PAPER

Cavernous Hemangioma of the Liver

Anatomic Resection vs Enucleation

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Hypothesis: Patient outcome and the development of major intra-abdominal postoperative complications following removal of cavernous hemangiomas of the liver are affected by methods of resection.

Design: Case-control study.

Setting: Hepatobiliary surgery and liver transplantation unit in a tertiary care referral medical center.

Patients: Between December 1, 1987, and December 1, 1997, 28 patients underwent the surgical removal of cavernous hemangioma either by hepatic resection or enucleation. Indications for the operation were pain, enlarging tumors, uncertain diagnosis, or rupture.

Main Outcome Measures: The technique of tumor removal, hospital course, and the development of intra-abdominal complications. Independent factors influencing the development of complications were ascertained by multivariate analysis.

Results: Twenty-four female and 4 male patients (age, 47.5 ± 12.4 [mean ± SD] years) underwent either enucleation (n = 23) or liver resection (n = 5). Lesions ranged from 2 to 16 cm in their postresection diameter. No surgical (30-day) mortality was observed. Four major intra-abdominal complications were found: 1 episode of intraoperative bleeding requiring abdominal packing and 3 intra-abdominal fluid collections requiring percutaneous drainage. Enucleation was the only independent factor found by univariate and multivariate analyses to be associated with a reduction in the number of intra-abdominal complications ($P = .04$).

Conclusions: Cavernous hemangiomas of the liver can be removed safely by either hepatic resection or enucleation. Enucleation is associated with fewer intra-abdominal complications and should be the technique of choice when tumor location and technical factors favor enucleation.

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CAVERNOUS hemangiomas represent the most common benign tumor of the liver.[1,2] These lesions consist of large vascular spaces lined by a monolayer of endothelial cells. Because most of these tumors are asymptomatic, the diagnosis is most commonly made by ultrasonography, computed tomographic (CT) scan, or during laparotomy for other intra-abdominal disease.[3] Occasionally, patients present with abdominal pain, early satiety, or a sensation of an abdominal mass. Rarely, a patient may present with consumptive coagulopathy (Kasabach-Merritt syndrome) resulting from sequestration and the destruction of platelets related to giant hemangiomas.[4,5]

For most patients, the natural history of cavernous hemangiomas in the liver remains uneventful, and surgical intervention can be avoided. The observation of asymptomatic lesions with routine follow-up with CT scan or ultrasonography is often sufficient.[2] Indications for the surgical removal of hemangioma may include the development of pain, especially in patients with rupture, rapidly enlarging lesions, profound thrombocytopenia, or an uncertain diagnosis of a liver mass.[6-8] In this study, we evaluated the outcome of patients who underwent the surgical removal of cavernous hemangioma and assessed factors affecting major complications postoperatively.

RESULTS

In 17 patients (61%), the tumor was located in the right lobe and, in 9 patients (32%), in the left lobe. Bilobar location was found in 2 patients (7%). Indications for surgical resection were pain alone in 16 patients (57%), pain and tumor growth in 3 patients (11%), uncertain diagnosis in 7 patients (25%), and rupture in 2 patients (7%).

The surgical removal of the tumors was by enucleation in 23 patients and anatomic liver resection in 5 patients. In the

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PATIENTS AND METHODS

PATIENTS

Between December 1, 1987, and December 1, 1997, 28 patients (24 women and 4 men) underwent surgical removal of a hepatic cavernous hemangioma in the Hepatobiliary Surgery and Liver Transplantation Unit at the Beth Israel Deaconess Medical Center, Boston, Mass. Patients underwent surgical removal by either anatomic resection (n = 5) or enucleation (n = 23). Patient medical records were reviewed for demographics, characteristics of the tumor (location and size), indication for the operation, the technique of removal (resection or enucleation), operative variables (operation time, amount of blood loss, transfusion requirement, and inflow occlusion time), hospital length of stay, and postoperative complications. Indications for the operation included pain, rapidly enlarging mass, uncertain diagnosis, and hemorrhage. No patient in the current series presented with coagulopathy associated with Kasabach-Merritt syndrome.

Methods for diagnosis included ultrasonography, CT scan, magnetic resonance imaging (MRI) scan, or combinations of more than 1 technique. Scanning using erythrocytes labeled with technetium Tc 99m was done in 4 patients to assist with the preoperative pathological diagnosis. Our current diagnostic preference is ultrasonography and dynamic CT scanning, followed by MRI, if necessary.

