

Graft loss and poor outcomes after living-donor liver transplantation owing to arterioportal shunts caused by liver needle biopsies

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Short title: APS after LT

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Abstract

Background. Arterioportal shunts (APSs) are well-known critical complications after liver transplantation (LT). The aims of this study were to assess the frequency and causes of APSs after LT and to analyze APS patients with poor outcomes. **Patients.** A total of 1415 LT recipients were evaluated. Among these patients, the APS cases were retrospectively investigated. **Results.** APSs were detected at least in nine patients, and the rate after LT was 0.6%. All patients accompanied with APS had a history of post-transplant invasive procedures (percutaneous transhepatic cholangio-drainage in six cases and liver needle biopsy (LNB) in three cases). Two patients with poor outcomes showed proximal APSs caused by LNBs. The other seven patients showed distal APSs, and had stable conditions. Imaging findings in the two proximal APS patients revealed drastic changes in the graft hemodynamics. Although they finally received re-LT, their outcomes were poor owing to fatal complications associated with advanced collaterals. **Conclusion.** We conclude that even careful LNBs can cause APSs at unexpected points, and that earlier and more aggressive treatments are required, especially in proximal APS patients, from the viewpoints of not only graft failure but also developed collaterals.

Introduction

We previously documented our experiences of portal venous complications after pediatric living-donor liver transplantation (LDLT),¹ and suggested that these complications may result in graft loss despite intensive treatments. Arterioportal shunts (APSs) are well-known critical complications of the portal vein (PV).² In this study, we focused on APSs after liver transplantation (LT). The aims of this study were to assess the frequency and causes of APS and to analyze APS patients with poor outcomes to improve future APS outcomes.

Patients and Methods

Since Kyoto University initiated its LDLT program in 1990, 1415 LTs have been performed until September 2009. We retrospectively investigated APS cases after LT among these patients. In addition, we further analyzed the details of two APS patients with poor outcomes.

Results

Frequency of APS

Postoperative screenings by ultrasound (US) were routinely performed in our institution. The

1 APSs detected in this series were identified on screening examinations. APS was detected at least in
2 nine patients (0.6%), and two of these patients finally died.

3 **Causes and characteristic findings of APS**

4 All patients accompanied with APS had a history of post-transplant invasive procedures.
5 Therefore, we investigated their histories of invasive post-operative treatments. We found that six
6 patients had undergone percutaneous transhepatic cholangio-drainage (PTCD) owing to biliary
7 complications after LDLT, while three patients had undergone liver needle biopsies (LNBs). Proximal
8 APS was defined as APS near the hilar bifurcation of intra-hepatic arteries, though distal APS occurred
9 at peripheral branches from hepatic hilus. Two patients with LNBs showed proximal APSs with fatal
10 outcomes owing to graft loss and complications associated with advanced collaterals. The remaining
11 seven APS patients showed distal APSs, and had stable conditions. It should be noted that the proximal
12 APSs in the former two cases appeared suddenly and immediately after the LNBs.

13 **APS patients with poor outcomes**

14 A 1.9-year-old boy underwent LDLT because of Byler's disease. He received a re-LDLT
15 accompanied by external biliary drainage via a hepaticojejunostomy owing to graft loss caused by
16 biliary complications at 5.6 years of age. Although extracorporeal membrane oxygenation for severe
17 respiratory failure and percutaneous drainage for an intraperitoneal abscess were required, these
18 complications were successfully treated and his general condition became stable. He received an LNB
19 by his local physician at 6.9 years of age, and liver function test abnormalities and ascites immediately

1 increased thereafter. He was referred to our facility again, and aortoangiography clearly revealed a
2 proximal APS (Fig. 1A and B). Although he received corresponding treatments, LNB findings after the
3 APS confirmed a disorder of the graft hemodynamics. Hepatic coma occurred at 7.1 years of age, and
4 a second re-LDLT was performed at 7.2 years of age. Esophageal varices suddenly ruptured at 17 days
5 after the second re-LDLT, and he died at 19 days after the secondary re-LDLT (4 months after APS
6 onset).

