Enucleation is Better for a Giant Hemangioma Proximal to the Hepatic Portal Vascular Structures

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Received: 9 August 2015 / Accepted: 20 October 2015 / Published online: 2 November 2015
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Abstract The aim of this study is to compare the effect of liver enucleation with resection of a giant hemangioma proximal to the hepatic portal vascular structures. From 2008 to 2014, 53 patients with giant hemangiomas proximal to the hepatic portal vascular structures underwent surgery in our hospital by the same surgical team. The indications for surgery included a tumor size greater than 8 cm, a middle size greater than 4 cm but with abdominal pain, a rapidly increased tumor size with uncertain malignancy, or tumor rupture. Thirty-two patients (60 %) had pain only, 15 (29 %) had pain with tumor growth, 5 patients (9 %) had an uncertain diagnosis, and 1 patient (2 %) had tumor rupture. Enucleation was performed in 31 patients and liver resection was performed in 22 patients. There were no significant differences in the size of the hemangioma (13.9 ± 3.1 vs 12.3 ± 5.5 cm; $P > 0.05$), preoperative liver function tests, hemoglobin levels, and platelet counts between the enucleation and resection groups. The mean intraoperative blood loss was significantly less in the enucleation group compared with the resection group (350.9 ± 89.8 vs 988 ± 91.7 mL; $P < 0.01$), and the enucleation group had a significantly shorter mean operative time (1.7 ± 0.4 vs 2.9 ± 0.9 h; $P < 0.01$) and significantly shorter duration of hospital stay (9.6 ± 4.2 vs 14.7 ± 3.7 days; $P < 0.05$). Five patients in the resection group and only 1 patient in the enucleation group had major postoperative complications. Compared to liver

resection, enucleation is safer and faster for liver hemangiomas proximal to the hepatic portal vascular structures and is associated with fewer complications.

Keywords Hepatic hemangioma · Enucleation · Hepatectomy · Hepatic portal system

Introduction

Hemangioma is the most common primary liver tumor and affects 0.4–7.3 % (at autopsy) of the general population [1–3]. A giant hemangioma of the liver has been defined as a lesion greater than 4, 6, or 8 cm in diameter [4–6]. Most giant hemangiomas are located in the proximity of the hepatic portal vascular structures and receive a blood supply from the hepatic artery. With the increased use of imaging modalities [ultrasonography, computed tomography (CT) scan, and magnetic resonance imaging (MRI)], asymptomatic giant hemangiomas (>4 cm in size) are detected more frequently. Giant hemangiomas may become symptomatic due to pressure on adjacent organs or the liver. Patients with hemangiomas may present with abdominal pain, early satiety, or abdominal distention due to an abdominal mass. Rarely, a patient may present with consumptive coagulopathy (Kasabach-Merritt syndrome) [7].

There is considerable controversy regarding the need for medical intervention in patients with giant hemangiomas of the liver. During the long-term follow-up of such lesions, researchers have proposed that most of these lesions do not require any treatment as the natural history of cavernous hemangiomas in the liver are uneventful in most patients. However, others have treated these lesions surgically, citing either symptoms in the patient or an increase in size, with an occasional case of rupture or diagnostic uncertainty [8, 9].

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There are two choices for surgical treatment: anatomic resection and enucleation, and the best treatment is still under debate. Hemangiomas do not have a capsule and their walls are very thin. Once broken, significant blood loss will occur. This can be avoided by choosing anatomical resection, in which the whole liver lobe containing the hemangioma is removed. However, a residual hemangioma is possible as the shape of the hemangioma is often irregular and one of its branches or corners may extend into the neighboring lobe. In addition, resection of large lesions may be accompanied by significant blood loss, high operative time, long hospital stay, and increased postoperative complications. Considering that a hemangioma has a clear boundary and is a benign tumor, enucleation has been developed to remove the hemangioma and spare the parenchyma. It is advocated by some surgeons as an option with fewer complications, which may be associated with maximum preservation of normal liver parenchyma, limited blood loss, and reduced risk of bile leak.

Here, we report our experience of these two surgical options to treat giant perivascular hemangiomas of the liver proximal to the hepatic portal vascular structures.

