Imaging of hepatic hypervascular tumors & clinical implications
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Management of Giant Liver Hemangiomas: An Update

Case Study 3

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Case study 3

INTRODUCTION

Hemangiomas are the most common benign tumors affecting the liver, occurring in the general population with incidences ranging from 0.4 to 20% [1]. Hemangiomas are composed of multiple, large vessels lined by a single layer of endothelial cells within a thin fibrous stroma.

Most hemangiomas are discovered between the thirs and fifth decade, with a mean age of 50 years at diagnosis [2] and are seen more often in females (female: male ratio = 3:1) [2]. The etiology is not understood, although a congenital anomaly has been suspected [1, 3]. Differential diagnosis include other hypervascular tumors, such as hepatocellular adenoma, hepatocellular carcinoma, metastasis of a neuroendocrine tumor or renal cell carcinoma. Most hemangiomas are small, asymptomatic and are usually incidental findings. Since the lesion is benign, these hemangiomas usually require no treatment of follow-up. Giant liver hemangiomas are defined by a diameter larger than 5 cm. In literature, there is no consensus regarding the optimal management of giant hepatic hemangiomas, be it a nonsurgical approach or resection, enucleation or selective embolization of the feeding hepatic artery.

The aim of this study is to review the current evidence concerning treatment strategies in giant hepatic hemangiomas, in combination with evaluation of management strategies for giant hemangiomas in our department. A systematic search of the literature was undertaken in PubMed, EMBASE, Ovid Medline (Ovid Technologies New York, NY, USA), and the Cochrane library database (Cochrana Database of Systematic Review) using the key words and medical subject headings ‘treatment’ and ‘giant hemangioma’ (figure 1). Two authors independently assessed study titles, abstracts and full texts, and selection was based on their relevance for the subject. The reference lists of all relevant articles appearing in the search results were scanned to check for additional publications. Only English articles were used for this study. No unpublished data were encountered.

DIAGNOSTIC IMAGING

The ultrasonographic appearance is highly suggestive of a liver hemangioma if a homogeneous, round or oval lesion is seen, which is hyperechoic, well defined and may exhibit posterior acoustic enhancement. Other imaging techniques, such as contrast-enhanced computed tomography (CT) or magnetic resonance (MR) imaging, are recommended for confirmation in case of inconclusive ultrasonographic results, or if a giant hemangioma requiring treatment is dealt with [4-6]. Characteristic, late, peripheral filling is seen after contrast administration, since the blood circulation within the tumor vessels is slow [1]. Another imaging option is the tagged red blood cell study for the characterization of hemangiomas [7]. Because of technical improvements of multiphase CT and MR imaging, liver scintigraphy, however, no longer used as routine imaging in clinical practice [8]. Frequent follow-up of imaging is not advised in patients with giant hepatic hemangiomas, since spontaneous changes are rare [9]. Previous studies have shown that the mean size of giant liver hemangiomas (n = 90) in patients who were observed, did not increase significantly, with an initial value of 7.4 ± 3.3 cm as compared with 7.6 ± 3.5 cm (P = 0.32) after a follow-up time of 5.1 ± 4.4 years [10]. A diagnostic biopsy to differentiate a hemangioma from a malignant lesion is not recommended because of the risk of hemorrhage in 1.8% of patients and the difficulty to obtain a definite diagnosis [2, 8].

Related symptoms & complications

Despite size, most patients with a giant hepatic hemangiomas are asymptomatic. A hemangioma increases in size in 10-20% of patients [11, 12] and, because it may occupy space and displace other organs, may become symptomatic with pain in the right upper quadrant of the abdomen, nausea and vomiting, mainly seen in left-sided giant hemangiomas of the liver [12, 13]. Typical abdominal pain is seen in 23-57% of patients with giant hemangiomas in the liver [14]. Schnell didorfer et al. reported chronic abdominal
**Treatment**

The management of giant hepatic hemangiomas is controversial. Several treatment strategies are available: non-surgical, expectative management, surgical (laparoscopic) resection or enucleation.

**Nonsurgical management**

Recently, a cohort study has been published by Schnellendorfer et al. in which 289 patients with giant hepatic hemangiomas are described [10]. In the nonsurgical group (n = 231), 30% of patients reported persistent complaints or new symptoms related to the hemangioma, including life threatening complications in 2% of patients. In the surgical group (n = 58), peri-operative complications were seen in 14 of patients, including 7% life threatening complications. In the latter group, no persistent or new complaints were reported after resection. Health status and quality of life were not significantly different between both groups. Therefore, the authors advise clinical observation in patients with severe symptoms or complications. Another study reported 249 patients with a giant hepatic hemangioma, of which 3.2% was treated surgically because of pain, an inconclusive diagnosis, or compression of the stomach [16]. A giant hepatic hemangioma was seen in 62 patients. These results were compared with 241 patients, who were treated nonsurgically. No complications were reported in both groups. Again, clinical observation was recommended for patients with giant hepatic hemangiomas in the liver [13]. In conclusion, clinical observation is justified in patients with giant hepatic hemangiomas, except for patients with persistent severe symptoms or with development of complications [16-18].