7 A 10.5-year-old boy underwent LDLT because of biliary atresia. Biliary stenosis was
8 successfully treated by additional surgery, and the postoperative course was subsequently uneventful
9 until he reached the age of 14.3 years. He received an LNB by his local physician and an APS
10 suddenly appeared thereafter. The PV flow became hepato-fugal, and he was referred to our facility
11 again. Distal and proximal APSs were detected by imaging studies. We performed interventional
12 radiology (IVR), and repeated embolizations using coils were effective for both APSs. However, the
13 proximal APS recurred, and IVR was repeated. Thereafter, follow-up histopathological analysis of an
14 LNB revealed a disorder of the graft hemodynamics. A re-LDLT was performed at 16.2 years of age,
15 and contrast radiography of the removed allograft clearly revealed a proximal APS (Fig. 1C and D).
16 Although he recovered after the re-LDLT, he died from sudden gastrointestinal bleeding at 16.9 years
17 of age (2.6 years after APS onset).

19 Discussion

1
2 Various complications after LT require invasive examinations and/or treatments, and these
3 invasive procedures inevitably involve some risks.^{3,4} Biliary complications after LT remain crucial
4 problems that require adequate treatments.^{5,6} However, PTCO often causes APSs, and several of our
5 cases with PTCO histories showed distal APSs. On the other hand, LNBs are invasive but
6 indispensable for a precise diagnosis after LT. In our facility, LNBs are performed only when necessary.
7 We have performed a total of 6520 LNBs over approximately two decades, and have encountered one
8 distal APS after an LNB. The rate of APSs caused by LNBs is 0.015% in our facility. The liver
9 functions in seven of our APS cases caused by PTCO and LNB were fortunately well maintained,
10 since the APSs occurred at distal points.

11 Proximal APSs caused by LNBs were detected in this study. To the best of our knowledge, there
12 are no previous reports of cases similar to our two cases. The coauthors based at the Mayo Clinic
13 Florida (Jacksonville, FL 32224, USA) have also had no experiences similar to these proximal APSs,
14 although they have experienced a total of 2005 LTs. We do not know how the proximal APSs were
15 caused, because we are unaware of the LNB procedures used by the local physicians of these patients.
16 However, these two cases appear to suggest that LNBs may cause APSs rarely but centrally compared
17 with PTCO, and that transplant surgeons must be aware that even careful LNBs can cause APSs at
18 unexpected points. US-guided LNBs are usually performed in our facility, and an education system
19 involving Doppler US in the LT field was previously recommended.⁷ We suggest that the screening

examinations by US should be performed after any invasive procedures to check the complication of APS.

The imaging findings in our proximal APS cases revealed drastic changes in the PV flow. Furthermore, hepatic vein flow was not confirmed even in the late phase. Moreover, turbulent flow made the hepatic artery appear tortuous, dilated and aneurysm-like. Hepato-fugal, rather than hepato-petal, PV flow caused by proximal APSs more easily leads to developed collaterals and shows more drastic cirrhotic symptoms.^{8,9} Even after PV flow restoration by LT, well-developed collaterals do not disappear immediately and some collaterals still remain after LT.¹⁰ Our proximal APS cases eventually died from collateral-associated complications (bleeding and rupture). The hepatic arterial complications after LT, such as pseudo-aneurysms and APS, are rare. However, these complications are characterized by a high mortality rate.¹¹ Portal venous complications are also fatal.¹

Iatrogenic complications should be treated non-invasively if possible. APSs are generally treated by transcatheter arterial embolization,⁸ and we consider that IVR ranks first among APS treatments even after LDLT. In our two cases, the treatments retrospectively seemed to be delayed. More aggressive and immediate treatments on the detection of proximal APS maybe improve the outcome of patients with proximal APS. We conclude that earlier and more aggressive treatments are required, especially for proximal APSs after LT, from the viewpoints of not only graft failure but also developed collaterals, if IVR is not successful.

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Figure legends

Figure 1. Impacts of proximal APSs on graft hemodynamics in imaging studies

Panels A and B show data for one patient, while panels C and D show data for the other patient. (A,B)

The hepatic artery (HA) phase (A) and delayed phase (B) in aortoangiographs approached from the celiac artery are shown. Aortoangiography clearly revealed a proximal APS (red arrow) and a serpentine aneurysm of the HA after the APS (yellow arrow). Contrast material from the HA directly filled the PV (green arrow). The hepatic vein was not detected even in the delayed phase, and the contrast material drained to the developed collaterals via hepato-fugal PV flow (blue arrow). (C,D)

Contrast radiographs approached from the HA in the removed allograft are shown. The coils placed by IVR for the proximal and distal APSs are easily confirmed. The proximal APS was clearly detected (red arrow), and the HA after the APS was tortuous and dilated (yellow arrow). The PV was directly filled with contrast material (green arrow), and the contrast material was drained by hepato-fugal flow via the PV (blue arrow). This examination also verified that the distal APS was successfully treated by IVR.

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