

Is regular follow-up scan for giant liver haemangioma necessary?

CME

Wilson WC Ng 吳咏志
 YS Cheung 張宇新
 KF Lee 李傑輝
 John Wong 黃 創
 Simon CH Yu 余俊豪
 Paul SF Lee 李醒芬
 Paul BS Lai 賴寶山

Objectives To review the reliability of radiological diagnosis and need of regular scans for giant liver haemangioma, in terms of long-term outcome and management options.

Design Retrospective study.

Setting Division of Hepato-biliary and Pancreatic Surgery, Prince of Wales Hospital, Hong Kong.

Patients Patients with giant liver haemangioma noted on initial imaging from February 1996 to July 2006.

Main outcome measures Patient demographics, clinical assessments, management, and outcomes.

Results There were 42 female and 22 male patients with a median age of 49 (range, 27-84) years with a suspected haemangioma. The median maximal diameter of the lesions was 5.5 cm (range, 4.0-20.3 cm). They were first detected by ultrasonography (n=45), contrast-enhanced computed tomographic scan (n=18), or magnetic resonance imaging (n=1). Besides regular follow-up scans, 22 patients were investigated further to confirm the diagnosis/exclude malignancy. Finally, 63 patients had a haemangioma and one had a hepatocellular carcinoma. Regarding the patients with haemangiomas, two were operated on for relief of pain and the rest were managed conservatively. The median duration of follow-up was 34 months. Most (54%) of the patients were asymptomatic, but in 17% the haemangioma enlarged to exceed its original size by more than 20%. There were no haemangioma-associated complications.

Conclusions Majority of patients having giant liver haemangioma are asymptomatic and do not suffer complications. If the diagnosis is uncertain, selective further investigations may be necessary. Lesions with a confirmed diagnosis tend to remain static in size; performing regular scans for asymptomatic giant liver haemangiomas may not be necessary.

Key words

Hemangioma; Liver neoplasms; Magnetic resonance imaging; Tomography, X-ray computed

Hong Kong Med J 2007;13:353-8

The Chinese University of Hong Kong,
 Prince of Wales Hospital, Shatin, Hong
 Kong:

Division of Hepato-biliary and
 Pancreatic Surgery, Department of
 Surgery

WWC Ng, FRCS (Edin), FHKAM (Surgery)

YS Cheung, MB, ChB, MRCS

KF Lee, FRCS (Edin), FHKAM (Surgery)

J Wong, FRCS (Edin), FHKAM (Surgery)

PBS Lai, MD, FHKAM (Surgery)

Department of Diagnostic Radiology and
 Organ Imaging

SCH Yu, FHKAM (Radiology)

PSF Lee, FHKAM (Radiology)

Correspondence to: Prof PBS Lai

E-mail: paullai@cuhk.edu.hk

Introduction

Haemangioma is the most common solid benign hepatic lesion, with a reported prevalence of 0.4 to 7.3% in western countries.¹ Most are small and remain asymptomatic. Diagnosis usually relies on imaging, including ultrasonography (USG), contrast-enhanced computed tomography (CT), and magnetic resonance imaging (MRI). Owing to the high prevalence of chronic hepatitis B virus infection in South-East Asia² and the current widespread use of these investigations for the screening of hepatocellular carcinoma, more and more liver haemangiomas are likely to be detected incidentally.

Liver haemangioma is a vascular malformation (not a neoplasm) and becomes enlarged by vascular ectasia. Morphologically it is a reddish, well-defined lesion, which is compressible on digital pressure. For small and asymptomatic liver haemangioma, conservative management with periodic review is the recommended management strategy. However giant (≥ 4 cm) haemangioma³ may give rise to symptoms, including: abdominal pain, abdominal distension, early satiety, and rarely Kasabach-Merritt syndrome (thrombocytopenia due to entrapment of platelets within haemangioma) or even rupture. Moreover, the latter lesions may also have atypical radiological features, generating diagnostic uncertainty and the need for further investigation. Hence, for patients having such

