

# A Feasible Surgical Approach for Treating Extensive Hepatoblastoma Using a Backup for Living Donor Liver Transplantation: Case Report

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## ABSTRACT

Hepatoblastoma is the most common type of malignant liver tumor in children and occurs most frequently in patients two years of age and younger. The outcomes for children with hepatoblastoma have been improving in recent years due to the introduction of cisplatin-based chemotherapy regimens. Recently, performing liver transplantation after neoadjuvant chemotherapy has become increasingly advocated as a primary surgical treatment for children with unresectable hepatoblastoma involving three or four sectors of the liver. Surgical exploration is frequently required to determine which tumors are resectable, which require liver transplantation and timing of resection. When the quality of the remnant liver is in question, the decision for transplantation versus resection should be made by a liver team in experienced center with capability of liver transplantation. This report presents the findings of the patient with hepatoblastoma who successfully underwent extreme resection with a backup for living donor liver transplantation. The patient was discharged home in good condition and the follow-up continued for three years with normal AFP levels observed.

**Keywords:** Hepatoblastoma; Unresectable Hepatoblastoma; Living Donor Liver Transplantation

## 1. Introduction

Hepatoblastoma is the most common type of malignant liver tumor in children and occurs most frequently in patients two years of age and younger [1]. The prognosis of a patient with hepatoblastoma is primarily dependent upon the surgical resectability of the tumor and the addition of postoperative chemotherapy. The overall survival rates of patients with hepatoblastoma are approximately 85% to 89% [2]. Higher survival rates have been achieved due to improvements in imaging, systemic cisplatin-contained neoadjuvant chemotherapy, and surgical resection [3,4]. Recently, performing a liver transplantation (LT) after neoadjuvant chemotherapy has become increasingly advocated as a primary surgical treatment for children with unresectable hepatoblastomas [5,6]. Initial studies of LT performed in children with unresectable hepatoblastomas report survival rates of 50%; however, survival rates of 87% have been observed in recent multicenter registries [5,7,8].

The excellent results obtained with primary LT to treat unresectable hepatoblastomas in children are in contrast with the poor outcomes reported for primary resection,

which can result in recurrence and the need for rescue transplants, and have led some to advocate an expanded use of primary transplantation [9]. The guidelines for early consultation with a transplant surgeon to perform primary LT to treat unresectable hepatoblastomas with multifocal pretreatment extent of disease (PRETEXT) grouping IV, unifocal centrally located PRETEXT II and III involving the three main hilar structures or all three of the main hepatic veins and POST-TEXT III with macroscopic vascular invasion have been suggested [10,11]. However, surgical exploration is frequently required to ultimately determine which tumors are resectable and which require LT. Such surgery should be performed at institutions experienced in both advanced pediatric hepatobiliary surgery and LT [12].

This report presents a case of treating hepatoblastoma with aggressive resection with a backup for living donor LT.

## 2. Case Report

The patient was a 1.4-year-old male weighing 9 kg. At eight months of age, abdominal distension and anemia

were noted during screening and the patient was admitted to the hospital for further evaluation. The patient was found to have an abdominal tumor. Laboratory values demonstrated hemoglobin of 6.4 mg/dL. A contrast-enhanced computed tomography (CT) scan of the patient's liver showed diffuse density, hepatomegaly without extrahepatic involvement, and a multicentric tumor. The patient's alpha-fetoprotein (AFP) level was markedly elevated at 1,393,900 ng/ml (normal range: <10 ng/ml). A histological examination of a liver biopsy revealed the presence of the embryonal and fetal types of hepatoblastoma. The PRETEXT staging system was used to classify the tumor, which occupied four adjacent liver sections and showed inferior vena cava (IVC) invasion at the time of admission, as PRETEXT IV (Figure 1). The patient was diagnosed as having an unresectable hepatoblastoma and received seven courses of neoadjuvant chemotherapy, including three courses of CITA and a combination of cisplatin (CDDP) and tetrahydropyran-doxorubicin (THP-ADR) and four courses of ITEC, ifosfamide, carboplatin, THP-ADR, and etoposide [13]. After the repeated courses of neoadjuvant chemotherapy were administered, the patient's AFP level increased from 3111 ng/ml to 7133 ng/ml and a CT scan showed the remaining tumor at the right-sided three sections with tumor invasion of IVC, the right hepatic vein, the middle hepatic vein, and the right portal vein, with close proximity to the left portal vein (Figure 2).

