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Technical refinement in living-donor liver transplantation for hepatoblastoma with main portal vein tumor thrombosis – a pullout technique

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Abstract: We present a case of a two-yr-old boy diagnosed with HBT with complete main PVTT. HBT was located in the bilateral lobe with PVTT involving the confluence of the SMV and the SpV. Cisplatin-based neoadjuvant chemotherapy was delivered; main tumor shrank and AFP levels decreased to below one hundredth. However, PVTT remained in the bilateral portal branches to the main trunk of PV. We describe the technical details of the portal venous tumor thrombectomy that was succeeded by a LDLT. The patient remained healthy 2.5 yr after LDLT, showing good patency of the PV with no evidence of recurrence of tumor.

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Key words: hepatoblastoma – liver transplantation – portal vein tumor thrombosis

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HBL is the most common malignant liver tumor in early childhood, accounting for 60–85% of all pediatric hepatic tumors (1). As it is a surgical tumor, the main form of treatment is surgical resection. Advances in imaging technology, systemic cisplatin-based neoadjuvant chemotherapy, and surgical resection have improved survival rates (2). Patients with HBL with resectable tumors have a disease-free survival rate of 80–90% (3). While more than 60% of lesions that appeared unresectable at initial imaging shrank with chemotherapy and eventually became resectable (2), some cases of HBL remained unresectable despite chemotherapy to control extrahepatic lesion. In such cases, whole liver resection is necessary, with liver transplantation being recognized as a valid therapeutic option to accomplish complete resection (4). HBL that invades the bilateral portal branches or the main portal trunk with tumor thrombosis is one of the most unresectable forms of tumor. Although macrovascular invasion posed as a

Abbreviations: FDG, F^{18}-fluoro-2-deoxy-D-glucose; HBL, hepatoblastoma; LDLT, living-donor liver transplantation; PET, positron emission tomography; POST-TEXT, post-treatment extent of disease; PRETEXT, pretreatment extent of disease; PV, portal vein.; PVTT, portal vein tumor thrombosis; SMV, superior mesenteric vein; SpV, splenic vein.

poor prognostic factor, the main aim is still to achieve complete resection for chemosensitive HBL through surgery (5).

Here, we report a pediatric patient with PVTT that remained in the SMV and the splenic venous junction (SMV-SpV junction) despite neoadjuvant chemotherapy. The patient eventually underwent complete surgical resection with PV thrombectomy and LDLT. We describe the details of the surgery of the PV thrombectomy that employed the use of a "pullout technique."

Case

The patient was a 2.5-yr-old boy 12 kg in weight. The chief complaint was abdominal distension. A computed tomography (CT) showed multifocal liver tumors occupying the whole liver with a PVTT that extended to the SMV-SpV junction (Fig. 1a). PET with FDG study showed that huge liver tumor, PVTT, and the segment 6 of the right lung were positive. At the time, serum AFP level was markedly elevated at 580 000 ng/mL (normal range: <10 ng/mL). The case was assessed using the PRETEXT grouping system for HBL, as PRETEXT IV, C1, E0a, F1, H0, M1p, P2a, and V1 (6). Needle biopsy findings showed fetal and embryonic mixed-type HBL. Neoadjuvant chemotherapy by cisplatin–pirarubicin (tetrahydropyranyl–adriamycin) (CITA) was introduced in accordance with the protocol of the Japanese Study Group for Pediatric Liver Tumor protocol-2 (7). At the end of the third cycle of CITA, AFP levels decreased to 2373 ng/mL and the size of the tumor size was reduced. While a lung metastasis was no longer present after the fourth cycle of chemotherapy by ifosfamide, carboplatin, tetrahydropyranyl–doxorubicin, and etoposide (ITEC), AFP levels rose again to 6450 ng/mL. It was determined at that stage that the primary liver tumors could not be sufficiently controlled, prompting the need for transarterial chemoembolization. In addition, a systemic chemotherapy comprising cisplatin, vincristine, and fluorouracil (C5V) was delivered due to the suspicion that the patient might have impaired response to the previous rounds of chemotherapy (8). Subsequently, AFP level decreased to 2532 ng/mL. However, the PVTT, which assumed an atrophic shape and was negative in FDG–PET study, remained in the SMV-SpV junction. CT showed enlarged and tortuous collateral vessels had developed along the common bile duct in the hepatoduodenal ligament (Fig. 1b). The case was assessed again using POST-TEXT grouping system for HBL, as POST-TEXT III, C0, E0, F1, H0, M0, P2a, and V0. We scheduled an LDLT for total resection of HBL and removal of PVTT by either thrombectomy or total resection (including PV). The patient's 40-yr-old mother volunteered to have her left lateral segment, weighing 242 g, donated as a graft. The graft-to-recipient body weight ratio was 1.95%.