是否必須為肝臟巨大血管瘤進行規律隨訪掃描？

目的 回顧肝臟巨大血管瘤的遠期結果及處理方法，以決定放射學診斷的可靠性和規律隨訪掃描的必要性。

設計 回顧研究。

安排 香港沙田威爾斯親王醫院肝膽胰外科。

患者 1996年2月至2006年7月期間，進行首次影像學檢查並診斷為肝臟巨大血管瘤的病人。

主要結果測量 患者的人口學資料、臨床評價、處理計劃和結果。

結果 共收集64例病人（42例女性，22例男性），其年齡中位數為49歲（介乎27至84歲）。最大血管瘤的中位數為5.5 cm（介乎4.0至20.3 cm）。首次進行影像學超聲波掃描、電腦斷層掃描和磁力共振造影掃描的病人數目分別為45：18：1。除了規律的隨診掃描外，22例進行了進一步的檢查以明確診斷和排除惡變。最後診斷63例為血管瘤，1例為肝癌。對於所有的血管瘤患者，2例接受手術治療緩解疼痛，其他病例均接受保守治療。隨訪時間的中位數是34個月。大部份病人（54%）沒有症狀，17%的病人血管瘤比原來增大了超過20%。隨訪期間沒有與腫瘤有關的併發症。

結論 大部分患有肝臟巨大血管瘤的病人沒有症狀並且在隨診時沒有併發症。當遇到不確定的病例時有必要選擇性使用進一步檢查。一旦診斷明確而血管瘤並無增大，可以不必對無症狀的肝臟巨大血管瘤進行規律掃描。

patients is limited. We therefore aimed to review (a) the reliability of radiological and related means for diagnosing giant liver haemangioma, and (b) the need for regular follow-up scans. At the same time, we also set out to review our experience in managing such lesions and their long-term outcomes.

Methods

We recruited all patients attending our institution, who were diagnosed to have a giant liver haemangioma (≥ 4 cm) at initial imaging between February 1996 and July 2006. A retrospective review of all relevant patient medical records was performed. Patient demographic data, presentation, tumour characteristics on imaging, other investigation findings, surgical procedures, and clinical outcomes were recorded. Moreover the results of corresponding blood tests (complete blood count, renal and liver function tests, serum α -foetal protein [AFP] level, carcino-embryonic antigen [CEA] level, and hepatitis B and C serology) were analysed and logged. Most patients with giant haemangioma had regular follow-up USG or CT scans yearly or half-yearly; during follow-up, their symptoms, investigation results, and any related complications were also recorded.

Statistical analysis was performed using Fisher's exact test for categorical variables with the aid of the Statistical Package for the Social Sciences (Windows version 14.0; SPSS Inc, Chicago [IL], US). A P value of less than 0.05 was regarded as statistically significant.

Results

A total of 64 patients (42 female and 22 male) were included. The final diagnosis was haemangioma in 63 patients and hepatocellular carcinoma in one. Hence 63 patients were used for the subsequent analysis. Their demographic and baseline clinical features are summarised in Table 1. In all, only 23 of the 63 patients were symptomatic (having upper abdominal pain) at presentation. Diagnosis based on initial imaging by USG or CT was uncertain in 11 of the patients, and suspicious of malignancy in four others. All 15 of these patients underwent further imaging (Table 2). The correct diagnosis of liver haemangioma was established in 73% of patients having an initial scan by USG and 78% having an initial scan by CT. Additional investigations were performed for seven patients because of atypical features on imaging, enlargement, and suspicion of malignancy (Table 3). Notably, one of these patients with an initial diagnosis of giant haemangioma by USG scan was subsequently found to have hepatocellular carcinoma. The radiological investigations, results and follow-up plan for these 64 patients are summarised in Figure 1. There were no procedure-related complications.

Due to the high prevalence of chronic hepatitis

TABLE 1. Demographic data and clinical features of 63 patients with a confirmed diagnosis of giant liver haemangioma

Demographics/clinical features*	Value
Mean age (SD; range) [years]	49 (10; 27-84)
Sex (M:F)	21:42
Median maximal diameter of tumour (range) [cm]	5.5 (4.0-20.3)
USG:CT:MRI as first imaging	44:18:1
No. symptomatic at initial presentation	23 (37%)
No. with hepatomegaly	8 (13%)
No. positive for HBsAg	10 (16%)
No. positive for anti-HCV Ab	0
No. with elevated AFP level	6 (10%)
No. with elevated CEA level	0
No. of operated patients	2 (3%)
Median follow-up duration (range) [months]	34 (1-115)