For patients who underwent anatomic resection, the following definitions are used for consistency[9]: *right hepatic lobectomy* includes the resection of Couinaud segments[10] 5, 6, 7, and 8, whereas *left hepatic lobectomy* refers to the resection of segments 2, 3, and 4. *Extended left hepatic lobectomy* refers to the resection of segments 2, 3, and 4 and portions of segments 5 and 8, whereas *extended right hepatic lobectomy* refers to the resection of segments 5, 6, 7, and 8 and portions of segment 4. *Left lateral segmentectomy* is limited to the resection of segments 2 and 3.[9] *Enucleation* refers to the creation of a plane between the normal liver parenchyma and the hemangioma without the removal of any normal hepatic parenchyma. *Major intra-abdominal complications* were defined as intra-abdominal infection, hemorrhage requiring reoperation and packing, and major bile leakage.

OPERATIVE TECHNIQUE

Enucleation

A right subcostal incision is used, with extension to the left side as needed. After the abdominal cavity is explored, the liver is fully mobilized by dividing the suspensory ligaments. Intraoperative ultrasonography is frequently used to assist with the identification of the lesion and its relations to intraparenchymal venous structures. Following the initial assessment of the location of the lesion, a 2.5-cm Penrose drain is placed around the hepatoduodenal ligament to provide inflow occlusion as indicated (Pringle maneuver). The capsule of the liver is coagulated with cautery to demarcate the extent of the resection and to initiate the development of a plane between the tumor and the hepatic parenchyma. The tumor is progressively separated from the parenchyma with a finger or a blunt instrument. Small bridging vessels are divided with the cautery, and the relatively few larger vessels are controlled with silk ligatures. After the hemangioma is removed, the residual cavity is manually compressed for several minutes to facilitate hemostasis. Residual bleeding points are controlled with suture ligatures, electrocautery, or argon-beam coagulation. For large defects, omentum can be placed in the bed of the cavity. A closed suction drain is placed to monitor for bile leaks and bleeding.

Hepatic Resection

Anatomic resection is performed using standard resection techniques. We prefer complete mobilization of the liver and the routine use of intraoperative ultrasonography to identify portal and hepatic venous structures. This is especially useful during right hepatic lobe resections, when large inferior right hepatic veins can be easily identified.

Once the extent of resection is decided, dissection of the porta hepatis is carried out. Generally, the portal vein and hepatic artery on the affected side are divided before bile duct division. This minimizes the risk of injury to the bile duct on the contralateral side. After the inflow vessels are divided, we generally prefer to control the hepatic veins at their level of entry into the inferior vena cava before hepatic parenchyma division. This reduces blood loss considerably and may obviate the need for total inflow occlusion (Pringle maneuver).

After the hepatic parenchyma is removed, manual compression of the cut surface is used to facilitate hemostasis. Residual bleeding sites are controlled with simple sutures, electrocautery, or argon-beam coagulation. We do not use large transhepatic compression sutures to avoid ischemic injury to the remaining segments.

STATISTICAL ANALYSIS

Results are expressed as mean ± SD. Continuous variables were compared by the Student *t* test. Univariate analysis was performed using the Fisher exact test for dichotomized variables. Multivariate analysis using logistic regression was performed to identify independent factors affecting abdominal complications. Differences were considered significant at $P<.05$ in all cases.

group undergoing anatomic resection, 2 patients had right hepatic lobectomies, 1 patient had extended right hepatic lobectomy, 1 patient had extended left hepatic lobectomy, and 1 patient had left lateral segmentectomy. The lesions ranged from 2 to 16 cm as measured after resection. Given the propensity for these vascular lesions to empty of blood during resection, the diameter of the lesions before resection was always much greater, with the largest lesion having a radiologically measured diameter of 45 cm.

