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Giant Haemangioma of the Liver: Observation or Resection?

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Key Points

1. Cavernous haemangioma are the most common benign solid tumour of the liver.
2. Giant haemangioma are defined as those measuring ≥5 cm in diameter.
3. The natural history of liver haemangioma is generally uncomplicated.
4. Liver function tests are usually normal.
5. The successful management of giant haemangioma depends on establishing the diagnosis, determining the requirement for surgical intervention and, where necessary, defining the optimal type of surgery.
6. Patients must be counselled that surgery may not alleviate their symptoms.
7. Surgery should only be considered for patients with complicated or symptomatic lesions, or where the diagnosis remains uncertain despite appropriate specialist investigation.

Introduction

Liver haemangioma are a common incidental finding, reflecting a high prevalence within the population. With increasing application and resolution of abdominal imaging modalities, haemangioma are detected more frequently. Originating from the mesodermal layer, these lesions represent a congenital, non-neoplastic hamartomatous proliferation of vascular endothelial cells [1]. Current evidence indicates that haemangioma have no malignant
potential. Macroscopically, haemangioma tend to remain stable in size. Weimann et al. [15] reported size increases in 11 (10.6%) of 104 patients with liver haemangioma. Jaundice is unusual and, despite reaching large dimensions, spontaneous rupture of a giant haemangioma is exceptional. While fewer than 50 cases of spontaneous rupture have been reported [10], the mortality rate can be appreciable, up to 60% in one series [16]. Traumatic rupture is a recognised but rare complication with a handful of cases described in the literature [17].

Liver function tests (LFT) are generally normal in the presence of giant haemangioma, although LFT abnormalities have been reported as a consequence of biliary compression by the mass [18]. Patients with a giant haemangioma may exhibit inflammatory features, and Bornman et al. [19] described a clinical triad in 4 patients, consisting of signs suggestive of an acute inflammatory process within the liver, normal white cell count and normal LFT. Haematological markers of inflammation, e.g. raised erythrocyte sedimentation rate, thrombocytosis and hyperfibrinogenaemia, may be detected in association with giant haemangioma and can be reversed by resection [20]. However, in a further small group of patients with giant haemangioma exhibiting inflammatory features, none displayed a leucocytosis [18]. Clinical features of polymyalgia rheumatica have also been described in association with a giant cavernous haemangioma. These features also resolved following resection of the lesion [21].

Kasabach-Merritt syndrome [22] is characterised by thrombocytopenia and consumptive coagulopathy in association with large haemangioma (fig. 1), and may prompt intervention. Platelet trapping in the haemangiomata is thought to result in activation of platelets and the clotting cascade, resulting in a consumptive coagulopathy [22]. The mortality rate of Kasabach-Merritt syndrome approaches 30% [23].

**Reported Experience**

In a series of 163 hepatic haemangioma, reported by Farges et al. [10], with a mean follow-up of 92 months, only 9 haemangioma increased in size and 7 decreased. Complications included 2 cases of Kasabach-Merritt syndrome, 1 intrahepatic bleed, and 2 cases of Budd-Chiari syndrome. 16 patients underwent intervention including 8 resections, 5 arterial embolisations, 2 transjugular intrahepatic portosystemic shunts, 1 right hepatic artery ligation, and 1 liver transplantation. Liver transplantation has been used by a number of groups for unresectable disease, and for Kasabach-Merritt syndrome [24].

**Cavernous Haemangioma: Presentation and Natural History**

Cavernous haemangioma are the most common benign solid tumour of the liver [5] and have been reported in up to 7.3% of autopsy studies [6]. These lesions are more usually found in women (female: male ratio = 5:1), with a mean age at diagnosis of 50 years, most lesions being detected between the 3rd and 5th decades. Prevalence is greatest in women with higher parity [7, 8]. Although there is no proven association with oral contraceptive use, this relationship remains controversial. Cavernous haemangioma occur more frequently within the right liver and multiple lesions occur in 10% of cases [6]. Similar haemangiomatous lesions may occur in other organs [9].

