Living donor liver transplantation in a pediatric patient with hepatic angiosarcoma: a case report

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Hepatic angiosarcoma (HAS) is a rare malignant disease in pediatric patients. We report the case of a 3-year-old boy with HAS, which was treated with neoadjuvant chemotherapy and living donor liver transplantation (LDLT). A previously healthy 3-year-old boy who presented with a firm mass in the upper quadrant of the abdomen was diagnosed with hepatoblastoma at a local general hospital and was referred to our institution. Percutaneous liver biopsy confirmed the diagnosis of HAS. The extent of the tumor was large, not allowing surgical resection; thus neoadjuvant chemotherapy was performed. The size of the tumor was markedly reduced after 2 cycles of chemotherapy for 2 months; thus LDLT was planned to remove the tumor completely. A left lateral section graft weighing 280 g was harvested from his 38-year-old father. The left lateral section graft was implanted according to the routine procedures of pediatric LDLT, including patch venoplasty of the recipient hepatic vein and portal vein. The explant liver showed a 9 cm-sized residual angiosarcoma with 60% regression. The patient recovered uneventfully and is doing well for 3 months with scheduled adjuvant chemotherapy. Although there are only a few pediatric liver transplantation cases showing prolonged survival, liver transplantation appears to be a viable treatment option for long-term survival for pediatric patients with unresectable HAS.

Keywords: Hepatic malignancy; Chemotherapy; Venoplasty; Pediatric transplantation; Recurrence

INTRODUCTION

Hepatic angiosarcoma (HAS) is a rare malignant disease in pediatric patients and it is found more often in adults. It is difficult to distinguish this disease from other vascular anomalies, such as infantile hemangioendothe-

lioma. Malignant liver tumors account for approximately 1% of childhood malignancies and HAS comprises only 1-2% of pediatric liver tumors [1,2]. Less than 50 pediatric cases have been reported in the literature worldwide [2,3]. The prognosis of HAS is very poor, regardless of the treatment or stage, with mean survival time ranging from only

10 months to 2 years [2,4]. Only six cases of disease-free survival have been reported in the literature [3,5]. Complete surgical resection appears to provide the best chance for long-term survival, but many patients have metastatic disease or their tumors are unresectable. Liver transplantation (LT) in such patients is controversial and often contraindicated because of the posttransplant tumor recurrence and mortality rates. Systemic chemotherapy yielded mixed results, but long-term remission was largely not achievable.

We report the case of a 3-year-old boy with HAS, which was treated with neoadjuvant chemotherapy and living donor liver transplantation (LDLT).

CASE PRESENTATION

A previously healthy 3-year-old boy who presented with a firm mass in the upper quadrant of the abdomen was diagnosed with hepatoblastoma at a local general hospital and was referred to our institution. The initial imaging diagnosis was hepatoblastoma with portal vein tumor thrombus, PRE-Treatment EXtent of tumor (PRETEXT) stage IV (Fig. 1). Percutaneous liver biopsy showed angiosarcoma, with immunohistochemical findings of CD31 positivity, non-contributory ERG, HEP PAR-1 negativity, and P53 neg-

ativity. The extent of the tumor was too large, not allowing surgical resection; thus neoadjuvant chemotherapy according to the Children's Oncology Group ARST0332 study using doxorubicin and ifosfamide was performed [6]. No significant side-effects occurred, with a normal-structured heart and an ejection fraction of 67%. The size of the tumor was markedly reduced after 2 cycles of chemotherapy for 2 months (Fig. 2); thus LDLT was planned to remove the tumor completely.

LDLT operations were performed in both the donor and recipient according to the routine procedures. Pretransplant computed tomography findings suggested that the left hepatic vein trunk, the confluence of the hilar portal vein and the second-order branch of the right hepatic artery were suspected to show tumor involvement (Fig. 2); thus dissection of the recipient liver was limited and it did not include dissection of these involved areas (Fig. 3).

A left lateral section graft weighing 280 g was harvested from his 38-year-old father. The graft left hepatic vein orifice was enlarged with patch venoplasty according to our institutional guidelines [7,8].

During recipient hepatectomy, the right and left hepatic arteries were transected below the involved tumor portion. The hilar portal vein was transected distal to the conflu-

Fig. 1. Initial radiologic study findings. At three months before the liver transplantation operation, computed tomography (A, B) and magnetic resonance imaging (C) studies show huge multiple tumors occupying the whole liver, and the abdomen is distended by the enlarged liver. Whole-body positron emission tomography (D) shows a heterogeneous mild hypermetabolic huge mass in the liver. The diagnosis from these imaging studies is hepatoblastoma and differential diagnoses include solid variant of mesenchymal hamartoma, inflammatory pseudotumor and hemangioma.

Fig. 2. Pretransplant computed tomography findings. The tumors show noticeable interval decrease in size (A), encasement of the middle and left hepatic veins (B), encasement of the right and left portal veins (C), and encasement of the second-order right hepatic artery branches (D).