Vascular inflow occlusion (Pringle maneuver) was used in 11 (48%) of 23 patients in the group having enucleation, for a mean of 14.7 minutes (range, 0-50 minutes), and in 3 (60%) of 5 patients in the group having resection, for a mean of 19.2 minutes (range, 0-45 minutes). Transfusion requirement, operative time, and length

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Table 1. Tumor Characteristics and Indications for Surgery Between the Group Undergoing Enucleation (n = 23) and the Group Undergoing Anatomic Resection (n = 5)*

Variable	Enucleation	Resection
Age, mean ± SD, y	47.6 ± 13.4†	47.2 ± 7.2†
Tumor size, mean ± SD, cm	6.0 ± 3.7†	8.6 ± 5.4†
Location		
Right lobe	14 (61)	3 (60)
Left lobe	8 (35)	1 (20)
Bilateral extension	1 (4)	1 (20)
Indications		
Pain	13 (56)	3 (60)
Uncertain diagnosis	6 (26)	1 (20)
Rapid growth	3 (13)	0
Rupture	1 (4)	1 (20)

*Data are given as number (percentage) of patients except as noted.
†Values are not statistically different by Student t test.

Table 2. Operative and Hospital Course in the Group Undergoing Enucleation (n = 23) and the Group Undergoing Anatomic Resection (n = 5)*

Course	Enucleation	Resection
Blood loss, mL	922.7 ± 1032.5†	2080.0 ± 1138.9†
Blood transfusion, U	1.2 ± 3.6	2.6 ± 2.8
Operative time, h	3.4 ± 1.2	4.3 ± 1.5
Time of vascular control, min	14.1 ± 17.8	19.2 ± 19.5
Hospital stay, d	8.2 ± 3.9	9.4 ± 2.2

*Data are given as mean ± SD.
†Blood loss statistically significant by Student t test, P = .04.

of hospital stay are summarized in the following tabulation. Packed red blood cells (PRBC) were administered to 10 patients, and 3 patients received only autologous blood.

Course	Mean ± SD (Range)
PRBC transfused, U	1.29 ± 2.88 (0-14)
Autologous blood, U	1.46 ± 3.47 (0-17)
Operative time, h	3.58 ± 1.31 (1.6-6.8)
Hospital stay, d	8.39 ± 3.65 (5-21)

As shown in **Table 1**, demographics, characteristics of the tumor, and indications for surgical resection were similar in the group of patients undergoing enucleation compared with those undergoing anatomic resection. Perioperative variables like amount of blood loss, transfusions, operative time, time of vascular inflow occlusion, and hospital stay between these 2 groups demonstrated that blood loss was significantly greater in the group undergoing anatomic resection than in the group undergoing enucleation ($P = .04$). **Table 2** demonstrates the tendency of a longer operative time, greater blood product usage, and prolonged vascular inflow occlusion and hospital stays in the group of patients treated with anatomic resection, without showing statistical significance.

Four major intra-abdominal complications were encountered. These included 1 case of persistent intraoperative bleeding that required packing and reoperation 24 hours later for pack removal; 2 patients in whom infected intra-abdominal fluid collections developed that were treated by percutaneous drainage under CT guidance, and 1 patient with a biloma in whom a bronchobiliary fistula eventually developed, requiring reoperation. There was no operative (30-day) mortality. Other significant complications included 1 nonfatal case of pulmonary embolus, 3 cases of atelectasis, 1 of urinary tract infection, 1 of postoperative ileus, 1 of antibiotic reaction resulting in anaphylaxis, and 1 of wound infection.

Table 3. Univariate Analysis of Variables Predicting Major Complications After Surgical Removal of Hepatic Hemangiomas

Parameter*	P
Operative time, h	
≥3.6	.12
<3.6	
Blood loss, mL	
≥1565	.06
<1565	
Resection vs enucleation	.01†
Vascular control time, min‡	
>15	.30
≤15	
Transfusions	
Yes	.32
No	
Vascular control used	
Yes	.20
No	

*The mean value was used as the threshold value for operative time, blood loss, and time of vascular control.
†Type of surgical resection significant by Fisher exact test, P<.05.
‡Vascular control time refers to minutes with inflow occlusion (Pringle maneuver).

UNIVARIATE AND MULTIVARIATE ANALYSIS

Univariate analysis revealed that enucleation of hemangiomas was associated with significantly fewer intra-abdominal complications compared with anatomic resection (**Table 3**). Enucleation was the only independent risk factor found by multivariate analysis to be associated with fewer intra-abdominal complications ($P = .04$). Although there was a strong trend for blood loss of greater than 1500 mL to be associated with a higher complication rate, this did not reach statistical significance ($P = .06$).