Materials and Methods

Patient Characteristics and General Data

A retrospective study was performed, which included 53 patients (42 women and 11 men), with a mean age of 46.5 years (range, 26–78 years), who underwent surgical treatment of a hepatic cavernous hemangioma in our hospital by the same surgical team between January 1, 2008 and July 1, 2014. All hemangiomas were in the proximity of the hepatic portal vascular structures. Routine hematological parameters and renal and liver function parameters were assessed with no differences between the two groups before surgery. Patients underwent surgical removal of the hemangioma by either anatomic resection ($n=22$) or enucleation ($n=31$). A detailed history was taken with emphasis on the patient's symptoms. Indications for surgery included tumor size greater than 8 cm, with or without pain, rapidly enlarging mass, uncertain diagnosis, and hemorrhage. No patient in the current series presented with coagulopathy associated with Kasabach-Merritt syndrome. Variables selected for analysis included age, sex, characteristics of the tumor (location and size), surgical approach, surgical variables (operation time, amount of blood loss, intraoperative transfusion requirement, and inflow occlusion time), pathological findings, duration of hospitalization, postoperative complications, morbidity, and mortality.

Our preferred diagnostic method was ultrasonography combined with dual-phase CT scan, which was performed in

on all patients. MRI was performed when necessary. Scanning using erythrocytes labeled with technetium Tc 99m and angiography with the intention of embolization was not performed in any of the patients.

Surgery

Enucleation Enucleation refers to separation of the hemangioma from the normal liver parenchyma along the potential space between them without the removal of any normal hepatic parenchyma. A right subcostal incision or midline incision with a right horizontal extension was used. Intraoperative ultrasonography was used to assist in identifying the lesion and its relationship with intraparenchymal venous structures.

The duration of occlusion of the hepatic inflow was approximately 30 min, which was well within the tolerance of healthy liver tissue in the patients with hemangiomas. An active silastic drain was placed near the raw area after enucleation to monitor bile leaks and bleeding for 24 to 72 h.

Hepatic Resection Hepatic resection was carried out by removing the hepatic parenchyma containing the hemangioma, and blood vessels and bile ducts were ligated and divided as necessary. Careful intraoperative ultrasound of the liver was performed in order to verify tumor extension, portal and hepatic venous structures, and the presence of unknown lesions in the contralateral lobe. The Pringle maneuver was used in an identical fashion to that in enucleation to reduce blood loss. After the hepatic parenchyma was removed, manual compression of the cut surface was used to facilitate hemostasis. Residual bleeding sites were controlled with sutures, electrocautery, or argon-beam coagulation. An active silastic drain was placed and then removed as in the enucleation technique.

All patients received the same postoperative care by the same team of surgeons and were monitored in the intensive care unit during the early postoperative period. Early enteral nutrition was given when bowel activity returned. All intraoperative and postoperative complications were recorded prospectively. Surgical complications were summarized according to Clavien's classification [10].

Statistical Analysis

Data were analyzed using SPSS 17.0 and expressed as mean±standard deviation (SD). Continuous data were analyzed using the Student *t* test. Univariate analysis was performed using the Fisher exact test and the Pearson χ^2 test for dichotomized variables. A *P* value less than 0.05 was considered statistically significant.

Results

Diagnosis and General Condition of the Patients

Ultrasound examination alone was used for diagnosis in 32 patients (60 %). CT scan confirmed the diagnosis in 46 patients (87 %), and MRI scan was diagnostic in 2 patients. Hence, the preoperative diagnosis was confirmed in 48 patients (91 %).

In 28 patients (53 %), the tumors were located in the right lobe and in 20 patients (38 %) in the left lobe. Bilobar location was observed in 5 patients (9 %). Indication for surgical resection was pain only in 32 patients (60 %), pain with tumor growth in 15 patients (29 %), uncertain diagnosis in 5 patients (9 %), and rupture in 1 patient (2 %) (Table 1). Liver function tests, hemoglobin levels, platelet counts, prothrombin time, and total bilirubin were comparable between the two groups with no statistical differences (Table 2).

