

Preoperative Transcatheter Arterial Chemoembolization of Hepatoblastoma in Infants

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ABSTRACT

Purpose: To evaluate the effect of preoperative transcatheter arterial chemoembolization of hepatoblastoma in infants.

Materials and Methods: Clinical data of 21 infants with hepatoblastoma treated between July 2008 and July 2012 in a single hospital were retrospectively analyzed. After preliminary diagnosis, surgical resection was performed in 9 infants (group I), and transcatheter arterial chemoembolization was performed in 12 infants (group II) before conventional resection. Surgical resection was performed when the tumor bulk appeared sufficiently reduced after transcatheter arterial chemoembolization alone or transcatheter arterial chemoembolization following chemotherapy in cases of pulmonary metastases.

Results: Tumor shrinkage ranged from 25%–91% with a mean reduction of 69% ($t = 3.816$, $P = .003$) in group II. α -Fetoprotein levels were markedly decreased from 49%–99% with a mean level of 95% ($t = 4.871$, $P = .000$) in group II. Specimens in group II showed massive necrosis with a mean percentage of 72% with no significant treatment-related toxicity. In group II, the surgical time was significantly shorter ($t = 3.438$, $P = .003$), intraoperative blood loss was considerably less ($t = 3.459$, $P = .003$), and the weight of the resected liver was significantly less ($t = 3.785$, $P = .001$). Of 21 patients, 16 survived for 50 months without recurrence.

Conclusions: Transcatheter arterial chemoembolization effectively reduced tumor volume, decreased α -fetoprotein, and reduced intraoperative hemorrhage. It represents a safe and effective adjuvant bridge to successful surgery for hepatoblastoma in infants.

ABBREVIATIONS

AFP = α -fetoprotein, PRETEXT = pretreatment extent of disease, PVA = polyvinyl alcohol, SIOPEL = International Childhood Liver Tumors Strategy Group

Hepatoblastoma is the most common hepatic malignancy in infants and children. It is most often detected before 3 years of age. Although radical tumor resection can prove successful (1–5), in more than half of infants with hepatoblastoma, the disease is too advanced at the time of diagnosis to allow effective surgical intervention (6). In addition, aggressive surgical intervention is associated with high mortality and survival < 30% (7,8).

Radiotherapy and chemotherapy regimens such as cisplatin and doxorubicin have proved successful since the 1970s as a pretreatment before surgical resection (9–12). Such regimens have been shown to shrink tumor mass, boost the rate of tumor resection, and increase the 5-year survival rate of infants with a diagnosis of hepatoblastoma to $\geq 75\%$ (13). However, systemic chemotherapy delivered via peripheral intravenous administration is associated with significantly reduced efficacy because the chemotherapeutic agents combine with plasma proteins before reaching the liver. Systemic chemotherapy is also associated with severe adverse effects, including bone marrow suppression and organ toxicity. High-dose chemotherapy also resulted in drug resistance and secondary malignancies (14). In the past decade, transcatheter arterial chemoembolization increasingly has been reported to be an effective preoperative adjuvant therapy for hepatoblastoma. Transcatheter arterial chemoembolization can achieve excellent efficacy with low systemic toxicity and a favorable

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safety profile (15–17). This article examines the therapeutic significance of transcatheter arterial chemoembolization of hepatoblastoma in infants before surgical resection.

MATERIALS AND METHODS

Subjects

The clinical data of 21 infants (age, < 3 y) with a diagnosis of hepatoblastoma who were treated between July 2008 and July 2012 in our hospital were retrospectively analyzed. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Guangzhou Women and Children's Medical Center.