Although the tumor was initially classified as PRETEXT IV, it thereafter decreased in size to that of POSTTEXT III. Right trisegmentectomy with caudate lobectomy were indicated because of the poor response to the repeated chemotherapy and the possibility for major vas-

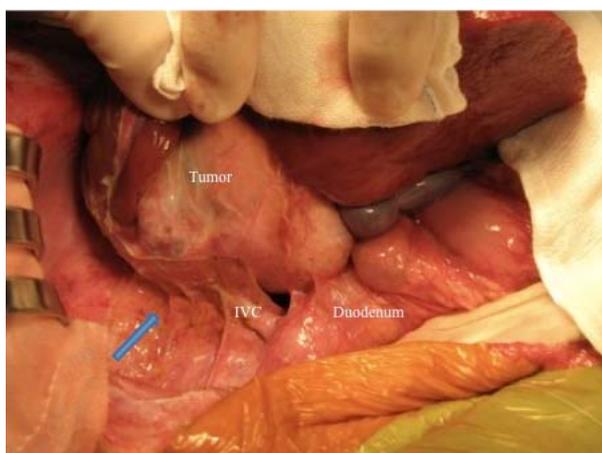


**Figure 1.** Computed tomography images obtained at the time of admission. A tumor occupying four adjacent liver sectors with inferior vena cava (IVC) invasion was classified as (PRETEXT) IV based on the radiological findings of the pretreatment extent.

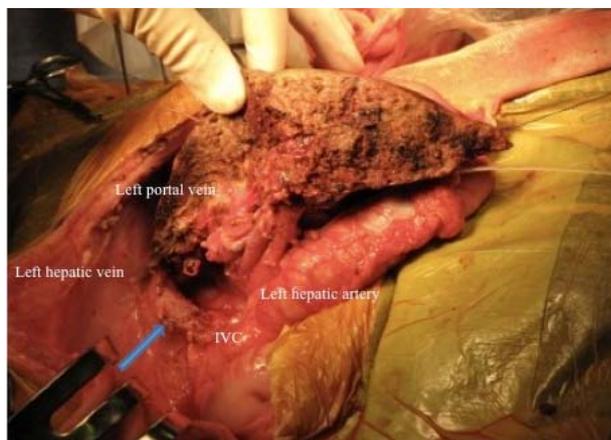
cular invasion. Since the remnant liver volume after trisegmentectomy with caudate lobectomy was estimated to be 28% of the standard liver volume, determined by preoperative CT volumetry, it was possible that hepatectomy might induce liver dysfunction; therefore, the parent had been completely evaluated as a living donor and prepared to donate, if necessary [14]. The operation revealed an enlarged right liver with tumors adhering to the IVC varying 7.2 cm in size (Figure 3). The right liver was fully removed by means of a partial resection of the right side of the IVC wall, which was successfully completed with side clump and direct closure, and right trisegmentectomy and caudate lobectomy were performed using the hanging method and the Glissonian anterior approach (Figure 4). The operation lasted 300 minutes and



**Figure 2.** The administration of neoadjuvant chemotherapy down-sized the tumor to Post-TEXT III; however, the tumor invaded the right sectors of the liver (right, middle, and caudate lobes) with invasion of the IVC, the right hepatic vein, the middle hepatic vein, and the right portal vein, with close proximity to the left portal vein.



**Figure 3.** The intraoperative findings revealed an enlarged right liver with tumors studded in the right adrenal gland and the IVC (arrow).



**Figure 4. Right trisegmentectomy and caudate lobectomy were safely performed with combined resection of the inferior vena cava (arrow).**

the amount of intraoperative blood loss measured 365 ml. The resected tumor measured  $7.2 \times 5.5 \times 4.0$  cm with a safe margin and the explanted liver volume measured 346 g. The patient's AFP level markedly decreased to 15.7 ng/ml by day 60 after the hepatectomy. The patient's postoperative course was uneventful. The follow-up continued for three years without the administration of postoperative chemotherapy and with normal AFP levels (4.5 ng/ml) observed.