The majority of evidence indicates that the natural history of liver haemangioma is uncomplicated [10–13] and most lesions are asymptomatic. Symptoms associated with haemangioma should be interpreted cautiously. In a series of 87 patients with liver haemangioma, Farges et al. [10] reported that 54% of these patients had other identifiable causes for their abdominal symptoms. While lesions <10 cm in diameter seldom cause symptoms, patients with larger lesions may present with abdominal pain, due to stretching of Glisson’s capsule, compression of local structures, intralesional thrombosis and infarction or, less commonly, haemorrhage. The risk of clinically relevant haemorrhage appears to be less than 1% [14]. Haemangio-
have also reported extracorporeal resection for ‘unresectable’ giant haemangioma [25]. Non-operative adjunc-
tive measures such as transarterial bland embolisation or
chemoembolisation have been reported as a ‘bridge to
surgery’ [26], as well as a unimodality treatment.

In a series of 115 patients, recognised as being selected
surgical referrals, Yoon et al. [27] reported 6 episodes of
thrombosis and 3 cases of infarctions or necrosis, but no
cases of rupture. The authors concluded that complica-
tions were uncommon and that indications for resection
should include severe symptoms, inability to exclude ma-
lignancy and complications. These authors advocated
enucleation, first described by Alper et al. [28] in 1988,
with good long-term outcomes [29].

Lerner et al. [4] reported outcomes from a case series
of 52 resections for giant cavernous haemangioma. This
group has moved towards a policy of enucleation rather
than resection over time. The perceived benefits of enu-
cleration over resection include reduced intraoperative
blood loss, reduced bile leak rates [30] as well as maximis-
ing preservation of functional hepatic parenchyma.

In a series from the Memorial Sloan-Kettering Center,
35% of resections were performed in asymptomatic pa-
tients. Haemangioma >10 cm were overrepresented in
the resected group (58%), the median size in this group
being 11 versus 4 cm in the unresected group. In this se-
ties, enucleation was performed in 14% of cases where
malignancy was suspected. Enucleation of potentially
malignant lesions is difficult to justify and data regarding
the long-term outcome of this approach are not available.

Management

The successful management of giant haemangiomata
depends on: (1) confirming the diagnosis; (2) determin-
ing whether the lesion requires surgical treatment; (3) de-
termining the optimal type of surgery, and (4) avoiding
unnecessary surgical intervention. A detailed history
should be obtained, addressing relevant risk factors.
Symptoms unrelated to an incidentally detected haeman-
gioma should be clarified and alternative cases, e.g. cho-
lelithiasis, liver disease, excluded. Liver biochemistry is
usually normal, although abnormalities may indicate
haemorrhage, infarction, neoplasia or be associated with
a non-haemangiomatous aetiology.

Management: The Case for Observation

In the face of a large body of evidence indicating a be-
ign and uncomplicated natural history for the majority
of haemangiomata, including giant haemangioma, a
policy of non-operative management will be the optimal
approach for the majority of patients. While morbidity
and mortality rates associated with liver resection and
enucleation in specialist centres are low, adverse events
do occur. The risk of potential complication must be care-
fully weighed against operative risk. Surgery should
therefore be reserved for cases of absolute necessity.

The decision to manage giant haemangioma expec-
tantly depends largely on the certainty of diagnosis,
which in turn is reliant on the quality of non-invasive
imaging and its interpretation. Transabdominal ultra-
sound is diagnostic in approximately two thirds of cases
[31]. However, axial imaging will usually also be under-
taken. Haemangioma tend to be hypodense on non-
contrast computerised tomography and show peripheral
followed by central enhancement. Isoenhancement with
the arteries is typical. Delayed scans show persisting con-
trast enhancement and features such as corkscrewing
and ‘cotton wool’ appearance reflect the abnormal ves-
sels within the lesion. Globular enhancement, isodense
with the aorta, has been shown to be 67% sensitive and
100% specific in differentiating haemangioma from
metastases [32].