Several ablative techniques have also been suggested for treatment of giant hepatic hemangiomas, including percutaneous radiofrequency ablation (RFA), which in a number of case series, resulted in reduction in size of the lesion [19-22]. Even laparoscopic RFA has been reported to show promising results for the treatment of giant hepatic hemangiomas [23]. In addition, transarterial embolization (TACE) can be applied to relieve symptoms of giant hepatic hemangioma, as well as in cases of disseminated intravascular coagulation. A decrease in size of the hemangioma is usually the results; however, recurrence is common because of vascular recanalization [24].

**Surgical intervention**

The preference for laparoscopic enucleation or resection of a giant hepatic hemangioma is dependent on the obtained certainty of diagnosis, localization, size and number of lesions, and growth pattern of the hemangioma [4, 25]. Enucleation versus resection

Several authors prefer enucleation of a giant hepatic hemangioma rather than resection [17, 25, 26]. Enucleation without a margin of normal liver parenchyma is justified treatment, since hemangiomas are benign lesions. Other reported advantages of enucleation are: less intraoperative blood loss (enucleation: 400 mL vs resection: 1350 mL; P = 0.004) [17], less risk of bile leakage (enucleation: 0% vs resection: 8-17%) [25, 26], maximum preservation of functional liver parenchyma and less overall complications [3, 16, 25, 27]. No randomized controlled trials have been published that compare enucleation and resection.

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**Mechanical complaints**

Mechanical complaints arise from displacement of other organs, stretching of Glisson’s capsule, infarction in the lesion, or bleeding. Although uncommon in small hemangiomas (<1%)[12, 15], complications, such as thrombosis, infarctions and hemorrhages, have been reported in giant hemangiomas, and are characterized by acute severe pain. A spontaneous or traumatic rupture of a giant liver hemangioma is also an uncommon finding (1-4%), which has been described in some case reports [15]. However, mortality in this patient group is high (36-39%) [11].

**The Kasabach Merritt syndrome**

The Kasabach Merritt syndrome is a rare but well known complication of giant hemangio- mas, which is characterized by the combination of a vascular tumor and consumptive coagulopathy. The coagulopathy can progress to disseminated intravascular coagulation. Patients uniformly show severe thrombocytopenia, low fibrinogen levels and high fibrin degradation products, due to secondary fibrinolysis and microangiopathic hemolysis. Aim of the treatment is to eliminate the hemangioma, which has been described in some case reports [15].

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have been published that compare enucleation and resection. With enucleation, the risk of injury of bile ducts and vessels is minimal, since enucleation is performed just outside of the fibrous capsule surrounding the hemangioma, which is composed of compressed liver parenchyma. Belli et al. showed positive results after enucleation of giant hepatic hemangiomas in four patients, with preservation of sufficient normal liver parenchyma [28]. In addition, Singh et al. reported that enucleation of giant hemangiomas in the liver is safer and quicker, with less morbidity (enucleation: zero out of nine versus resection: five out of 12 patients; P = 0.045) [26]. Kuo et al. compared patients with giant hepatic hemangiomas who underwent enucleation (n = 10) with a control group (liver resection, n = 10) [29]. Patients in the enucleation group showed 49% less blood loss (400 ± 129 mL vs 742 ± 116 mL; P < 0.05) with less blood transfusions (two vs six). They concluded that enucleation is a safe alternative compared with resection for liver hemangiomas [29]. Mortality rates after liver resection for giant hemangiomas are low (0-4.3%) [30]. However, severe complications can develop after liver resection, of which intraoperative bleeding is life threatening [11, 31]. Other complications are bile leakage and infection. Postoperative insufficiency of the remnant liver is less important, since relatively little liver parenchyma is removed with resection of a giant hepatic hemangioma.

Liver tumors can also be resected by laparoscopic approach, depending on size and localization. This method can be considered in patients with hemangiomas in the left liver lobes or ventral segments. However, many surgeons are reluctant to perform laparoscopic resection in patients with large hemangiomas because of the risk of bleeding. Main case reports on laparoscopic surgery of liver hemangiomas have been described [31, 32]. Laparoscopic surgery has many advantages, such as smaller wounds and a faster return to full activity. Laparoscopic resection of giant hepatic hemangiomas will remain challenging, and is preferably performed by surgeons with a lot of experience in (open) liver surgery as well as in laparoscopic surgery [33].