* AFP denotes α -foetal protein, CEA carcino-embryonic antigen, CT computed tomography, HBsAg hepatitis B surface (antigen), HCV hepatitis C virus, MRI magnetic resonance imaging, and USG ultrasonography

giant and/or symptomatic haemangiomas, enucleation or even lobectomy is the usual recommended treatment.^{4,7} However, published information on the natural course of giant liver haemangioma in Asian

TABLE 2. Further imaging performed for 15 patients with uncertain diagnosis or suspicion of malignancy based on the first imaging*

Reasons	No. of patients	Investigations	Results
Uncertain diagnosis			
USG	9	4 CT scan, 2 liver biopsy, 2 USG, 1 RBC scan	Haemangioma in all cases
CT scan	2	1 PET scan, 1 liver biopsy	
Suspicion of malignancy			
USG	2	1 CT scan, 1 liver biopsy	Haemangioma in all cases
CT scan	2	1 liver biopsy, 1 hepatic angiogram and day-10 lipiodol CT scan	

* CT denotes computed tomography, PET positron emission tomography, RBC red blood cell, and USG ultrasonography

TABLE 3. Additional investigations for seven cases of giant liver haemangioma*

Reasons	No. of patients	Investigations	Results
Increased in tumour size	3	2 liver biopsy, 1 RBC scan and liver biopsy	Haemangioma in all cases
Suspicion of malignancy† (due to raised AFP)	1	1 hepatic angiogram + day-10 lipiodol CT scan	Hepatocellular carcinoma
Atypical features in follow-up scan	1	1 liver biopsy	Haemangioma
Confirmation by more accurate scan	2	2 RBC scan	Haemangioma in all cases

