Management of giant liver hemangioma.

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Abstract

Liver hemangiomas are the most common benign vascular neoplasms of the liver and are often diagnosed incidentally during abdominal surgical procedures or in abdominal imaging studies. Liver hemangioma is qualified giant when its diameter exceeds 5 cm. The natural progression of giant hemangiomas is not clearly defined and the risk of life-threatening complications is not well established. Reported single centers studies demonstrated the safety of expectant management of even very large asymptomatic hemangioma with very low risk of adverse events. Therefore, tumor size alone as an indication for surgery is not supported by any published data. Based on published studies results, the indications of surgery are well defined and with the improvement of liver surgery, surgical resection of liver hemangioma can be performed with nil mortality and very low morbidity. Other therapeutic options as Radiofrequency Ablation (RFA) and Transcatheter Arterial Embolization (TAE) can be considered in some situations.

Keywords: Giant liver hemangioma, Resection, Observation.

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Introduction

Liver hemangiomas are congenital vascular malformations and are the most common benign liver tumors. Their prevalence varies from 5% to 20%. Most hemangiomas are asymptomatic, small (<4 cm) and often diagnosed incidentally on abdominal imaging studies. A hemangioma is qualified giant when having a diameter of more than 5 cm. Giant hemangiomas can become symptomatic and even may cause complications such as mechanical complications and coagulopathy [1]. The reported studies demonstrated that the expectant management of asymptomatic giant hemangiomas even very large size can be safely conducted with lower rate of adverse events. Symptomatic giant hemangiomas with severe incapacitating symptoms, consumptive coagulopathy, diagnostic uncertainty, lesion growth and complications as bleeding and rupture, are the most indications for surgical treatment [2-6]. Surgery is become the most effective method procedure to treat Hemangiomas with a low risk of morbidity and mortality [7,8]. However other treatment options can be considered, including transcatheter arterial embolization (TAE) [9], radiofrequency ablation (RFA) and liver transplantation when liver resection is not technically feasible or in patient with high risk of surgical complications [10-13].

Literature Review

Expectant management approach (observation)

