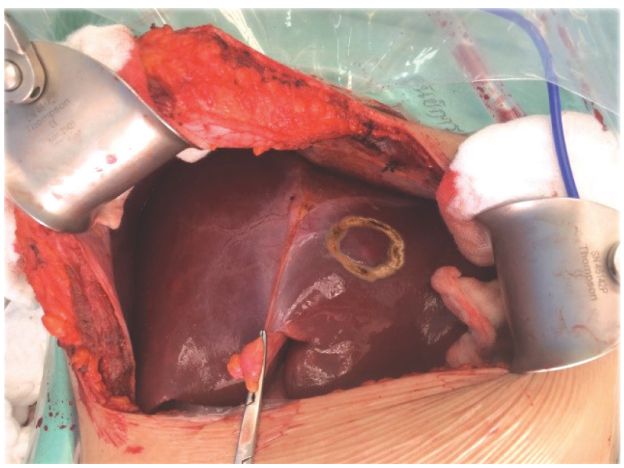

Figure 1c Intraoperative picture showed liver mass size 1.5 cm. segment 3 was marked by electrocautery.

Case 2

A 1-year-old Thai female with an unknown case of cholestasis jaundice with a differential diagnosis of Neonatal intrahepatic cholestasis caused by citrin deficiency. Her presenting symptom was neonatal jaundice without a pale stool; the intraoperative cholangiogram showed that contrast could pass from the hepatic duct to the duodenum. Then she was turned to decompensated cirrhosis with PELD 19 and was needed for liver transplantation. Her weight was 8.95 kg.

The living donor was her mother, a 33-year-old Thai female without any underlying disease. Physical examination was unremarkable; her laboratory test was within normal limits. Computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a solid enhancing mass of about 2.3 cm with a central scar at segment VII, which was suspected of focal nodular hyperplasia (FNH) from correlation with the imaging characteristic (Figure 2a, 2b) Estimated left lateral segment was 336.5 cm^3. The estimated GWRWR was 3.7%.

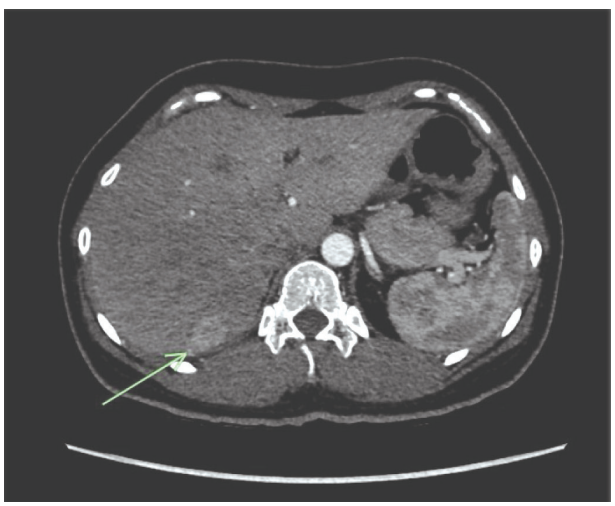

Figure 2a Contrast CT scan shows the mass size of 2.3 cm at segment VII in the arterial phase.

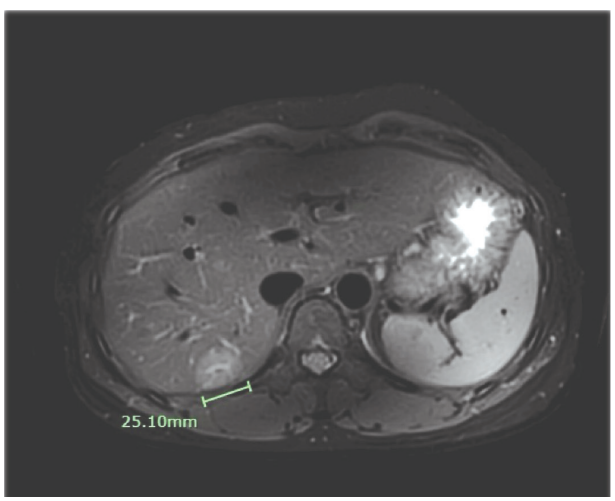

Figure 2b MRI scan shows the mass size of 2.5 cm at segment VII.