* AFP denotes α -foetal protein, CT computed tomography, and RBC red blood cell

† Not related to first imaging

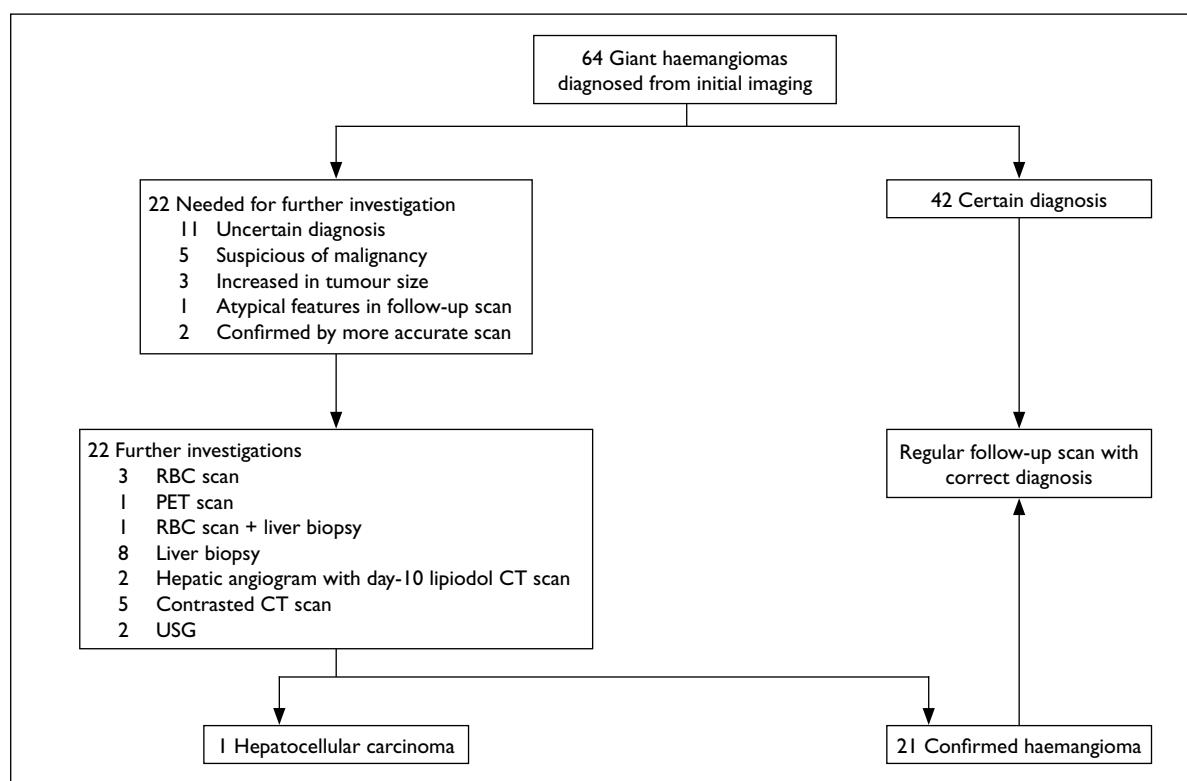


FIG 1. Flowchart of investigations for giant liver haemangioma after initial radioimaging

CT denotes computed tomography, PET positron emission tomography, RBC red blood cell, and USG ultrasonography

TABLE 4. Comparison of surgical resection rates for liver haemangioma in our patients and three other large series

Study	No. of patients	Rate of surgical resection
Present study, 2007	63	3.2%
Yoon et al, ⁹ 2003	115	45.2%
Ozden et al, ¹⁰ 2000	171	24.6%
Farges et al, ¹¹ 1995	163	4.3%

B virus infection (8.8%) in Hong Kong,² hepatitis B serology was checked in all patients, 10 (16%) of whom were found to be antigen carriers. Fifty-three patients had hepatitis C serology tested but none was found to be a carrier. The AFP level was checked in all patients; it exceeded the reference level (<7 µg/L) in seven patients—being 99 µg/L in a pregnant woman, and ranged from 7 to 15 µg/L in the rest. The CEA level was checked in 43 patients only and all the results were within the normal range. No thrombocytopenia was observed in our patients.

Two female patients had their giant haemangioma surgically resected, both of whom had intractable abdominal pain. One underwent open left lateral segmentectomy 7 years after the diagnosis, though the tumour size had remained static all along. The other underwent laparoscopic left lateral segmentectomy 3 weeks after the diagnosis, because of pain and unrelieved anxiety. She had already undergone oesophagogastroduodenoscopy to exclude other causes of abdominal pain and was provided adequate preoperative counselling about the benign nature of the tumour for the patient. Both patients had complete resolution of abdominal pain after the surgery and both pathologies were confirmed to be liver haemangioma.

One hepatitis B carrier was wrongly diagnosed to have giant haemangioma by initial USG scan. A hepatic angiogram was performed for the patient to rule out malignancy because of his elevated AFP level (12 µg/L). His hepatic angiogram showed a hypervascular tumour in Couinaud's segment IV B supplied by an enlarged middle hepatic artery, and the day-10 post-lipiodol CT scan had increased lipiodol uptake by the tumour. These features were all suggestive of hepatocellular carcinoma. Non-anatomical liver resection of Couinaud's segment IV B was performed for the patient; pathology confirmed it was a hepatocellular carcinoma.

The median duration of follow-up for these patients was 34 (range, 1-115) months. Six asymptomatic patients complained of upper abdominal pain during subsequent follow-up, and thus 46% of our patients were symptomatic. Among the symptomatic patients, 15 (52%) underwent oesophagogastroduodenoscopy to rule out co-existing upper gastro-intestinal tract diseases. Among the latter, five had acute gastritis,

two had peptic ulcers, two others had ischaemic heart disease, and four had gallstones or gallbladder polyps that might also have accounted for their symptoms.

Compared to its original size, in 11 (17%) patients, the respective haemangiomas enlarged by at least 20%, and in four by more than 40%. In these 11 patients, the median rate of enlargement was 7.8 mm (range, 3.6-26.6 mm) per year. At the latest follow-up scan, seven of the corresponding lesions had nevertheless remained static in size. There was a tendency for symptomatic patients to have enlarging lesions with an odds ratio of 2.4 (confidence interval, 0.6-9.2; $P=0.32$), but the association did not reach statistical significance. No rupture of a haemangioma or Kasabach-Merritt syndrome ensued.