Studies assessing expectant management or observation of asymptomatic giant hemangiomas are retrospective, limited to single center studies [14-23]. The primary outcomes including development of new symptoms and adverse events were analyzed in most of these studies. Thus, the interpretation of the data is limited to center specific and often inadequately defined practices in the management of giant hemangiomas. Nevertheless, the trends in outcomes provide insight into the safety and lower rate of adverse advents with expectant management or observation of asymptomatic giant hemangiomas. Reported the most recent study evaluating the management of 307 patients with giant hemangiomas [15]. Two hundred nineteen asymptomatic patients were managed expectantly (Observation). Elective surgery was performed in 94 patients principally for symptomatic lesions (62 cases), diagnostic uncertainty (11 cases) and for fear of future complications (21 cases). However surgical resection was indicated for tumor growth in observation group in only 9 cases (4.1%). In contrast to other studies, the authors reported a 9% of major complications rate in the observation group with two fatalities from traumatic hemangioma rupture. Mortality was nil and symptom resolution was achieved in 88% of operated symptomatic patients with lower morbidity rate [14] reviewed 74 patients who were managed for giant liver hemangiomas in regional hepatobiliary referral center. Thirty-four patients underwent observation. Surgical resection was initially performed in 33 patients and indication of surgery was mainly abdominal symptoms and diagnostic uncertainty. In the observation group, only 7 of 14 tumors which demonstrated growth underwent surgical resection and 5 of resected tumors had an additional indication for resection as abdominal pain and Kasabach-Merritt syndrome. The tendency to enlarge decreased over time and there was no significant increase in mean lesion size or development of new symptoms during the follow-up period in the observation group. Another single institution study which supported the safety of expectant management of asymptomatic giant hemangiomas was reported by Terkivatan et al. [20]. During the period study, 49 patients with giant hemangiomas were included for management. Thirty-eight patients were managed with observation. There was no significant difference in the mean diameter of lesions in the observation group. Abdominal pain, which was noted in 12 patients on initial evaluation, was not attributed to the hemangioma and it resolved in each case during follow-up. None of the asymptomatic patients developed new symptoms during a mean follow-up period of 59 months. However, one
asymptomatic patient who developed growth by exhibiting 5 cm of growth over 36 months follow-up had been operated. As for surgical group, resection was performed in 10 symptomatic patients and indication for surgery was exclusively abdominal symptoms related to hemangioma. As reported by Yeo [17] in a large retrospective single-institutional cohort study evaluating the rate of hemangioma-associated complications and quality of life in patients with giant hepatic hemangioma after both clinical observation and surgical management. Among 450 patients managed for liver giant hemangioma, only 289 patients (64%) have been evaluated including 233 (81%) patients categorized into the observation group and 56 (19%) patients into the surgical group. Twenty (20%) of observed patients developed new-onset symptoms or complications with 2% being life-threatening. Resolution of symptoms (persistent or new-onset symptoms) was observed in 46 patients (20%) and only 32 patients (14%) developed enlargement in size of 1 cm during follow-up. Surgery was necessary in 14 symptomatic patients (6%). In 56 patients of surgical group, hemangioma resection. In the operative group, surgery was mainly indicated for abdominal pain and complications (jaundice, hemorrhage). Interestingly, neither size nor numbers of hemangioma were associated with adverse events in either group. Health status and quality of life varying from good to excellent were similar in both resected and observed patients leading to conclude that observation was safe in most patients. Regarding the obtained results cited above, expectant management of asymptomatic giant hemangiomatas is still justified, even in large lesions, when it is possible to control related hemangioma complaints with analgesics [24,25]. Published studies from many centers demonstrated that asymptomatic giant hemangiomas even very large lesions can be safely observed with low rate of adverse events and tumor size alone is not supported as an indication for surgery in asymptomatic lesions [14-23].

**Surgical Approach**

**Indications for surgery**

The indications of surgery for giant hemangioma are well defined. Symptomatic giant hemangioma with abdominal pain and discomfort not controlled by medical treatments is commonly the major indication for surgery. However before considering surgical therapy, it is mandatory to confirm the relationship between symptoms and hemangioma by excluding other possible causes of abdominal pain, such as, gallstones, peptic ulcer disease or gastroesophageal reflux disease. As reported in surgical series, the complaints relief was observed in 82% to 100% of patients correctly assessed before surgery [20,26,27]. Considering the benign and non-progressive nature of the disease, it is currently accepted that a giant hemangioma is not necessarily an indication for surgery just because of its size, and continued observation in asymptomatic patients or patients with minimal abdominal symptoms seems to be justified [21,28]. The growth rate of lesion is considered as the second reason for indication of surgery, but it remains a controversial and the trajectory of growth over long term follow-up and its implication for lesion rupture risk is uncertain and not clearly defined. Thus, hemangioma size is usually stable and reported increase in size varied from 8.7 to 14% [10,14,15,20] and a minimum of 25% increase in largest diameter over a period of 6 months was defined as a rapid growth justifying indication of surgery for asymptomatic hemangiomas [18]. The increasing in lesion size can raise the suspicion of malignancy; and as speculated, diagnostic error is higher in patients with rapid tumor growth. Although, there is no provided clinical data to support the claim of increased risk of diagnostic error with rapid growth, however the lesion should carefully be assessed [26]. Diagnostic uncertainty is the third most common indication of surgery for vascular liver tumor when a definitive diagnosis cannot be made from radiologic studies, particularly in the setting of known extra-hepatic malignancies or in the presence of risk factors for the development of liver malignancy (cirrhosis, hepatitis, steatosis).