### 3. Discussion

Surgery and the administration of optimal chemotherapy regimens have substantially improved the survival outcomes of children with hepatoblastoma, with 5-year survival rates of 80.9% now being achieved [13]. Although the administration of neoadjuvant chemotherapy allows for primary tumors to be resected in from 75% to 85% of all cases, factors which may limit the possibility of performing radical resection still remain, including invasion of the main vascular trunks, extension of the tumor to all hepatic lobes, poor responses to chemotherapy, and intrahepatic recurrence [15,16]. In our country, the treatment of hepatoblastoma follows the protocol proposed by the Japanese study group for pediatric liver tumor (JPLT) [13]. This protocol outlines the chemotherapy regimen and timing of surgical intervention to be used based on the PRETEXT staging and the existence of extrahepatic lesions. When considering surgical intervention, the decision to perform resection or LT could be worrisome for liver surgeons. The radiological investigation of tumors using all kinds of modalities is the key in order to provide macroscopic details of vascular invasion, the presence of which might be a significant factor in making the decision regarding surgical intervention. In this report, the tumor showed macroscopic invasion of the right hepatic vein, the middle hepatic vein, and the right portal

vein, with extrahepatic involvement of the IVC. These tumor characteristics were important in our decision to perform resection instead of LT. A judgment regarding the possibility of obtaining safe tumor margins, which may be made based on the radiological findings, is crucial for making a decision to perform resection versus LT. Recent advances in imaging techniques could provide more realistic information regarding the oncological viability of tumors; however, preoperative PRETEXT staging tends to be over-staged compared with the pathological findings of the explanted liver [2]. Calculation of the remnant liver volume that would remain if resection were to be performed is another important criterion for the decision to perform resection or LT. The quality of the remnant liver should be considered in addition to the volume because patients with hepatoblastoma receive repeated courses of chemotherapy before undergoing surgical intervention. Although the volumes of the remnant livers in the current cases were estimated to be more than 25% of the standard liver volumes, there might have been the potential for liver dysfunction. Preparing a backup for living donor LT can facilitate the intraoperative diagnosis, lead to an accurate diagnosis, and, moreover, provide a safety net for performing an aggressive resection.

Previous studies have found that total hepatectomy with LT might be an attractive modality to treat unresectable hepatoblastomas [17]. Moreover, according to these studies, the presence of solitary or multifocal hepatoblastomas involving all four liver sectors (PRETEXT IV) is a clear indication for LT, while the presence of unifocal, centrally located hepatoblastomas (PRETEXT III) may also indicate LT if surgical resection does not seem feasible [18-21]. A recent report from King's College showed the overall actuarial patient and graft survival rate for treatment of hepatoblastoma with primary LT at 5 years to be 77.6% [22-24]. In contrast, there are several significant risk factors for the development of tumor recurrence after LT. The presence of macroscopic vascular invasion or extrahepatic lesions detected at the time of LT might be a relative or absolute contraindication for LT because of the high incidence of tumor recurrence [25]. In the setting of LT, immunosuppressants may have a negative impact on tumor recurrence. Furthermore, patients who have undergone transplantation must receive life-long immunosuppression therapy, which can be associated with severe side effects, even after successful LT. Although postoperative chemotherapy after liver transplantation has remained a controversial subject, most patients might opt to receive it despite the risks of immunosuppression and post-transplant complications. Preserving a patient's long-term quality of life and maximizing survival while minimizing unnecessary morbidity should be taken into consideration when selecting a

treatment modality.

Reports regarding aggressive resection of advanced hepatoblastomas have shown 88% overall survival rates at five years despite patients being potential candidates for primary transplantation [12]. Although the decision to perform hepatectomy should be carefully considered on a case by case basis, patients with patent hepatic and portal veins should be candidates for aggressive hepatectomy when performed by experienced pediatric hepatobiliary and transplant surgeons. Moreover, the use of backup for living donor LT provides excellent results in children with hepatoblastoma because it allows for the optimal timing of the LT operation given the absence of a delay between the completion of neoadjuvant chemotherapy/aggressive hepatectomy and the planned LT [9,10,25].

#### 4. Conclusion

In summary, the patient in this case report underwent aggressive resection with a backup for living donor LT to treat centrally located hepatoblastomas. The consideration of using a backup for living donor LT as a therapeutic option for patients becomes more important in countries such as Japan which has extremely few deceased donors. Long-term observations of patients with hepatoblastoma may be necessary in order to collect sufficient data to establish the optimal surgical treatment protocol for these patients.

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