All patients had no history of treatment for hepatoblastoma before admission. Patients presented with abdominal ultrasound, computed tomography (CT) scan, or magnetic resonance imaging showing a huge liver malignancy infiltrating most of one or both hepatic lobes. We identified 21 patients, 13 boys and 8 girls (age range, 3 mo–2 y 8 mo; average, 12.76 mo \pm 8.06). Hepatoblastoma was considered unresectable when it affected both lobes of the liver, involved most of the hepatic vein and inferior vena cava, was composed of multiple diffuse lesions, or included distant metastases. Among 21 patients, 9 patients with a diagnosis of resectable hepatoblastoma were treated with immediate surgical intervention (group I), and 12 patients with a diagnosis of unresectable hepatoblastoma underwent needle biopsy plus transcatheter arterial chemoembolization until the hepatic malignancies shrunk to a safe volume for surgery (group II).

Based on preoperative staging (pretreatment extent of disease [PRETEXT]) (18), group I included three patients in stage III, four patients in stage II, and two patients in stage I. Group II included two patients in stage IV, seven patients in stage III, and three patients in stage II. All cases of hepatoblastoma were confirmed pathologically.

Transcatheter Arterial Chemoembolization Procedures

Treatment included immediate surgical resection or preoperative transcatheter arterial chemoembolization combined with surgical resection. Using the Seldinger technique, right femoral artery catheterization was performed routinely under general anesthesia. Sequentially, a 4-F pediatric sheath was placed followed by conventional heparinization (100 U/kg [75 U/kg if weight was < 10 kg]). Abdominal aortography and abdominal angiography were performed using a 4-F Cobra catheter (Terumo, Tokyo, Japan) to investigate thoroughly the anatomy of the hepatic artery for abnormal blood vessels; the location, size, number, or type of feeding artery; and the presence of arteriovenous fistula or portal

vein obstruction. A 2.7-F Progreat microcatheter (Terumo) was selectively inserted into the artery that supplied the tumor, and chemotherapeutic drugs dispersed in ethiodized oil (Lipiodol; Laboratoire Guerbet, Roissy Charles de Gaulle, France) contrast medium were slowly injected into the liver tumor through the microcatheter.

Embolization Agents

Complete embolization of the main feeding artery and preferably all feeding arteries was achieved by administering polyvinyl alcohol (PVA) particles dissolved in contrast medium to prevent ethiodized oil contrast medium from being washed away and contributing to avascular necrosis of the tumor. The size of PVA particles used was based on the time lapsed from the appearance on imaging of the artery supplying the tumor to the appearance of the backflow vein; 300–500 μ m PVA particles were used for cases in which this time was > 3 seconds, and 500–700 μ m PVA particles were used for cases in which the time was 2–3 seconds. For some cases with larger feeding arteries, additional PVA was used to ensure complete embolization of the artery.

If the artery supplying the tumor was too big, absorbable gelatin sponge (Gelfoam; Upjohn, Kalamazoo, Michigan) particles were inserted to block the artery. In addition to the right or left hepatic arteries, branches of the superior mesenteric artery, renal artery, inferior phrenic artery, and lumbar artery were involved in supplying the tumor.

The ethiodized oil emulsion consisted of cisplatin 60 mg/m² with pirarubicin 30 mg/m² and 60% ethiodized oil 0.4–1 mL/N, where N represents the maximum diameter of the tumor in centimeters, determined by cross-sectional CT scan (13). Tumor response and indication for surgical resection were evaluated by CT scan and α -fetoprotein (AFP) analysis 4 weeks after transcatheter arterial chemoembolization. Surgical resection was carried out when tumor bulk was sufficiently reduced to allow safe resection. For infants who were found to have pulmonary metastases during transcatheter arterial chemoembolization, systemic chemotherapy was administered, repeatedly where necessary, until metastases were confirmed by CT to have disappeared. The chemotherapy regimen for patients with pulmonary metastases included 500 mg/m² carboplatin on day 1 and 30 mg/m²/d pirarubicin on day 1 and 2.

Evaluation of Therapeutic Effect

Tumor volume reduction, rate of decline, and necrotic area of the largest section of the resected specimen were compared before and after transcatheter arterial chemoembolization. The tumor reduction rate was calculated by the following formula (19): Volume (V) = Length (L) \times diameter (D)² \times 1/2.

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