**Discussion**

Nowadays, diagnostic uncertainty has become much less common with advances in medical imaging modalities and experience at high-volume centers. Therefore, the diagnostic certainty can be established in most cases by combined use of various imaging techniques. The diagnostic uncertainty as an indication for surgery was significantly decreased during last 10 years due to the significant impact of advances in medical imaging [23]. Percutaneous biopsy is considered dangerous because of the risk of bleeding and tumor rupture [29]. However, surgery is indicated when the doubt persists and in such situation, patients are more likely to be asymptomatic and having a smaller lesion with history of malignancy [21]. Consumptive coagulopathy or Kasabach-Merritt syndrome requires a surgery, but its incidence is extremely rare. Emergency surgery for complicated liver hemangiomas is seldom necessary and bleeding, spontaneous rupture, and tumor thrombosis have been exceptionally reported [15]. Patient anxiety and his willingness due to the undesirable feeling of living with a hepatic tumor, even if asymptomatic, should not be considered a good indication for surgery anymore [30]. Even if the patient’s wish has to be considered, the surgeon must well explain the risk of liver surgery comparing to the benign natural history of the disease and the safety of observation option. The hemangioma size is supported by some authors as an indication for surgical treatment of asymptomatic lesion, suggesting resection for large left liver hemangiomas which carry a risk of hepatic trauma. This prophylactic indication has never been established or supported by conclusive prospective observational data. There is not an absolute size threshold for indication of surgery in the reported more recent studies. However, it seems reasonable to indicate surgery for the safety of the patient with giant hemangioma carrying the risk of trauma [26].

**Surgical procedure**

Technical aspects of surgical treatment may vary greatly between centers. Hepatic resection and enucleation are the most commonly used surgical procedures to treat surgically liver hemangiomas. The choice between these two techniques is still an open matter; depending on the experience and results of high volume centers. The enucleation is preferred by some authors because there is a dissection plane between hemangioma and liver parenchyma making transversing vessels ligation much simpler decreasing the risk of blood loss, and the risk of
postoperative bile leak is much lower due to the absence of bile ducts in the enucleation dissection plane. Also, enucleation preserves the healthy liver parenchyma avoiding unnecessary parenchyma loss for the treatment of benign tumor [21,26]. Compared to peripherally located hemangiomas, enucleation of centrally located hemangiomas is more likely associated with longer operative time and higher rate of blood loss and transfusion [31]. Recently reported, the risk of bleeding and blood transfusions is to be more related to hemangioma size than to the type of surgical technique [14]. As reported by some authors, enucleation can be performed with fewer intra-abdominal complications compared to hepatic resection [20]. Furthermore, evolution toward enucleation over resection even for large hemangiomas over time with less blood loss and transfusions and less complications have been documented and reported [32]. Liver resection is the first surgical method used to resect hemangioma and since Couinaud defined the segmental anatomy and the avascular planes, performing hepatectomy had become a safer surgical procedure. Some authors prefer anatomic liver resection [15] and considerable number of studies suggested that hepatic anatomical resection can be performed with reduced intraoperative blood loss and reduced need to blood transfusion [33]. Recently reported [34], hepatic resection and enucleation of giant hemangioma are associated with similar rate of blood loss and transfusions. Furthermore, the risk of bleeding and blood transfusions was more related to tumor size [34] and blood transfusion was more needed in patients with hemangiomas larger than 10 cm in size [15]. When indicated, liver resection for hemangiomas can be performed safely with low morbidity and nil mortality rates [14,20,30-34]. However recent multi-institutional studies reported a complications rate ranging from 10% to 27.3% following surgical resection and the overall rate of Clavien grade 3 complication or higher was 5.7% including bile leaks and bleeding after surgical management of liver hemangiomas [35]. Hence the documented risks of surgery must be carefully weighed against the severity of symptoms and the very low risk of complications associated with observation. Laparoscopic surgical procedures for liver benign tumors including hemangiomas have been increased up to 26% during the last two decades because no radical margins are requested, and healthy parenchyma is more manageable than diseased liver [36,37]. However, the above indications for surgery should be maintained and cannot be widened by the possible laparoscopic approach. Limited resections of the anterior segments of the liver can be easily performed by mini-invasive surgery. Thus, the impact of a minimal access approach in reducing operative risk or complications is not clearly defined. On the other hand, giant hemangiomas located in the right liver, are usually very close to intrahepatic major vessels and are difficult to be manipulated, leading to increase the risk of the laparoscopic approach. [33,38-40]. Liver transplantation has already been performed to treat an extremely rare cases of diffuse hepatic hemangiomatosis and lesions anatomically unresectable by conventional approaches in patients with the Kasabach-Merritt syndrome [10,12,13,41].