Magnetic resonance imaging (MRI) may be of value in
establishing the diagnosis. Typical features include high
signal intensity on T2-weighted series and discontinuous
nodular peripheral enhancement (fig. 2). In some cases,
MRI features can be correlated with histological ones, e.g.
presence of hypocellular myxoid tissue [33].

Applying a combination of axial imaging modalities
will generally allow the diagnosis of haemangioma

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Giant Haemangioma

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Fig. 1. Giant haemangioma of the right lobe which was associated
with thrombocytopenia and consumptive coagulopathy: Kasab-
bach-Merritt syndrome.
to be made with an adequate degree of certainty to justify a plan of expectant management. The static nature of giant haemangiomata means that once the diagnosis is established, further follow-up may be unnecessary [34].

**Management: The Case for Operative Management**

**Established Complications.** In the minority of cases that present as a surgical emergency due to haemorrhage, rupture, thrombosis and infarction, surgical management may be the only appropriate course of action. There is also a role for the elective surgical management of giant haemangiomata, albeit in a highly selected group of patients. As demonstrated by the data presented above, an operative approach with the objective of preventing future complications of giant haemangiomata is less easy to justify.

**Diagnostic Uncertainty.** Despite improvements in non-invasive imaging technology, cases of diagnostic uncertainty continue to pose a challenge. In situations where it is not possible to exclude malignancy, surgical intervention by formal liver resection may be indicated. In almost all situations, the use of percutaneous liver biopsy for the differentiation of giant haemangiomata from malignant liver lesions cannot be justified. The risks of haemorrhage as a result of biopsying a giant haemangioma are appreciable and, together with the risks of needle track seeding and intra-abdominal dissemination of a potentially curable malignancy, mean that biopsy in this setting must be avoided.

**Incapacitating Symptoms.** Having taken all possible steps to ensure that symptoms are attributable to the haemangioma, surgical resection may be justified on grounds of intractable symptoms. Patients with clearly defined abdominal compressive symptoms may be more likely to derive benefit from surgery than patients with non-specific abdominal discomfort, although this is not backed up by a meaningful body of evidence. Management of this group of patients is, by necessity, highly individualised. Despite apparently satisfactory surgical management, symptoms persist in approximately 25% of patients following resection of seemingly symptomatic haemangiomata.

**Conclusions**

Decision-making with regard to the optimal management of giant haemangiomata depends on a high level of confidence in diagnostic imaging. Diagnostic biopsy to differentiate giant haemangiomata from malignant lesions should in general be discouraged. The risks of potential complications and the severity of symptoms need to be carefully weighed against surgical risk. Patients must be counselled that surgery may not alleviate their symptoms and an individualised approach is essential. Despite limitations and alternative modalities, surgery remains the only consistently effective curative treatment for giant haemangiomata and should be considered for patients with complicated or symptomatic lesions, where operative risk is acceptable, or where the diagnosis remains uncertain despite appropriate specialist investigation. The choice of enucleation versus formal resection depends upon factors including the certainty of diagnosis and anatomical considerations such as the location and extent of the lesion. Formal resection may be preferable for potentially malignant lesions, and for lesions that totally replace an anatomical section of the liver. However, enucleation offers the benefit of potentially lower operative morbidity.

The advent of minimally invasive resectional liver surgery offers the possibility for the further reduction of perioperative morbidity and mortality. While this development should not substantially lower the threshold for selecting haemangiomata patients for surgery, if individual surgeons can demonstrate more favourable outcomes for those treated laparoscopically than by open surgery, this approach may alter the balance of risk and benefit in favour of surgical management of giant haemangiomata in a small proportion of symptomatic patients.
References