Resection for Primary Liver Tumors in Children: An Experience of 52 Cases at One Institution

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Objective: *To review the authors' experiences of liver resection for primary tumors in children.*
Material and Method: *The children who had undergone liver resection for any masses between January 1996 and December 2005 were studied. Their clinical data and pathological reports were reviewed for descriptive study. Surgical data including the extent of lesions, type of resection, and post-operative complications within 60 days after surgery were analyzed. Data are expressed as mean and standard deviation (SD).*
Results: *Fifty-two children, with a male to female sex ratio of 28:24, underwent resection for primary liver tumors. Their average age was 36.64 ± 4.05 months and average weight was 12.02 ± 6.76 Kg. Asymptomatic mass was the main complaint. Ultrasonography was the initial investigation and CT scan was performed later in all patients with suspected liver mass to confirm the diagnosis and to assess the resectability. CT scan was also useful for the diagnosis of liver tumor in six cases which ultrasonography could not differentiate from other abdominal tumors. The tumors were assessed to be unresectable in 28 of 52 (53.8%) patients who had preoperative chemotherapy and became resectable later. Surgical procedures were as follows: 39 hepatic lobectomies, six extended hepatic lobectomies, and seven segmentectomies. Mean operative time was 251.04 ± 89.22 min. Mean ICU stay was 2.8 ± 3.2 days. Pathology revealed 38 hepatoblastomas, five hemangioendotheliomas, four hepatomas, two harmatomas, and three other lesions. Post-operative complications occurred in 15 children (29%) including intra-abdominal bleeding (3), subphrenic collection (1), acute liver failure (3), wound infection (2), and atelectasis (6). No mortality within 60 days after surgery occurred. Most of the patients were discharged within 10 days after surgery.*
Conclusion: *With the advancement of preoperative evaluation, more accurate diagnosis of liver tumors, and the extent of lesions has led to the proper, more effective surgical resection and further treatment, then led to zero mortality rate related to liver resection for primary tumors in the present series. Although there were significant complications, mostly minor problems and all both minor and major complications were manageable; their fatal potentials should not be underestimated.*

Keywords: *Liver resection, Hepatectomy, Liver tumors, Children*

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Liver resection is the gold standard treatment for most hepatic tumors in a pediatric population. Generally, primary liver tumors in children are uncommon. Among them, two-thirds are malignant lesions[1]. The only chance for cure for malignant primary liver tumors is the complete resection of the tumors prior to chemotherapy or any other modalities. Statistically, malignant liver tumors account for only 0.2 to 2.8% of all pediatric malignancies[2] but they are listed as the third most common abdominal solid tumor in children, after neuroblastoma and nephroblastoma[3].

Couinaud's description of the segmental anatomy of the liver based on portal venous inflow, hepatic venous outflow, and the suggested subdivision of eight segments (segment I through VIII) were key steps in the discovery and modification of

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safe, anatomic hepatic resection[2,4,5]. Such surgical refinement has allowed hepatic operative procedures to evolve to a level at which they can be performed with an acceptable morbidity and mortality related to the function of the liver after resection. However, liver resection in children who are more vulnerable to blood loss than in adults is still considered as a major operation with significant morbidity that requires skillful experienced pediatric surgeons. The objective of the present study was to review the experience of liver resection in children at one institution, represents medical school based and tertiary care hospital, regarding clinical presentations, types of procedures, pathological diagnosis, and early post-operative complications.

Material and Method

Clinical data

Between January 1996 and December 2005, pediatric patients (less than 15 years old) who underwent liver resection for liver masses at Chulalongkorn University Hospital (King Chulalongkorn Memorial Hospital) were retrospectively studied. Demographic data, clinical presentation, imaging studies, pathological reports, and information regarding types of procedures, operative time, blood loss, intra-operative complications, and post-operative complications within 60 days following the surgery were evaluated.

Investigation

Ultrasonography was the first investigation of choice in all patients with the provisional clinical diagnosis of abdominal mass. The masses were confirmed with more details about the precise location, organ of origin, characters of mass. Vascular flow of the mass may be useful information for the suspected hemangioma. However, once the liver tumor was confirmed by both clinical and ultrasonographic study, CT scan was performed to evaluate the extent of lesion(s), vascular supply, adjacent organs involvement, lymph nodes involvement and the relation of the mass to major vessels, i.e., portal vein, hepatic arteries, and veins. Then, all the information was gathered for the treatment plan including type of surgical resection.