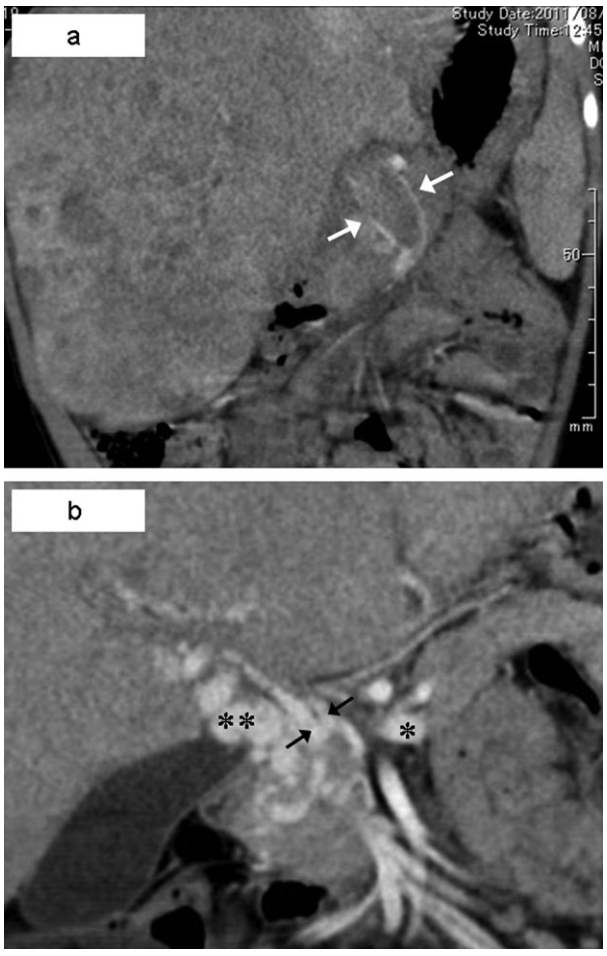

Fig. 1. (a) Large PV thrombosis (white arrow) in coronary view revealed by computed tomography. (b) Thin and long PV thrombosis (black arrow) from the bilateral portal branch to the confluence of the SMV and the SpV (asterisk). A collateral vein was present in the hepatoduodenal ligament (double asterisk).

Surgical procedures

Both collateral vessels and the PV were isolated and taped with vessel loops, and preserved until total hepatectomy. Intra-operative ultrasonography provided definitive imaging of the location of the PVTT which extended into the SMV-SpV junction; however, it was atrophic and appeared "floating." The SMV-SpV junction was exposed with meticulous dissection of the tributaries into the portal venous system. The SMV and the SpV were isolated and clamped at a distal site of the

junction (Fig. 2a). The PV was dissected from the posterior of the pancreas toward the liver and was easily pulled out through the dorsal side of the pancreas in a safe manner (Fig. 2b). The PVTT was completely thrombectomized by this "pullout" technique; intra-operative histology of the PVTT revealed no viable tumor cells within the excised specimens and the surgical margin of the PV. Subsequently, the PV was returned to its original position without using an interposed vein graft. PV anastomosis was accomplished at the confluence of the recipient PV and the left PV of the graft.

Pathological examination of the explanted liver showed a multicentric tumor with PVTT extending to the bilateral branches of the PV and the main trunk. About 35% of the whole tumor revealed necrotic changes, while viable tumor was composed of fetal and embryonic mixed-type HBL. The excised thrombus in the main portal trunk measured 22 ×2 × 2 mm with no viable tumor cells.

Tacrolimus and low-dose steroids were used for immunosuppression. The patient managed to wean off the steroids over three months (9).

After surgery, AFP levels decreased significantly. On postoperative day 13, the patient had mild acute cellular rejection, but was successfully treated with bolus administration of steroids. The patient was discharged 30 days after LDLT. Adjuvant chemotherapy with C5V commenced 40 days after LDLT. The patient remained in good health 2.5 yr after LDLT with normal AFP levels (5.6 ng/mL), good patency of the PV, and no evidence of recurrence of tumor.