Process and Relevant Information of Surgical Treatments

Enucleation was performed in 31 patients to remove the tumor, while anatomic liver resection was carried out in 22 patients including the 5 patients with an uncertain diagnosis. The mean size of the hemangiomas was 13.1 ± 4.3 cm (range 5–23 cm) and was similar between the two groups [enucleation group 13.9 ± 3.1 cm (range, 6–23 cm); liver resection group 12.3 ± 5.5 cm (range, 5–21 cm)]. Forty-seven patients had a single giant hemangioma, 5 patients had two hemangiomas, and 1 patient had three hemangiomas. Anatomical liver resection was carried out with extended right hepatectomy

Table 1 Tumor characteristics and indications for surgery in patients undergoing enucleation ($n=31$) and those undergoing anatomic resection ($n=22$)

Variable	Enucleation	Resection
Age, mean $\pm$ SD, years	45.4 $\pm$ 8.9	47.6 $\pm$ 11.7
Sex		
Male	7	4
Female	24	18
Tumor size, mean $\pm$ SD, centimeters	13.9 $\pm$ 3.1	12.3 $\pm$ 5.5
Location		
Right lobe	17 (55 %)	11 (50 %)
Left lobe	11 (35 %)	9 (41 %)
Bilateral extension	3 (10 %)	2 (9 %)
Indications		
Pain	19 (61 %)	13 (59 %)
Uncertain diagnosis	2 (6 %)	3 (14 %)
Rapid growth	9 (29 %)	6 (27 %)
Rupture	1 (3 %)	0 (0 %)

Table 2 Operative and hospital course in patients undergoing enucleation ($n=31$) and those undergoing anatomic resection ($n=22$)

Variable	Enucleation	Resection	<i>P</i> value
AST (U/L)	16 $\pm$ 2.6	13 $\pm$ 3.5	>0.05
ALT (U/L)	17 $\pm$ 4.2	16 $\pm$ 1.8	>0.05
Hemoglobin (g/L)	142 $\pm$ 16.4	134 $\pm$ 23.2	>0.05
Platelet ($\times 10^9/\text{mm}^3$)	230 $\pm$ 76.4	245 $\pm$ 56.4	>0.05
Prothrombin time (s)	11.5 $\pm$ 5.2	12.1 $\pm$ 4.3	>0.05
Total bilirubin (mg/dL)	9.6 $\pm$ 3.1	6.8 $\pm$ 5.6	>0.05
Blood loss (mL)	350.9 $\pm$ 89.8	988 $\pm$ 91.7	<0.01
Blood transfusion (U)	0.4 $\pm$ 0.6	2.9 $\pm$ 1.5	<0.05
Operative time (h)	1.7 $\pm$ 0.4	2.9 $\pm$ 0.9	<0.01
Time of vascular control			
Minutes	30.4 $\pm$ 0.5	32.8 $\pm$ 3.5	>0.05
Hospital stay (days)	9.6 $\pm$ 4.2	14.7 $\pm$ 3.7	<0.05

($n=4$), right hepatectomy ($n=7$), extended left hepatic lobectomy ($n=3$), left hepatic lobectomy ($n=6$), and bilateral extension ($n=2$). The mean blood loss was 988 ± 91.7 mL (range, 150–2600 mL), and the mean operative time was 2.9 ± 0.9 h (range, 1.5–5.1 h) in the resection group.

Vascular inflow occlusion (Pringle maneuver) was performed in 21 of 31 (48 %) patients in the enucleation group, for a mean of 30.4 ± 0.5 min (range, 0–45 min), and in 10 of 22 (60 %) patients in the resection group, for a mean of 32.8 ± 3.5 min (range, 0–45 min). The period of vascular occlusion was similar in both groups ($P>0.05$). Transfusion requirement, operative time, and length of hospital stay are summarized in Table 2. Packed red blood cells (PRBC) were administered to 27 patients, and no patient received autologous blood.

Enucleation Preferred Over Resection

As shown in Table 1, the demographics, characteristics of the tumor, and indications for surgery were similar in patients undergoing enucleation and those undergoing anatomic resection. Analysis of perioperative variables such as amount of blood loss, transfusions, operative time, time of vascular inflow occlusion, and hospital stay between these two groups demonstrated that blood loss was significantly greater in the group undergoing anatomic resection than in the group undergoing enucleation ($P<0.01$) (Table 2). In addition, patients who underwent anatomic resection had a significantly longer operative time, greater blood product usage, and prolonged hospital stay ($P<0.05$).