Surgical technique

A transverse incision was preferred because of good exposure and cosmetic appearance. No matter which segment or lobe involvement, the liver was fully mobilized in every case by detaching all ligamentous attachments to the anterior abdominal wall and diaphragm. Then the liver was flipped up to expose the inferior surface where important vessels and biliary duct were easily identified and the extent of tumor together with the resection possibility was easily assessed. Hilar structures were controlled by extrahepatic dissection of porta hepatis in the hepatoduodenal ligament and ligation of the related branches of portal vein, hepatic artery, and extrahepatic biliary ducts. Whenever possible, suprahepatic inferior vena cava was exposed for easy control if necessary, hepatic veins were exposed and right, middle, or left hepatic vein was isolated and secured depending on the type and the extent of resection. Apart from the anatomical site, extension, and involvement of the tumor, another important factor to be evaluated for possible major resection was the degree of liver cirrhosis and fibrosis. When the type of resection was decided, the related vascular and biliary structures were identified and isolated then ligated and transected according to the resection type for the control and less blood supply to the resected part. Parenchymal dissection was mostly carried out by cauterization followed by finger fracture technique and ligations of corresponding branches of portal veins, hepatic arteries, and bile ducts in the liver tissue. The procedure was followed by monopolar cauterization of the raw surface.

For the last 5 years, Argon gas coagulator has been used to seal the raw surface of the liver. Intraoperative blood loss was calculated as the sum of the blood aspirated from the operative site into a suction bottle and the weight of blood soaked sponges (dry sponge weight was subtracted). Postoperatively, peritoneal drainage using Penrose drain was routine. The patients were transfused as necessary with fresh frozen plasma, packed red cell and dextrose solution. For the children with the diagnosis of hepatoblastoma that were initially considered clinically unresectable, preoperative chemotherapy would be administered to reduce the size of the tumor and improve the possibility of complete removal.

All patients were followed up for evaluation of postoperative general condition, detection of any complications and later the condition of liver function and the residual or recurrent tumor. The records were reviewed and data including preoperative, perioperative period and post-operative period within 60 days after the operation were collected for analysis.

Results

During the 10-year period, 52 pediatric patients with liver masses were managed surgically at Chulalongkorn University Hospital. There were 28 boys

and 24 girls (7:6). Their age range was between 2 and 180 months old (36.64 ± 44.05 mo) and mean weight was 12.02 ± 6.76 kg.

Ultrasonography (US), the first investigation of choice, was able to confirm the diagnosis of liver tumor in 46 cases. However, in the other six cases, US could not differentiate between liver tumor and other tumors originating from neighboring areas; CT scan was the most useful investigation method for confirming the diagnosis and the extent of lesion. CT scan was also accurate in indicating five cases of hemangioendothelioma from their characteristic appearance in the CT images.

There were 28 out of 52 cases (53.85%) assessed by clinical evaluation and imaging technologies as unresectable ones and these children (27 with hepatoblastoma (71.05%) and one case with hepatocellular carcinoma (20%)) had got chemotherapy prior to operative treatment and all responded well and were operated on later.

Surgical procedures used for resection were 39 hepatic lobectomies, six extended hepatic lobectomies, four segmentectomies, and three multiple segmentectomies. Histological examination for pathological study revealed 38 hepatoblastomas (HB), five hemangioendotheliomas, four hepatocellular carcinomas (HCC), two harmatomas, and three other conditions (embryonal sarcoma, focal nodular hyperplasia and teratoma each), as shown in Fig. 1. Mean operative time was 251.04 ± 89.22 minutes. Mean intraoperative blood loss was 52.68 ± 66.03mL/kg (range 5.6 to 270 mL/kg.). Mean ICU stay was 2.8 ± 3.2 d. (0-14 d).