Non-surgical therapies

When indicated, surgery remains the definitive treatment of giant liver hemangioma. However other less effective options have been proposed and consisted of non-surgical therapies including: Hepatic artery ligation (HAL), Trans arterial embolization (TAE) and Radiofrequency ablation (RFA). Hepatic artery ligation advocated for unresectable tumors, has been shown to arrest the growth of some lesions and even effect partial regression of others. This method has disadvantages including limited experience and its ineffectiveness in some patients. So, in the era of “safe” liver surgery, hepatic artery ligation should no longer be recommended [26]. Trans arterial embolization has been used as an alternative treatment for symptomatic hemangiomas [42]. A reduction of symptoms may be possible, but tumor size remains stable after the procedure and recurrence is common. Trans arterial embolization is widely performed both in the setting of acute management to stabilize ruptured hemangioma and preoperatively to reduce vascular inflow and to decrease size in very large tumors making surgical resection less risky [43].

Radiofrequency ablation has also been used to control symptomatic giant hemangiomas with promising results. A single institution initial experience using RFA to treat giant hemangiomas (41 patients) have been reported by [43] The use of RFA in lesions with diameter higher than 10 cm had a very high rate of complications (100%) including life-threatening complications (lower esophageal fistula and acute respiratory distress syndrome) suggesting its inappropriate use in lesions larger than 10 cm. However, RFA use was successful to controlling symptoms with only minor complications in smaller lesions (5-10 cm diameter). Medical therapies such as the anti-angiogenic agent bevacizumab and the tyrosine kinase inhibitor sorafenib have been reported to decrease the size of large hemangiomas, but published data is limited to case reports. Therefore, application of non-surgical therapies may lead to a less invasive and safer management approach of hemangiomas in the future.

Conclusion

In summary; published retrospective studies from many centers demonstrated that asymptomatic giant hemangiomas even very large lesions can be safely observed, and tumor size alone is not supported as an indication for surgery in asymptomatic lesions. Furthermore, surgical resection or another alternative treatment modality should be considered if symptoms or complications occur. The indications of surgery for giant hemangioma are well defined and surgical approach is widely accepted in symptomatic giant hemangiomas. The symptom development is the most often indication for surgical resection. However, the relative risks of surgery are balanced by a direct benefit of symptom resolution. Though symptom resolution after resection varies in published studies, a high rate of symptom relief is expected if initial symptoms were really related to giant hemangiomas. Rapid tumor growth is considered as an indication for surgery during observation periods, but the risk of rupture related to increase in size is not clear. However rapid lesion growth may prompt further investigation to confirm diagnostic and exclude malignancy. Diagnostic uncertainty is accepted as the most common indication for resection. Nowadays, the combined use of developed various imaging techniques can establish the diagnostic certainty in most cases. Surgical management
is required for hemangioma complications such as Kasabach-Merritt syndrome or consumptive coagulopathy and rupture or bleeding. Regarding patient anxiety and fear of complications, anxiety should be managed non-operatively and explaining to the patient the very low risk of adverse events associated with observation. When surgery is indicated, both liver resection and enucleation can be employed as surgical procedure to resect giant liver hemangiomas with low morbidity and nil mortality rates.

**Conflict of Interest**

The authors have no conflict of interest to report.

**References**


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