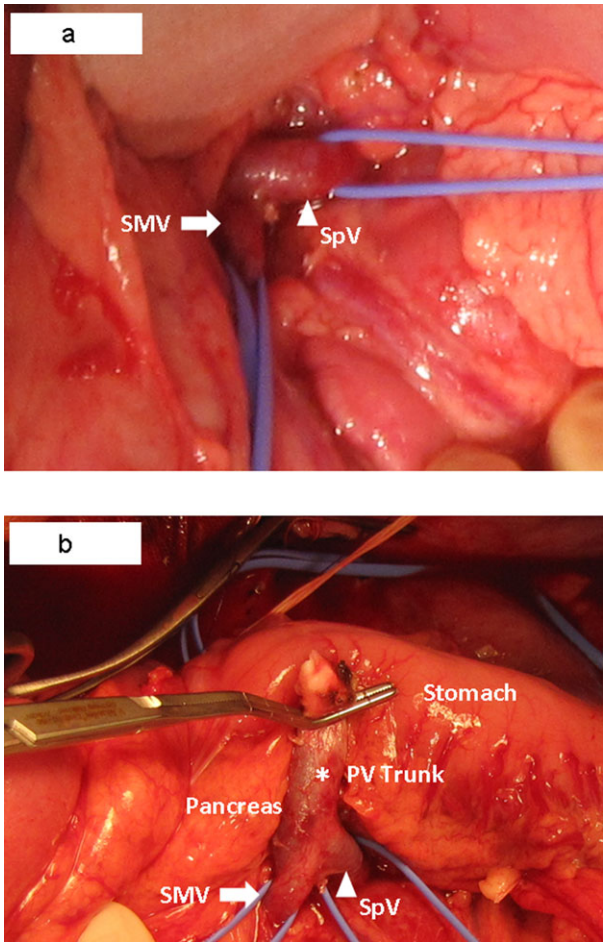

Fig. 2. (a) The SMV and the SpV were isolated and each taped with vessel loops. (b) The technical highlights showed the PV being drawn from superior to inferior border of the pancreas.

Discussion

The guidelines for early consultation with a transplant surgeon to perform primary liver transplantation to treat unresectable HBL include: (1) HBL having characteristics of multifocal PRETEXT IV without extrahepatic lesion, (3) unifocal centrally located PRETEXT II and III involving the three main hilar structures, or (2) all three of the main hepatic veins and POST-TEXT III with macroscopic vascular invasion (5). In our case, the HBL invaded bilateral portal branches with tumor thrombosis in the main portal trunk. While neoadjuvant chemotherapy succeeded in shrinking the size of the PVTT, it persisted in the main portal trunk and extended into the SMV-SpV junction. In the event that chemotherapy is effective, PVTT can become atrophic and mostly replace blood clots. When the risk of residual malignant cells in the PVTT is ruled out, the operative management of PVTT in patients undergoing liver transplantation would be dependent on the extent of PVT and the method of portal reconstruction according Yerdel's classification (Grade 1–4) (10). It has been reported previously that no special technique is required for the reconstruction of the PV in Grade 1 cases. PVT classified as Grade 1 is defined as minimally or partially thrombosed PV, in which the thrombus is mild or at most confined to <50% of the vessel lumen, with or without minimal extension into the SMV. Hence, only thrombectomy with cramping PV on the SMV-SpV junction is usually required. In our case, the PVTT decreased in size after neoadjuvant chemotherapy. It was classified as Grade 1 as it was confined to <50% of the vessel lumen.

Although neoadjuvant chemotherapy has been reported to reduce AFP level and allowed negative FDG–PET uptake into PVTT, our patient required complete thrombectomy due to the

potential risk of residual malignancy in the PVT. However, we decided against using total replacement with interposition vein graft as a first-line procedure because the PVTT went through a dramatic atrophic change after chemotherapy. Instead, the PV was clamped at the SMV-SpV junction. There were two reasons to our judgment. There was a risk of residual malignancy due to the cramp nipping at the edge of the PVTT. Hence, the SMV and the SpV were clamped separately at a distal site from the junction. We adopted a "pullout" technique to achieve good operative and visual field for complete thrombectomy. Even in such a case, a set of the procedures were performed safely in good operative field acquired by pullout techniques. In the event that malignant cells were present on the margin of the PV through the intra-operative rapid diagnosis, portal reconstruction using interposition vein graft may be performed as a second-line procedure.

The other reason was that our patient developed collateral vessels, which resulted in cavernous transformation in the hepatoduodenal ligament. We had to retain the collateral vessels in order to avoid intestinal congestion until PVTT was resected and the native liver removed. There was a high risk of bleeding when approaching the PVTT from the side of hepatoduodenal ligament that contained the distended collateral vessels.

In view of the factors, the "pullout" technique was very useful in resecting the PVTT completely. Furthermore, this technique can be combined with a portal reconstruction using interposition vein graft when the PV is sclerotic and had undergone atrophic change in recipients; for example, in patients with biliary atresia, direct anastomosis of PV cannot be performed due to an insufficient front flow because of some collateral vessels derived from the main PV. We have applied the "pullout" technique in such cases and achieved positive outcome (11).

In conclusion, our patient underwent LDLT for HBL with PVTT that extended to the SMV-SpV junction. The "pullout" technique allowed a good operative field to perform complete thrombectomy safely.

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Authors' contributions

H. Kanazawa: Participated in research design and writing of the paper, conducted research, provided reagents of analytic tools, and analyzed the data; S. Sakamoto, A. Fukuda, and M. Kasahara: Participated in research design and conducted research; K. Sasaki, H. Uchida, M. Matsunami, T. Shigeta, R. Tanaka, K. Matsumoto, and A. Nakazawa: Conducted research.

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