Discussion

Liver haemangioma may be a congenital or acquired lesion. In our series there was the characteristic female predominance. The association of hepatic haemangioma with female sex hormones is not entirely clear, and may be influenced by both endogenous and exogenous factors. A significant increase in the size of liver haemangiomas was demonstrated in women exposed to hormone therapy.⁸ The majority (63%) of our patients were asymptomatic at presentation, and of these most remained symptom-free during long-term follow-up. In the minority of symptomatic patients, the cause of abdominal pain is unclear. Postulated mechanisms include: increase in tumour size with liver capsule distension, intra-tumoural thrombosis, tumour inflammation, tumour haemorrhage or even rupture. Intractable pain, complications (haemorrhage or rupture), and inability to exclude malignancy are the usual indications for tumour enucleation or liver resection.^{4,7} However, pain alone as an indication for surgery remains controversial. Adequate pain control and counselling to relieve anxiety should be offered before recommending surgery. Common diseases such as ischaemic heart disease, peptic ulcer, gallstone, or musculoskeletal disorder can be the cause of upper abdominal pain and should be considered as alternative causes of symptoms. The surgical resection rate for liver haemangioma in our study was 3% (2/63 patients) and none were treated by trans-arterial embolisation. Compared to other large series published in the literature, our resection rate was relatively low (Table 4⁹⁻¹¹). This may be due to the high proportion (54%) of asymptomatic patients in our series or that they had greater pain tolerance. Diagnostic uncertainty is another commonly encountered problem in the management of liver haemangioma. Ultrasonography, contrast CT, and MRI are the usual imaging investigations performed for liver haemangioma. The typical features of giant haemangioma on USG are heterogenous

areas interspersed within an hyperechoic mass.⁴ In contrasted CT scans (Fig 2), haemangiomas usually demonstrate a peripheral nodular pattern of contrast enhancement with a hypodense centre.¹² In MRIs, there is a hyperdense signal in the T2-weighted images.¹³ However, some haemangiomas (especially small lesions) can have atypical features.¹⁴ In the study carried out by Yoon et al⁹ at the Sloan-Kettering Cancer Center, the diagnosis of haemangioma was established by USG in 57%, by CT scan in 73%, and by MRI in 84% of the patients. Most of our patients had their radioimaging performed in our centre. However, the first imaging was performed in other hospitals or by a private radiologist in Hong Kong. Evidently red blood cell (RBC) or MRI scans are regarded as the most accurate imaging tools for diagnosing liver haemangioma. The reported sensitivity and specificity being 89 and 100% respectively for RBC scans, and 90 and 92% respectively for MRIs.^{15,16} In our study one patient had an MRI and four had RBC scans; these scans confirmed the original diagnosis.



FIG 2. Radiological features of giant liver haemangioma in contrasted computed tomographic scan

Eight of our patients underwent liver biopsy at which the diagnosis of haemangioma confirmed and none developed any biopsy-related complication. Although needle biopsy of the liver is associated with local complications (bleeding, infection or injury to adjacent organs, and possibility of needle track seeding of tumour cells), the rate can be kept below 3%, depending on the size of needle.¹⁷ In a report by Tung and Cronan,¹⁸ who performed percutaneous needle biopsies on 38 patients with cavernous hepatic haemangioma, no complications were encountered except transient right upper quadrant pain in five individuals; the latter received no special treatment. They attributed improved safety of the procedure to the following: (1) selection of patients with no bleeding diathesis; (2) better design of smaller-diameter needles (eg 20-gauge needle) allowing effective core biopsy; (3) imaging-guided biopsy to allow precise localisation and reduction in the number of passes to enable adequate sampling; (4) ensuring interposition of normal liver between liver capsule and the cavernous haemangioma so that any bleeding from the lesion could be contained.

In our retrospective study, the rationale for further investigations (eg hepatic angiogram, contrasted CT scan, liver biopsy, RBC scan, MRI, etc) was not always clearly stated in the records. We believe such decisions should be individualised based on the overall clinical suspicion for malignancy. In our study, liver function tests had little bearing on distinguishing benign from malignant liver tumours, because a significant proportion (16%) of our patients