Intraoperative complications occurred in six patients (11.5%). They were all related to Inferior vena cava (IVC). The IVC was involved with the tumor at the time of operation needed for partial resection in four cases and unintention injuries in two cases. Massive bleeding occurred however, they were controlled and the IVC sites of resection or injury were successfully repaired. In addition, post-operative complications were noted in 15 patients (Fig. 2); six cases of lung atelectasis with successful medical treatment and physical therapy and two cases of wound infection. Major complications include three cases with intra-abdominal bleeding requiring re-operation occurred in the first 5-year-period. One case had hepatocellular carcinoma with cirrhosis and coagulopathy and two cases had good liver tissue but faced acute liver failure. There were three cases with acute liver failure, and all recovered spontaneously after conservative treatment. One case had subphrenic collection and was successfully treated by percutaneous drainage. There was no mortality within 60 days after surgery in this report.

Discussion

Primary liver tumors in children, which are uncommon compared to those in adults, are rare and account for only 1-2% of all childhood cancer. Based on pediatric surgical articles[1,4,6-8], the authors report quite a large number of children undergoing liver resection. The most common symptom and main complaint is an upper asymptomatic abdominal mass or generalized abdominal enlargement recognized during bathing. Therefore, frequent careful examination of the abdomen by their parents or physicians might be able to detect early lesions. In the present series, even though US is proven to be good in detecting the liver tumor but is still not good enough to evaluate the extent of lesion and invasion to the important adjacent organs or structures for the precise assessment about the resectability of the masses, so CT scan was carried out on all patients. This finding matches the previous concept that anything less than CT scan of the upper

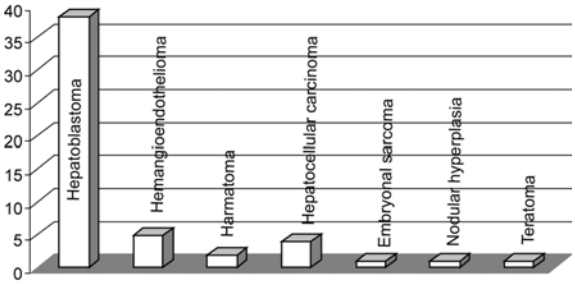

Fig. 1 Surgical pathology from 52 primary liver tumors in children over 10 years

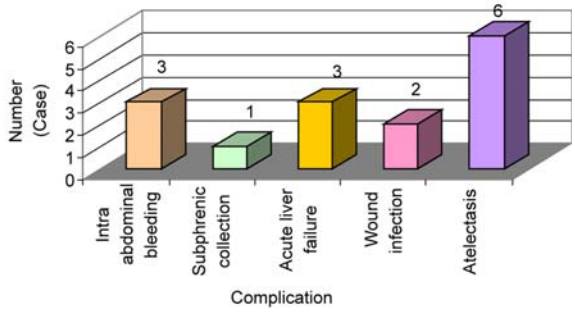

Fig. 2 Post-operative complications of resection for primary liver tumors within 60 d after surgery

abdomen was regarded as inadequate for liver tumors[1] but CT scan is also not recommended as initial investigation in every case with clinical suspicion of an abdominal mass. The authors found that CT scan is essential to guide surgeons, either to decide the choice of surgical procedures with the aim for total resection of tumors with good margin and saving most of the good liver tissue, or to give pre-operative chemotherapy for down-staging or reducing the huge mass which is hard to resect. For malignant lesions, the authors consider bi-lateral involvement that requires more than 75% resection of the liver mass or tumor invasion of portal vein and hepatic vein as unresectable tumors. Pre-operative chemotherapy would be given until the tumor size reduces enough for resection[9,10]. In the present series, 27 out of 38 patients (71.05%) with hepatoblastoma were given pre-operative chemotherapy before the surgery. This indicated that most of the hepatoblastoma cases came late for treatment and may differ from well-developed countries. Up to 85-90% of the liver may be safely resected in children if the remaining parenchyma is healthy[11,12]. Even though the results in the present series clearly demonstrates the same experience, major liver resection in children whose liver are not cirrhotic, can cause significant blood loss, which is potentially a fatal complication.