The recipient and donor operations were performed as standard procedures. The donor procedure was performed first to evaluate liver mass and intraabdominal organs. The liver mass wedge resection was performed, and segment VII using intraoperative ultrasound guide and electrocautery without Pringle maneuver. The specimen was sent for pathologic examination intraoperatively. After the pathological report was confirmed, FNH with free margin. The explanation of the recipient's liver was started simultaneously with the donor's left lateral segmentectomy. The donor's total operative time was 270 mins, and total blood loss was 250 ml. Actual left lateral segment weight was 317 grams, and actual GRWR was 3.5%.

Implant liver grafting was performed with the standard procedure – no massive bleeding at the cutting surface and wedge resection area after reperfusion. Total recipient operation was 580 minutes, and total blood loss was 800 ml.

Case 3

A 2-year-old Thai female with a known case of biliary atresia with a history of Portoenterostomy (Kasai's operation) at 3-month-aged. She had a history of recurrent cholangitis at age 8 and 11 months, bleeding esophageal varices. Her PELD score was 11. Physical examination finding: Body weight 12 kg with marked jaundice and marked hepatosplenomegaly. Laboratory test finding: Hematocrit 31% platelets 131,000 per microliters, prothrombin time international normalized ratio 1.21, total bilirubin 9.6 mg/dl., albumin 2.7 g/dl. The indication for liver transplantation in this patient was the failure of Kasai's operation with recurrent cholangitis.

The living donor was her mother, a 24-year-old Thai female without any underlying disease. Physical examination was unremarkable; her laboratory test was within normal limits. Computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a solid enhancing mass of about 1.6 cm at segment V, which was suspected of focal nodular hyperplasia (FNH) from correlation with the imaging characteristic (Figure 3). Estimated left lateral segment was 176.3 cm^3. The estimated GWRWR was 1.4%.

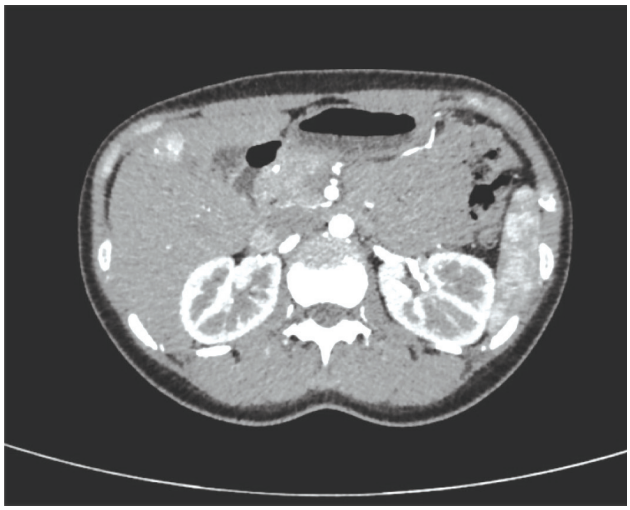

Figure 3 Contrast CT scan shows the mass size of 1.5 cm at segment V.

The recipient and donor operations were performed as standard procedures. The donor procedure was performed first to evaluate liver mass and intraabdominal organs. The segment V wedge resection was performed under intraoperative ultrasound guide and electrocautery without Pringle maneuver. The specimen was sent for pathologic examination intraoperatively. After the pathological report was confirmed to be FNH with free margin. The explanation of the recipient's liver was started simultaneously with the donor's left lateral segmentectomy. The donor's total operative time was 585 mins, and total blood loss was 300 ml. Actual left lateral segment weight was 168 grams, and actual GRWR was 1.6%.

Implant liver grafting was performed with the standard procedure – no bleeding at the cutting surface and wedge resection area after reperfusion. Total recipient operation was 570 minutes, and total blood loss was 1,500 ml.

