

Therapeutic approaches of giant hepatic hemangiomas

Abstract

HH are the most common benign tumor of liver. The wide use of imaging tests for various indications has increased the diagnostic rate of HH. GHH are defined as hemangiomas larger than 4cm in diameter and they can give symptoms. Not all cases of GHH require therapeutic intervention, being a part treated conservatively with observation. Other cases need therapeutic approach, which may be surgical or radiological procedures. To avoid the risks of surgery, several studies are trying to prove the efficacy and safe of the minimally invasive techniques in the clinical practice. In this review, we are going to discuss the main therapeutics strategies available for GHH.

Keywords: giant hepatic hemangioma, treatment, surgery, minimally invasive procedures

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Abbreviations: HH, hepatic hemangioma; GHH, giant hepatic hemangioma; RF, radiofrequency; TAE, trans-catheter arterial embolization

Introduction

Hepatic Hemangioma is the most common benign tumor of liver, with a prevalence ranging from 3 to 20% in autopsy series.¹ The lesions are considered to be congenital vascular malformations that enlarge by ectasia rather than neo-plastic growth.² The incidence of HH is highest in third to fifth decade of life and is more common in women by the exposure to high levels of estrogen and progesterone.³ The wide use of imaging tests for various indications has increased the diagnostic rate of HH.⁴ Most HH are small in size (<4cm in diameter) and remain asymptomatic, requiring no treatment. Giant Hepatic Hemangiomas (GHH), by other side, is defined as hemangiomas larger than 4cm in diameter and can give symptoms.⁵

Indications of surgery include the presence of progressive abdominal symptoms, spontaneous or traumatic rupture, rapidly enlarging lesions, Kasabach-Merritt syndrome and unclear diagnosis.⁶ Size alone, is not an indication of surgery.⁷ Although operative resection is the most effective and the gold standard treatment method for GHH symptomatic-enlarging, resection is invasive, and the operative morbidity and mortality ranging up to 27% and 3%, respectively. To avoid this operative risk, many attempts have been made to treat HH by minimally invasive procedures.⁸ In this perspective, this review seeks to understand and analyze the scientific publications that discuss the most current treatment alternatives for HHG.

Discussion

Management of GHH ranges from observation to a variety of radiological and surgical interventions. Most patients with HH are asymptomatic and have their tumor detected incidentally during routine imaging or investigation of other conditions.⁹ Considering the benign and non-progressive nature of the disease, it is currently accepted that the diagnosis of GHH is not necessarily an indication for surgery. A continued observation in asymptomatic patients or in patients with minimal abdominal symptoms appears to be justified.¹⁰

Rare complications may occur, particularly when the HH are large and superficially located. Intra-peritoneal bleeding from rupture, which can occur either spontaneously or traumatically, is a very rare but life threatening complication.¹¹ Nevertheless, prophylactic surgical intervention is not broadly applicable.¹² Schnellendorfer T et al.¹³ demonstrated that non-operative management of GHH asymptomatic is safe even in patients with extremely large hepatic hemangiomas. Patients with uncompensated anxiety triggered by diagnosis, independent of lesion size or symptoms, could be an exceptional indication for prophylactic resection.¹³

When patients have complaints, other causes such as dyspepsia and functional abdominal pain must be discarded. GHH may compress adjacent organs and structures and cause symptoms such as abdominal pain and early satiety.⁹ The most common indications for treatment in symptomatic patients include pain, mass growth, risk of malignancy, local compression, and rupture.¹⁴ In several studies, the number of symptomatic patients that did not appear to benefit from surgical treatment ranged from 0 to 27%.¹¹ A variety of techniques can be used for surgical treatment, as enucleation, hepatic resection, laparoscopic approaches and liver transplantation. Recent advances in surgical techniques and established perioperative management have now made it possible to perform liver resection or enucleation safely in most specialized units. However, massive intra operative hemorrhage remains a risk, especially GHH >10cm in size, because of the likelihood of major vascular injury.¹² Thus, operative intervention should be recommended only in patients with symptoms that are sufficiently severe to affect lifestyle and to justify operative risk.¹⁵