Surgical resection offers the only chance of cure in children with malignant liver tumors. Cure rates of 60% can be expected with HB and 33% in HCC if the tumor can be completely excised[3,8,12]. Nevertheless, major hepatic resection is one of the most formidable procedures in pediatric surgery. Awareness of anatomic variations in vascular and biliary anatomy is essential. The decision of resection type and refinement of operative techniques are supported by the advancement of the imaging technologies. Major intra-operative risks are bleeding, tumor embolism, hyperkalemia from tumor lysis, and bile duct injury[2,6,11]. In the present series, all intra-operative complications were bleeding related to IVC problems either involving the tumor needing partial resection or injury. Therefore, great care with prompt vascular instruments should be undertaken when performing IVC dissection.

Early post-operative complications of liver resection have been variably reported including hemorrhage, bile leak (usually from the parenchymal transection and resolving spontaneously with drainage), bile fistula, biliary obstruction, subphrenic abscess, pulmonary complications, adhesive bowel obstruction, wound problems, cardiac arrest, cardiac failure, liver abscess, liver failure, gastric perforation, respiratory insufficiency, and CNS changes[2,6,7,13]. Because of these serious complications, the authors suggest that post-operative care in the intensive care unit (ICU) is mandatory for children undergoing major liver resection. In the present series, postoperative complications occurred in 15 patients or 29% but eight of them were lung atelectasis and wound infection. Seven children (13%) experienced fatal complications; three bleedings requiring urgent re-operation, one subphrenic collection successfully treated by percutaneous drainage, and three acute liver failures with spontaneous recovery.

The review of hepatic resections in children have shown an overall operative mortality rate of 0 to 13 percent[1,3,7,12,14-17], which is less than adult cases due to less degree of underlying liver cirrhosis. It has also been agreed that operative mortality for liver resection in non-cirrhotic patients should be less than 5%. There was no mortality within 60 days after surgery in the present series based on the more careful evaluation, assessment for resection and decision about the surgical procedures.

Conclusion

Resection of primary liver tumors in children requires expertise in pediatric surgical practice. The present series showed no mortality directly related to liver resection. Although all complications were manageable, its fatal potentials should not be underestimated. Surgeons' experiences, advances in imaging technologies and pediatric anesthesia, and the availability of sophisticated intensive care are necessary for the improvement of surgical outcome.

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การผ่าตัดรักษาเนื้องอกปฐมภูมิของตับในเด็ก การศึกษาย้อนหลังผู้ป่วยจำนวน 52 ราย

สุทธิพร จิตต์มิตรภาพ, ตะวัน อิ่มวิเศษ, ไพศาล เวชชพิพัฒน์

วัตถุประสงค์: *เพื่อศึกษาข้อมูลทางคลินิกของการผ่าตัดรักษาเนื้องอกปฐมภูมิของตับในเด็ก*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังผู้ป่วยเด็กที่ได้รับการผ่าตัดรักษาเนื้องอกปฐมภูมิของตับตั้งแต่เดือนมกราคม พ.ศ. 2539 ถึง เดือนธันวาคม พ.ศ. 2548 โดยศึกษาเพื่อแสดงถึงข้อมูลทางคลินิกและทางพยาธิวิทยาของเนื้องอกของตับ ขณะเดียวกันก็วิเคราะห์ถึงความรุนแรงของโรค วิธีการผ่าตัดและข้อมูลที่เกี่ยวกับศัลยกรรมโดยเฉพาะในแง่ของภาวะแทรกซ้อนที่เกิดขึ้นภายใน 60 วันหลังการผ่าตัด*