The donor's ultrasound of the upper abdomen was performed 6 months after the surgery and showed no recurrent FNH in the period of the follow-up.

In all cases, their family did not have any other candidate living liver donors and low-rate suitable quality organs from deceased donors in our country. By ethical issues, we have approved LDLT for these cases by the institutional ethics committee and followed the Thai Red Cross's living donor rule. After that we gave family information and asked for their inform and consent.

DISCUSSION

To the best of our knowledge, this is the first reported case of an adult-to-pediatric living donor liver transplantation (LDLT) using a liver allograft with focal nodular hyperplasia (FNH). Due to lower rates of deceased organ donation in Asian countries caused by various factors, living liver donors have become increasingly important in improving recipient quality and reducing mortality rates in these regions.[1,2] In Thailand, while we continuously strive to promote and support deceased organ donation, obtaining good-quality livers suitable for pediatric split liver transplantation remains exceptionally rare each year. Consequently, our center primarily relies on living liver donors, typically parents or cousins, for pediatric liver transplantation.

FNH is the second most common benign liver tumor and has a very low recurrence rate following resection.[3] Only three cases of liver transplantation from liver allografts with FNH have been reported previously (Table 1).[4-6] These cases demonstrated no tumor recurrence and favorable outcomes. Generally, for small pediatric LDLT, the left lateral segment of the liver is sufficient. However, the functional capacity of the liver allograft must adequately meet the recipient's needs without compromising the donor. We calculated the future liver volume (FLV) after left lateral segmentectomy to be 80% of the total liver volume. The safe graft-to-recipient weight ratio (GRWR) for pediatric LDLT typically falls between 1-4%.[7,8] In these cases, as the liver tumor was small, we anticipated minimal volume loss after wedge resection without compromising the functional capacity of the liver. For safety, in the case that the tumor is in the liver graft, which will be transplanted, we estimated the tumor with a margin volume by simulating a sphere without the sphere cap volume, considering that the tumor was located on the liver surface (Figure 4). The tumor diameter was 1.5-2.5 cm, and we estimated a 1 cm margin of resection around the tumor to maximize liver volume loss. The equation calculating the sphere volume without the sphere cap volume is $4/3\pi r^3 - 1/3\pi h^2 (3r - h)$. Consequently, the estimated volume of the liver allograft after tumor resection was 168-317 cm^3, resulting in an estimated GRWR of 1.6-3.5%.

Table 1 The literature that published about liver allograft with focal nodular hyperplasia

Case No.	Author	Year	Reference	Deceased/ living donor	Adult/pediatric recipient	Whole/partial liver allograft
1	Tan M, et al	2001	(4)	Deceased	Adult	Whole
2	Gokcan H, et al.	2016	(5)	Living	Adult	Partial
3	Li G, et al.	2017	(6)	Living	Adult	Partial
Our case series	Arpornsujaritkun, et al.	2024		Living	Pediatric	Partial

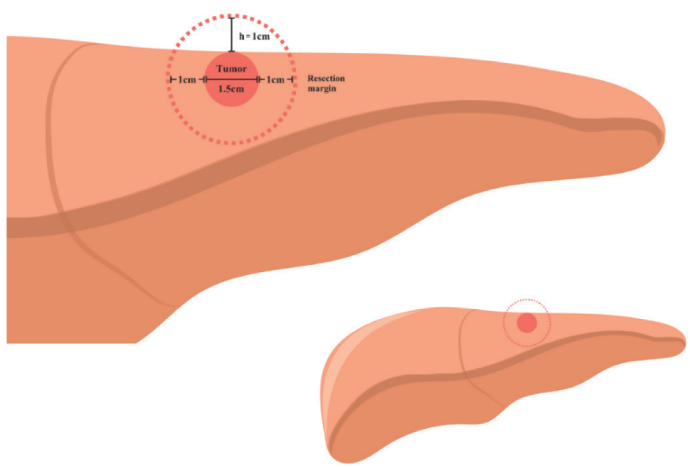

Figure 4 Simulate picture of liver tumor and margin. The tumor diameter is 1.5 cm, and the estimated margin is 1 cm around the tumor. The total diameter is 3.5 cm. The volume of the sphere without a sphere cap (V_3) is the difference between sphere volume (V_1) and sphere cap (V_2).; $V_1 = 4/3\pi r^3$, $V_2 = 1/3\pi h^2 (3r-h)$, $V_3 = V_1 - V_2 = 4/3\pi r^3 - 1/3\pi h^2 (3r-h)$.