No operative (30-day) mortality was observed. One patient (3 %) experienced major morbidity after enucleation as compared to 5 patients (23 %) after liver resection. In the enucleation group, 1 patient developed pleural effusion requiring percutaneous treatment. In the resection group, 2 patients

had a postoperative bile leak; 1 patient had fever, persistent vomiting, and ascites, which was considered ileus; 1 patient had atelectasis; and one patient had a wound infection. All of these complications were managed conservatively. The mortality rate was zero and the mean hospital stay was 11.9 days (range, 7–23 days). Due to postoperative morbidity, the hospital stay was significantly prolonged in the liver resection group compared to the enucleation group (14.7 vs 9.6 days; Table 2).

Discussion

In many patients, hemangiomas are asymptomatic and are discovered incidentally during a surgical procedure or imaging studies for unrelated diseases [11]. Advances in imaging technology have resulted in the increased detection of hepatic hemangioma [12]. The most commonly used techniques include ultrasonography, CT scan, erythrocyte scanning, and MRI scanning, used alone or in combination [13–16]. Because improved CT and MRI scanning techniques have evolved, scanning with technetium-labeled erythrocytes has been used less extensively in recent years. Core biopsy and fine-needle aspiration are reportedly safe but may be associated with pain or bleeding and are not recommended for diagnosis [17, 18].

From the literature and from our experience, surgical treatment is performed to relieve symptoms of the hemangioma and to treat complications such as severe abdominal pain and

distension, thrombocytopenia, hemorrhage, jaundice, and rupture [19, 20]. Surgical treatment should also be considered when the tumor size is greater than 8 cm or the diagnosis is uncertain [21–23]. In our opinion, asymptomatic patients with a diagnosis of hemangioma greater than 8 cm in size or a special location, such as the caudate lobe, require an operation.

Enucleation was first described in 1988 [24], and since then, many researchers have reported their experiences with this technique [22, 25–28]. Many institutions reported that enucleation can be performed safely, even with total vascular occlusion, when the hemangioma is very large or at a dangerous anatomical location adjacent to the inferior vena cava or a major hepatic vein. As enucleation is carried out along the relatively avascular capsule, the amount of normal functioning parenchyma removed is minimal. Thus, disturbance of liver function is usually insignificant. The residual cavity can be dealt with by meticulous dissection and good hemostasis, with or without omentum placement in the cavity.

In this interface between hemangioma and normal liver tissue, the hemangioma can be effectively enucleated and the vessels entering or leaving the tumor can be ligated and divided one by one (Fig. 1). Vascular inflow occlusion may be used intermittently for a longer period. We preferred enucleation as there was no excessive blood loss and less morbidity. Because there are no bile ducts traversing the plane between the liver and the hemangioma, enucleation does not result in postoperative bile leak, which is an infrequent, but troublesome,

Fig. 1 **a** Computed tomography scan of a giant hemangioma (15.6×13.1×6.9 cm) and proximity of the hepatic portal vascular structures (IVC). *Irregular line*: cutting edge. **b** and **c** Intraoperative photograph of enucleation of the giant hemangioma. **d** Giant hemangioma specimen

complication of liver resection; hence, the intra-abdominal complication rate was low. On the other hand, considering that most hemangiomas have an irregular shape, enucleation can excise the tumor thoroughly without leaving a residual tumor.

Although enucleation is the preferred method, caution is required. Firstly, when dealing with major blood vessels located very close to the hemangioma, if possible, surgeons should try to protect the trunk of the hepatic vein to reduce disturbance of returning blood flow to the liver. When tears in the hepatic vein occur, the preferred treatment method is compression with gauze to achieve hemostasis followed by suturing with 5–0 Prolene sutures. This approach is reliable and safe. To prevent an air embolism, the central venous pressure should be increased by slightly increasing the PEEP rate of the respirator. Secondly, during enucleation, separation should be along the interface between the hemangioma and normal liver tissue to avoid damaging the capsule, reduce hemorrhage, and avoid entering the normal liver parenchyma to reduce postoperative bile leak. Thirdly, when the hemangioma is deeply located and has an infiltrative character into the liver parenchyma, the best approach for a symptomatic giant hemangioma may be formal resection or angio-embolization [28]. Angio-embolization has been reported in recent years as a possible successful therapy for treating hemangioma; however, it carries the risk of damaging the blood supply in the intrahepatic bile duct and may result in biliary cirrhosis [29, 30].

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

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