were hepatitis B carriers, some of whom had liver cirrhosis with deranged liver function. Among the two serum tumour markers, only the AFP levels appeared helpful (in one patient). To exclude hepatocellular cancer, further investigations were carried out on 21 (33%) of our patients, who also continued to have yearly or half-yearly follow-up scans thereafter. The remaining 42 (67%) patients with a certain diagnosis of giant haemangioma at presentation also underwent regular follow-up scans, but only 11 lesions were subsequently noted to enlarge significantly (>20% of the original size). There was no false-negative diagnosis in this group of patients. Only two patients with giant haemangiomas underwent surgery for intractable symptoms, while the others were kept under observation. For asymptomatic patients with a certain diagnosis of giant haemangioma, the need for regular scans is questionable as they would appear to be a waste of medical resources. In summary, the majority of patients with giant liver haemangioma are asymptomatic and are not liable to late complications. Selective further investigations are necessary if the diagnosis is uncertain, depending on the overall clinical assessment of the patient and the level of suspicion for malignancy. Once the diagnosis is confirmed and the lesion tends to remain static in size, the practice of undertaking regular scans for patients with asymptomatic giant liver haemangiomas may not be necessary.

References

1. Ochsner JL, Halpert B. Cavernous hemangioma of the liver. *Surgery* 1958;43:577-82.
2. Mohamed R, Desmond P, Suh DJ, et al. Practical difficulties in the management of hepatitis B in the Asia-Pacific region. *J Gastroenterol Hepatol* 2004;19:958-69.
3. Adam YG, Huvos AG, Fortner JG. Giant hemangiomas of the liver. *Ann Surg* 1970;172:239-45.
4. Lise M, Feltrin G, Da Pian PP, et al. Giant cavernous hemangiomas: diagnosis and surgical strategies. *World J Surg* 1992;16:516-20.
5. Brouwers MA, Peeters PM, de Jong KP, et al. Surgical treatment of giant haemangioma of the liver. *Br J Surg* 1997;84:314-6.
6. Kuo PC, Lewis WD, Jenkins RL. Treatment of giant hemangiomas of the liver by enucleation. *J Am Coll Surg* 1994;178:49-53.
7. Lerner SM, Hiatt JR, Salamandra J, et al. Giant cavernous liver hemangiomas: effect of operative approach on outcome. *Arch Surg* 2004;139:818-23.
8. Glinkova V, Shevah O, Boaz M, Levine A, Shirin H. Hepatic haemangiomas: possible association with female sex hormones. *Gut* 2004;53:1352-5.
9. Yoon SS, Charny CK, Fong Y, et al. Diagnosis, management, and outcome of 115 patients with hepatic hemangioma. *J Am Coll Surg* 2003;197:392-402.
10. Ozden I, Emre A, Alper A, et al. Long-term results of surgery for liver hemangiomas. *Arch Surg* 2000;135:978-81.
11. Farges O, Daradkeh S, Bismuth H. Carvernous hemangiomas of the liver: are there any indications for resection? *World J Surg* 1995;19:19-24.
12. Leslie DF, Johnson CD, Johnson CM, Ilstrup DM, Harmsen WS. Distinction between cavernous hemangiomas of the liver and hepatic metastasis on CT: value of contrast enhancement patterns. *AJR Am J Roentgenol* 1995;164:625-9.
13. Egglin TK, Rummeny E, Stark DD, Wittenberg J, Saini S, Ferrucci JT. Hepatic tumors: quantitative tissue characterization with MR imaging. *Radiology* 1990;176:107-10.
14. Kim T, Federle MP, Baron RL, Peterson MS, Kawamori Y. Discrimination of small hepatic hemangiomas from hypervascular malignant tumors smaller than 3 cm with three-phase helical CT. *Radiology* 2001;219:699-706.
15. Kudo M, Ikekubo K, Yamamoto K, et al. Distinction between hemangioma of the liver and hepatocellular carcinoma: value of the labeled RBC-SPECT scanning. *AJR Am J Roentgenol* 1989;152:977-83.
16. Birnbaum BA, Weinreb JC, Megibow AJ, et al. Definitive diagnosis of hepatic hemangiomas: MR imaging versus Tc-99m-labeled red blood cell SPECT. *Radiology* 1990;176:95-101.
17. Shankar S, van Sonnenberg E, Silverman SG, Tuncali K. Interventional radiology procedures in the liver. Biopsy, drainage, and ablation. *Clin Liver Dis* 2002;6:91-118.
18. Tung GA, Cronan JJ. Percutaneous needle biopsy of hepatic cavernous hemangioma. *J Clin Gastroenterol* 1993;16:117-22.