COMMENT

Hepatic hemangiomas are common tumors and have an incidence of 0.4% to 7.0% in the general population.[11,12] For most persons, these tumors remain asymptomatic and are discovered incidentally during a surgical procedure or imaging studies for unrelated problems. When symptomatic, abdominal pain, early satiety, and distention are most common.[1] Rarely, platelet sequestration with thrombocytopenia or spontaneous rupture with intraperitoneal or intrahepatic hemorrhage can occur and can be life-threatening.[2] In this study, 2 patients (7%) presented with severe pain and intrahepatic hemorrhage due to rupture.

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A computed tomographic scan showing a nodular peripheral enhancement with hypodense center after the administration of contrast medium, typically seen in hepatic hemangiomas.

The strategic approach to diagnose these lesions varies among institutions, with ultrasonography, CT scan, erythrocyte scanning, and MRI scanning used alone or in combination.[13-17] Rarely is arteriography necessary to ascertain the diagnosis or resectability. The precise diagnostic criteria for cavernous hemangiomas of the liver vary with each diagnostic procedure. For lesions found on ultrasonography, small hemangiomas are described as hyperechoic homogeneous masses.[14] Large or massive hemangiomas have heterogeneous areas interspersed within the hyperechoic mass on ultrasonography.[18] With contrast-enhanced CT scans, a peripheral nodular pattern of enhancement with a hypodense center is often seen[19] (**Figure**). Scintigraphic studies using red blood cells tagged with technetium Tc 99m show delayed filling from the periphery of the lesion, whereas a hyperintense signal is seen during T_2-weighted MRI scanning.[14,20]

The diagnostic algorithm used in our institution has been to focus on ultrasonography to assess initial tumor characteristics, followed by dynamic CT scanning to better identify anatomic relationships. We generally restrict the use of MRI to adjunctive use if the diagnosis is in doubt or if a more complete delineation of the tumor's relationship to hepatic venous structures is desired. Scanning with technetium-labeled erythrocytes has been used less extensively in recent years because improved CT and MRI scanning techniques have evolved. Core biopsy and fine-needle aspiration are reportedly safe but may be associated with pain or bleeding, and we do not recommend them for diagnosis.[21-23]

Because most patients with cavernous hepatic hemangiomas remain asymptomatic, the decision to remove these lesions surgically has been a point of controversy in previous reports.[6,24] In this series, only hemangiomas causing severe abdominal pain or those with an indeterminate diagnosis or hemorrhage were removed. In these patients, the benefit of palliating pain, excluding the diagnosis of a possible malignant tumor, or controlling life-threatening hemorrhage, justifies the risk of surgery. In an asymptomatic patient with a secure diagnosis of a cavernous hemangioma, surgical resection cannot be justified.

Once the decision to remove a symptomatic hemangioma has been made, an important surgical management issue relates to the technique of removal. Both anatomic resection and enucleation can be effective in removing the lesion. In this study, enucleation was found to be associated with fewer complications postoperatively compared with anatomic resection. Occasionally, the tumor location precludes safe enucleation, and anatomic resection can be performed more expeditiously. Given the potential for life-threatening intraoperative and postoperative complications, the surgical treatment of hepatic cavernous hemangiomas should be performed by surgeons comfortable with their removal using a variety of techniques, which will ensure a low rate of morbidity and mortality.

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DISCUSSION

Giles Whalen, MD, Farmington, Conn: Dr Gedaly and colleagues focused their gaze on this rather uncommon problem. It is the most common benign liver tumor, but it is an uncommon clinical problem, as indicated by only 28 patients during a 10-year period. It is even more uncommonly operated on. The reason is that these are often large tumors. They are bloody, may be awkwardly situated, and, perhaps most important, their natural history is not as worrisome as used to be thought. It is clear that these generally do not go on to rupture, which was previously a fear. Interestingly, you have 2 patients in this series who did appear to have rupture. Because the usual precipitating event, at least in most of the literature, has been a biopsy, or mucking around with it in some way, I would be interested in knowing whether or not those patients who had presented with a rupture, in fact, had had a previous biopsy, or were they being watched? As is expected, the most common indication for operating on 1 of these tumors is pain. I would like to hear how much pain did the patients need to be in to have an operation? Some of the pain is perhaps due to thrombosis of the vessels. The natural history of the tumor in patients with pain is not entirely clear, and it can be a difficult call. You performed these operations with your expected success and excellence, a 14% major abdominal morbidity rate and no mortality. These are large operations with large incisions, and you have demonstrated how well the technique of enucleation works. The rest of my questions go directly to your central claim: Why do you think enucleation is a better technique for these operations? Even though there is a nice univariate and multivariate analysis, I feel a bit statistically challenged. Five of the operations are resections, and there are only 4 complications. I wonder whether the operations that were resections were performed for an emergency rupture, in which case one might expect to find a higher morbidity.