We performed wedge resection in vivo as it provides better control over bleeding after reperfusion. In these cases, the liver tumor with the margin volume was relatively small, which did not significantly affect the left lateral segment of the liver. It is possible that the resection margin was smaller than estimated, and the cutting surface was about 1 cm away from the falciform ligament. We used these calculations and sphere volume estimation to anticipate scenarios where a more giant tumor may be encountered, necessitating a strict calculation of liver volume, particularly for the right lobe of the liver allograft. We did not observe any recurrent liver tumors one year after liver transplantation. Therefore, living donor liver allografts with FNH appear to be a feasible option for expanding liver transplantation.

The importance of liver surgery for donors with suspected FNH (Focal Nodular Hyperplasia) lies in the necessity of confirming the pathology results from a pathologist beforehand, ensuring that the nodule is indeed FNH and not another malignancy disease such as HCC (Hepatocellular Carcinoma) or liver metastasis, before proceeding with liver graft transplantation to the recipient. Therefore, when performing wedge resection of FNH, consideration should be given to obtaining a free margin of the nodule to account for the possibility of the nodule transforming into cancer.

Consequently, surgical planning and assessment of liver graft volume must be meticulously evaluated, considering the portion of the liver to be resected and ensuring an adequate future liver remnant for both the donor and recipient. In cases of other benign liver masses, consideration for liver donation may be possible if there is an assessment of adequate liver graft volume for the recipient and an adequate future liver remnant for the donor. If the pathology report confirms a benign disease, it may not necessarily be a contraindication for liver transplantation.

In terms of long-term follow-up care, FNH has a low incidence of recurrence and no malignant potential. Therefore, long-term patient care may not primarily involve imaging follow-up.

Conclusion

This report shows that the liver allograft with focal nodular hyperplasia can be safely used for transplantation. But the important thing is the confirmation of the diagnosis by a pathologist before the transplantation and the adequate future liver remnant for the recipient and donor. Previous reports show that the lesion can be left in situ with closed follow-up without any clinical difference (Table 2).

Finally, a limitation of this report is that it includes only three cases, with only one case involving a liver graft with focal nodular hyperplasia. Therefore, future studies with larger sample sizes are necessary to validate and expand upon these findings, ensuring that the results are robust and applicable to a broader population.

Table 2 The summary of the cases

No.	Total liver volume (cm^3)	Estimated liver graft volume (cm^3)	Estimated GWRWR (%)	Size of FNH (cm)	Location of FNH	Segment of liver graft	Actual graft weight (g)	Actual GWRWR (%)
1	1,126.32	230.49	1.7	1.4	IVa	Left lateral segment	250	1.8
2	1,637.3	336.5	3.7	2.3	VII	Left lateral segment	317	3.5
3	1,100	176.3	1.4	1.5	V	Left lateral segment	168	1.6

Ethical Approval

This study was reviewed and approved by the Ramathibodi Hospital Institution Review Board. No. MURA2023/690.

Conflict of Interest

The authors have no conflicts of interest to declare.

Authorship Contribution Statement

N.A. participated in research design, the writing of the paper, data collection, critical revision, and approval of the final version of the article. N.K. participated in writing the paper, data collection, analysis, and interpretation, and the article was approved. P.S., C.T., A.B., S.L., B.S., G.G., V.A., and S.S. participated in the data

acquisition and approved the article. P.C. participated in data collection and analysis.

Abbreviations

FNH – Focal Nodular Hyperplasia

LDLT – Living Donor Liver Transplantation

PELD score – Pediatrics End-stage Liver Disease score

GRWR – Graft weight to Recipient Weight Ratio

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