**Management of hemangiomas in the AMC**

In our department, 22 patients with giant hepatic hemangiomas were evaluated (1991-2011). Figure 2 shows all patients classified according to size of hemangiomas. In this patient group, 73% of patients presented with abdominal pain. Surgical enucleation or resection was performed in 14 patients (64%) after a period of observation of 30.2 months (range: 4-96 months). The mean age of these patients was 44 ± 10.4 years (all women). Progressive abdominal pain was the indication for surgery in 12 patients. Enucleation was performed in four patients, a bi-segmentectomy in six patients, a right hemihepatectomy in two patients, a left hemihepatectomy in one patient. It should be noted that most giant hemangiomas were removed by resection, as with enucleation of these large, space occupying lesions, little parenchyma of the tumor-bearing segments would have been spared.

The mean size of resected giant hemangiomas was 13.0 cm (range 6.5-20.0 cm) compared with 9.5 cm (range 5.0-11.0 cm) in patients that did not undergo resection (P = 0.037). Abdominal complications were resolved after resection in 92% (11 out of 12) of patients with symptomatic giant hepatic hemangiomas. However, one patient had persistent complaints of pain in the right abdomen 18 months after partial liver resection for a giant hepatic hemangioma of 8.0 cm. This was possibly due to a nonspecific form of neuralgia of the abdominal wall. The median hospital stay was 8 days (range 3-21). Figure 3 shows the findings of one of our patients (female 30 years of age). Figure 3 shows the findings of one of our patients (female 30 years of age).
age), in whom a giant hepatic hemangioma was discovered during follow-up of treatment for hepati-
tis B. Because this patient did not have complaints, clinical observation was justified with outpatient
follow-up. Repeated ultrasonography 6 years later showed an increase in size reported abdominal com-
plaints. A right hemihepatectomy was decided and histological examination confirmed a cavernous he-
mangioma. A CT scan repeated 7 years postoperatively showed a marked hypertrophy response of the
remaining, left liver lobe. The image of figure 4 are of a 54-year-old female with morbid obesity, who
presented with fatigue and upper abdominal complaints, enucleation of the larger left hemangioma was
performed. In conclusion, liver hemangiomas are the most benign liver tumors. Hemangiomas of the
liver are readily demonstrated by abdominal ultrasonography or enhanced CT or MR imaging. Giant
liver hemangiomas are defined by a diameter larger than 5 cm. As complications are rare, observation
is justified in the absence of symptoms. Surgical resection is indicated in patients with abdominal
(mechanical) complaints or complications, or when diagnosis remains inconclusive. Enucleation is the
preferred surgical method according to existing literature and the authors’ own experience.

**Expert Commentary**

Hemangiomas are the most common benign tumors affecting the liver. Although they usually do not
require any treatment, there is a great deal of confusion regarding the complications and treatment of
giant hepatic hemangiomas (> 5 cm). Additionally, there is no consensus in the literature regarding
optimal management of these large tumors. Expert information, therefore, is necessary concerning
complications of giant hepatic hemangiomas, diagnostic imaging and treatment options.

The surgical risks of liver resection have greatly decreased in the past decade in specialized centers.
Whereas benign tumors, even when large and symptomatic, would previously have been declined for
resection, patients can now undergo safe liver resections with zero mortality in many centers. Giant
hepatic hemangiomas (> 5 cm) are more likely to give rise to complaints and are readily demonstrated by
contrast enhanced CT or MR imaging.

**5 Year View**

In 5 years time, the field will evolve, resulting in even more accurate imaging of giant liver hemangi-
omas and a tailored surgical approach. We suggest that enucleation will be the surgical method of choice
and that with increasing experience, more giant liver hemangiomas are amenable to a laparoscopic
approach.
Liver hemangiomas are the most common benign liver tumors, and are usually incidental findings.

Liver hemangiomas are readily demonstrated by abdominal ultrasonography, computed tomography or magnetic resonance imaging.

Differential diagnoses include other hypervascular tumors, such as hepatocellular adenoma, hepatocellular carcinoma, metastasis of a neuroendocrine tumor or renal cell carcinoma.

Giant liver hemangiomas are defined by a diameter larger than 5 cm.

In patients with a giant liver hemangioma, observation is justified in the absence of symptoms.

Surgical resection is indicated in patients with abdominal (mechanical) complaints or when diagnosis remains inconclusive. Enucleation is the preferred surgical method according to existing literature and our own experience.

Spontaneous or traumatic rupture of a giant hepatic hemangioma is rare, however, the mortality rate is high (36-39%).

An uncommon complication of a giant hemangioma is disseminated intravascular coagulation (Kasabach-Merritt syndrome); intervention is then required.