The other question is, if it is such a wonderful technique, are there times when you would not use it? Are there particular circumstances when you feel that it is not indicated? If you have embarked on it and have encountered some technical difficulties, do you have any tricks that you would like to impart as to how to get out of trouble while enucleating the tumor?

Mark Callery, MD, Worcester, Mass: Dr Whalen makes some important points in this mysterious lesion. My question pivots on your patient selection. How much pain do they have to have for you to operate on them? And what are your results from relieving the pain? How do you know which patients are probably going to have a good result?

Robert Beazley, MD, Boston, Mass: I have grown up with the fear that hemangiomas may rupture, but I have never heard of one or seen one that has ruptured. These are the first 2 cases I have heard reported. Would you give us some background on the cause of the rupture, whether they were iatrogenic, steering wheel, or what?

My other question is more of a philosophical one. I think enucleation is a major advance in the management of these tumors because it is so much better than a resectional approach, so much easier and less bloody. I question whether you might know if anyone has started to do these laparoscopically?

Richard Swanson, MD, Worcester: One question on the indications. You talked about pain. Do you use size alone as an indication, or a change in size? Was that 45-cm tumor operated on purely because of the size?

Dougald MacGillivray, MD, South Portland, Me: If uncertainty in the diagnosis was the reason for operation, did you approach these lesions with plans for enucleation, or were those the patients who had resection?

Dr Gedaly: I had 2 questions concerning rupture as the cause of the surgical intervention. We have 2 patients in our series with this rare and unusual complication, representing 7% of our patients. I have found only 29 other cases of spontaneous rupture of these tumors that have been reported in the literature. Most cases of hemorrhage from hemangiomas are iatrogenic, associated with biopsies or trauma, as described in previous studies.

Another important issue is, how much pain do patients have to have to need surgery and is there any way to anticipate good results in these patients? Let me answer the second part of the question first. It is essential that the surgeon rule out other important causes of pain in the right upper quadrant, even in those patients with giant tumors that obviously seem to be the source of their symptoms. This should be performed to have a certain amount of confidence that the hemangioma is the cause of pain and to subsequently optimize the results. Some authors have described the pain as severe or incapacitating to justify surgery. Yes, we think that enucleation is an excellent operation for benign tumors, not just because it was associated with a low rate of intra-abdominal complications compared with anatomic resection in both univariate and multivariate analyses in this series. We have demonstrated that this procedure can be performed with a low major morbidity rate and no mortality, with excellent results in terms of the resolution of the symptoms.

As I said in the conclusions, both anatomic resection and enucleation can be effective in removing these tumors, and enucleation should be considered the technique of choice. In some patients, however, the location of the tumor and technical aspects preclude safe enucleation. A good example may be total lobar replacement by the hemangioma or nearly total replacement of 1 lobe in a patient with a suggestion of a malignant neoplasm in which the only way to get adequate margins is to perform a right or left hepatic lobectomy. In these circumstances, anatomic resection is a reasonable alternative, but each case should be evaluated individually.

Changing to the next question regarding laparoscopic resection of hepatic hemangiomas, I have found only a few reports of laparoscopic removal of these tumors in studies regarding laparoscopic resection of hepatic tumors. The last question was in respect to the size as an indication of surgery. Size itself is not an indication. Rapid growth may increase the suspicion that you are dealing with a hepatic cancer. In this case, uncertainty of diagnosis is the real indication for surgical exploration. I want to be clear in this particular point: indications for surgery are severe abdominal pain, uncertain diagnosis, rupture, and profound thrombocytopenia and coagulopathy associated with Kasabach-Merritt syndrome.

Dr Jenkins: The important thing is to make sure that you take your time doing this. You cannot push with your fingers very much, but it really is extraordinarily easy to develop this plane and skeletonize everything so that when you look down at the end of it with a large tumor, you have a view of the vena cava, hepatic veins, and biliary radicals. Obviously, if you get into a difficult situation, you might have to do a major hepatic resection, but this is much easier. I get calls every year from surgeons who have cut across a hemangioma at the base of it as they were doing a liver resection. They call me from the operating room and say, "What shall we do now? The patient's bleeding to death." Enucleation is a much safer way to do this.

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