The size and location of the lesion influence the decision to perform either a segmental resection or an enucleation.³ Operative series comparing enucleation and lobectomy have shown that complications, such as bleeding from damage to blood vessels and bile duct injury, were significantly more common and more serious after lobectomy. Moreover, avoiding unnecessary loss of healthy liver parenchyma is always desirable in this benign disease.¹² Therefore, enucleation is preferred when feasible for symptomatic GHH.¹⁶ However, for larger lesions, enucleation would be more difficult resulting in greater blood loss and lobar resection maybe the preferred option.³ The resection

laparoscopy offers many advantages compared to laparotomy, such as decreased blood loss, shorter hospital day, more cosmetic scars and early return to normal life. The currently acceptable indications for this technique include patients with solitary lesions of <5cm diameter located in liver segments 2 to 6.¹⁷ Liver transplantation is an option for cases of symptomatic patients with un-resectable lesions, acute and chronic hepatic failure and occurrence of Kasabach-Merritt syndrome.¹⁸

Seeking to reduce the risk of surgical resections, much has been studied about the minimally invasive techniques. A Radiofrequency (RF) ablation has been used widely in the past decade for local destruction of hepatic malignant neoplasms because of its many advantages over resection, including minimal invasiveness, low complication rate, decreased cost and decreased duration of hospital stay. This therapy also has been performed successfully in HH, resulting in promising outcomes. The benign biological nature of HH determines advantages in at least three aspects compared to malignant neoplasms. First, the ablation of HH does not require ablative margins of the normal parenchyma. Second, a well-performed ablation of HH may lead to an obvious collapse of tumor tissue around the ablation zone, making ablation more efficient and easier than in malignancy. Third, residual tumor, if it occurs, will not grow rapidly nor send distant metastases.⁸

Several studies shown that symptomatic patients benefit from the RF ablation with pain relief and shrinkage of lesions, HH with a diameter of less than 10cm can be treated safely e effectively with RF. Its application for lesions over 10cm is still controversial due to greater technical difficulty and risk of complications.¹⁹ The complications, including hemoglobinuria, anemia, jaundice, and mild renal failure, were direct results of hemolysis and their severity was directly proportional to the extent of haemolysis.²⁰ This procedure can be performed via percutaneous, laparoscopic approach or laparotomic approach.²¹ Another kind of ablation is a microwave technology, which produce ablation zones that are hotter, larger, form faster and are more reproductive than RF ablation. This method appears to be safe and effective in initial studies.²²

Another promising treatment option is the Trans-Catheter Arterial Embolization (TAE). This method is used to shrink the GHH through blocking vascular reserve, consequently leading to decrease hemorrhage rates during surgery.²³ However, it is still not established whether TAE can be used alone for HH. Recently, combined TAE with RF ablation has attracted attention as a more promising technique for improving the local control of hepato cellular carcinoma, even in wide lesions.¹⁹ In HGG, this combination appears to be safe and effective treatment. The common complications of TAE for the treatment of HH are nausea, vomiting, abdominal distention, fever, hepatic dysfunction, abnormal embolization and intra-hepatic bile duct injury.²⁴ The prominent symptom in post embolization syndrome is abdominal pain and it is solved within 48hours.²⁵ Radiotherapy has been used successfully to treat the symptoms and induce involution of hemangioma in few institutions, but the rarity of this occurrence makes the result difficult to interpret. On the whole, the data justifying the use of radiotherapy in hemangioma is scant.²⁶ Non-surgical treatment of GHH in stable patients includes the use of interferon. This drug is known to inhibit endothelial cell migration and proliferation in vitro and an angiogenesis in vivo, exerting a suppressive effect on the vascular endothelium.²⁷ A few case reports have described its efficacy in the treatment of vascular malformations and neoplasm. Some patients demonstrated symptomatic and radiological improvement with its use.²⁸

Conclusion

The gold standard treatment for symptomatic GHH is still the surgery. However, the minimally invasive technique has shown promising results in several studies, with satisfactory pain control and shrinkage of the HH, having enough potential to reduce the need for surgery, still lacking studies with higher level of evidence to validate the true role of minimally invasive techniques.

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Conflict of interest

Author declares that there is no conflict of interest.

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