Fig. 3. Intraoperative findings showing the extent of hepatic angiosarcoma at the dome (A) and hilar area (B).

ence portion. The recipient common bile duct was transected and closed. The major hepatic vein stumps were transected without leaving any hepatic parenchymal tissues. Because the tumor was located very close to the left hepatic vein trunk, the left hepatic vein stump was resected further and the resection margin was sent for frozen section biopsy, which revealed a tumor-negative finding. The left hepatic vein stump was very short and could not be reconstructed directly; thus a small patch of iliac vein homograft was attached to facilitate graft hepatic vein reconstruction

(Fig. 4). Since the recipient portal vein appeared relatively small compared with the graft portal vein and a branch patch was not available, a small iliac vein homograft patch was attached to widen the portal vein orifice (Fig. 5).

A left lateral graft was implanted according to the routine procedures of pediatric LDLT, including size-matched reconstruction of the graft hepatic vein and portal vein, single left hepatic artery reconstruction using surgical microscopy, and Roux-en-Y hepaticojejunostomy (Fig. 6).

The explant liver showed residual angiosarcoma mea-

Fig. 4. Intraoperative findings showing patch venoplasty of the recipient hepatic vein stump. (A) The major hepatic vein stumps are transected without leaving any hepatic parenchymal tissues. (B) Because the tumor is located very close to the left hepatic vein trunk, the left hepatic vein stump is resected further. (C, D) The left hepatic vein stump appears to be very short and cannot be re-constructed directly; thus a small patch of iliac vein homograft (arrows) is attached.

Fig. 5. Intraoperative findings showing patch venoplasty of the recipient portal vein. (A) The recipient portal vein appears relatively small due to removal of the hilar bifurcation portion. (B) A small longitudinal incision is made at the portal vein stump. (C, D) A small iliac vein homograft patch is attached to enlarge the portal vein orifice.

Fig. 6. Intraoperative findings showing implantation of the left lateral section graft. (A–C) Size-matched reconstruction of the graft hepatic vein. The intervening vein patch is visible (arrow). (D, E) Size-matched reconstruction of the graft portal vein. The intervening vein patch is visible (arrow). (F) Gross finding of the left lateral section graft after portal vein reperfusion.

Fig. 7. Gross photographs of the explanted liver. There is a large viable tumor with extensive necrosis.

suring 9.2 cm × 7.8 cm × 5.2 cm in size in segments II, IV, V, VI, VII and VIII (Fig. 7). The tumor showed moderate grade of regression, in which the regressed area was approxi-

mately 60%. There was presence of Glisson capsule invasion with absence of lymphovascular invasion and perineural invasion.

This patient recovered uneventfully from the LDLT operation (Fig. 8) and is doing well for 3 months to date. He is currently undergoing scheduled adjuvant chemotherapy.

DISCUSSION

Pediatric HAS is a rare and aggressive vascular malignant tumor of endothelial cell origin that often presents with a rapidly enlarging abdominal mass and occasional pain [4]. The overall prognosis of HAS is very poor regardless of the treatment modalities. Because of the rarity of this tumor, there are no treatment consensus guidelines as yet. Treatment approaches vary widely, but they often include surgical treatment combined with systemic therapy. The results of treatment are mixed, but the overall outcomes and prognosis remain very poor.

Platinum-based chemotherapy regimens have often been attempted, as well as targeted therapy with sirolimus and vascular endothelial growth factor inhibitors including

Fig. 8. Computed tomography findings at five days after transplantation. (A) The graft hepatic vein reconstruction shows only a slight stenosis at the anastomotic site (arrow). (B) The funnel-shaped recipient portal vein is well visualized (arrow).

bevacizumab [2,5]. A sizable tumor response to bevacizumab, gemcitabine, and docetaxel was reported in a case of metastatic HAS, but the pediatric patient died after 16 cycles of chemotherapy [9]. Adriamycin combined with cisplatin was reported to significantly reduce the size of an unresectable HAS [10]. After complete resection and over one year of alternating courses of varying cytotoxic agents, the patient remained disease-free for 44 months [11]. Sclerotherapy, directed embolization, and radiation therapy have also been attempted, with little success [2]. Although many different agents have been tried with varying benefit as briefly commented above, the majority of patients never achieve remission or long-term survival.

Complete surgical resection appears to provide the best survival advantage for children with HAS; however, LT in such patients remains controversial because of the poor long-term survival outcomes. A retrospective review of the European Liver Transplant Registry concluded that HAS should be considered an absolute contraindication to LT due to poor outcomes [11]. The majority of patients with HAS will succumb to the diagnosis or related complications, and there are only a few reports of long-term survival. Among the six reported surviving pediatric patients with HAS, all patients underwent successful tumor excision with four patients undergoing LT and were still disease-free at the time of publication [1-3]. Interestingly, five out of these six patients were not diagnosed with HAS until after surgical excision or LT.

Our case report presents a patient with localized HAS that was not amenable to surgical resection and who was treated with neoadjuvant chemotherapy and LDLT. Although there are only a few pediatric LT cases showing prolonged survival, LT appears to be a viable treatment option for long-term survival of pediatric patients with unresectable HAS.

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CONFLICT OF INTEREST

All authors have no conflicts of interest to declare.

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AUTHORS' CONTRIBUTIONS

Conceptualization: SH. Data curation: GCP, SH. Methodology: SHO, KMK. Visualization: SH. Writing - original draft: SH, JMN. Writing - review & editing: SH.

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