ผลการศึกษา: *การศึกษาแสดงให้เห็นว่ามีผู้ป่วยเด็กทั้งหมด 52 คน (ชาย 28 คนและหญิง 24 คน) อายุเฉลี่ย 36.64 ± 4.05 เดือน ที่ได้รับการผ่าตัดรักษาเนื้องอกปฐมภูมิของตับในช่วงเวลาดังกล่าว น้ำหนักเฉลี่ยของผู้ป่วยเท่ากับ 12.02 ± 6.76 กิโลกรัม อาการส่วนใหญ่ที่นำมาพบแพทย์คือพบก้อนในท้องโดยบังเอิญ การตรวจด้วยคลื่นเสียงความถี่สูงเป็นวิธีการตรวจวิเคราะห์เบื้องต้นสำหรับผู้ป่วยที่สงสัยว่ามีก้อนในท้อง แต่ข้อมูลแสดงให้เห็นว่ามีการศึกษาวิเคราะห์เพิ่มเติมโดยใช้เอกซเรย์คอมพิวเตอร์ (ซีทีสแกน) ในผู้ป่วยทุกรายเพื่อยืนยันถึงโรค ขอบเขตของรอยโรค และเพื่อประเมินโอกาสที่สามารถจะตัดก้อนเนื้องอกตับนั้นออกได้ การใช้การตรวจด้วยเอกซเรย์คอมพิวเตอร์พบว่า ได้ประโยชน์ในการยืนยันการวินิจฉัยเนื้องอกในตับซึ่งการตรวจด้วยคลื่นเสียงความถี่สูงไม่สามารถให้ข้อสรุปได้ในผู้ป่วยจำนวน 6 ราย จากการประเมินพยาธิสภาพเห็นว่าไม่สามารถผ่าตัดเนื้องอกได้และต้องให้เคมีบำบัดก่อนซึ่งช่วยลดขนาดของเนื้องอกจนถึงระดับที่สามารถผ่าตัดออกได้ในผู้ป่วย 28 ราย สรุปการผ่าตัดมีดังนี้คือ การตัดตับเฉพาะกลีบใดกลีบหนึ่งหรือ hepatic lobectomies 39 ราย, การตัดตับออกมากกว่าเฉพาะกลีบหนึ่ง ๆ หรือ extended hepatic lobectomies 6 ราย, และการตัดเฉพาะส่วนย่อยของตับหรือ segmentectomies 7 ราย ค่าเฉลี่ยของเวลาผ่าตัดเท่ากับ 251.04 ± 89.44 นาที ค่าเฉลี่ยของระยะเวลาที่อยู่ไอซียูเท่ากับ 2.8 ± 3.2 วัน รายงานทางพยาธิวิทยาพบว่าเป็น มะเร็งตับชนิด hepatoblastomas 38 ราย, เนื้องอกของหลอดเลือดในตับหรือ hemangioendotheliomas 5 ราย, มะเร็งตับชนิด hepatomas 4 ราย, เนื้องอกตับชนิด harmatomas 2 ราย และเนื้องอกอื่น ๆ อีก 3 ราย มีภาวะแทรกซ้อนหลังผ่าตัดเกิดขึ้น 15 รายดังนี้ ปอดแฟบ 6 ราย เลือดออกในช่องท้อง 3 ราย, ตับวายเฉียบพลัน 3 ราย, แผลผ่าตัดติดเชื้อ 2 ราย, น้ำขังใต้กะบังลม 1 ราย ไม่มีการเสียชีวิต ที่เกิดขึ้นจากการผ่าตัด ในระยะเวลา 60 วันหลังผ่าตัด ผู้ป่วยเกือบทั้งหมดกลับไปพักฟื้นที่บ้านได้ภายใน 10 วันหลังผ่าตัด*

สรุป: *การพัฒนาในด้านการรักษาซึ่งประกอบด้วยการใช้เครื่องมือช่วยในการวินิจฉัยมากขึ้น ทำให้สามารถวินิจฉัยภาวะเนื้องอกของตับ ความรุนแรงของรอยโรค ได้อย่างดีและมีประสิทธิภาพมากขึ้น ส่งผลให้เห็นได้ว่าไม่มีการเสียชีวิตที่เกิดจากการผ่าตัดรักษาเนื้องอกตับปฐมภูมิในการศึกษาครั้งนี้ และถึงแม้ว่าภาวะแทรกซ้อนที่เกิดขึ้นมีจำนวนไม่น้อยแต่ส่วนใหญ่ก็เป็นปัญหาเล็กน้อย อย่างไรก็ตามถึงแม้จากการศึกษานี้จะพบว่าภาวะแทรกซ้อนที่พบทั้งหมดนั้นสามารถแก้ไขได้ แต่ภาวะแทรกซ้อนที่เกิดขึ้นดังกล่าวมีโอกาสที่จะมีความรุนแรงจนกระทั่งอาจเป็นอันตรายต่อชีวิต ดังนั้นปัญหาแทรกซ้อนหลังผ่าตัดที่อาจเกิดขึ้นเป็นสิ่งที่ไม่ควรมองข้ามหรือละเลยไป*