



CT and MRI studies of hepatic angiosarcoma

L.-L. Yi^a, J.-X. Zhang^a, S.-G. Zhou^a, J. Wang^a, Y.-Q. Huang^a, J. Li^a, X. Yu^{b,**},
R.-N. Wang^{c,*}

^a Department of Radiology, Foshan Hospital of Traditional Chinese Medicine, Foshan, 528000, China

^b Key Laboratory for Biorheological Science and Technology of Ministry of Education (Chongqing University), Chongqing University Cancer Hospital & Chongqing Cancer Institute & Chongqing Cancer Hospital, Chongqing, 400044, China

^c Minimally Invasive Center, Tumour Hospital, Sun Yat-Sen University, Guangzhou, 510060, China



ARTICLE INFORMATION

Article history:

Received 21 June 2018

Accepted 19 December 2018

AIM: To analyse the computed tomography (CT) and magnetic resonance imaging (MRI) manifestations of hepatic angiosarcoma.

MATERIALS AND METHODS: Nineteen patients with hepatic angiosarcoma underwent preoperative abdominal unenhanced and contrast-enhanced CT (11 cases) or (eight cases) MRI.

RESULTS: The results of a coagulation examination showed varying degrees of abnormalities in 12 (63.16%) cases (most were prolonged prothrombin time and an increased proportion of prothrombin time), which were the most common abnormalities on the laboratory tests. Unenhanced CT of the lesions showed homogeneous or heterogeneous hypointense with hyperintense haemorrhagic lesions, contrast-enhanced CT was performed for six cases (6/11, 54.5%) with centripetal heterogeneous filling. All lesions showed heterogeneous intensity at MRI, including heterogeneous hypointense T1WI and homogeneous or heterogeneous hyperintense T2WI. Haemorrhage lesions showed higher hyperintensity with spot or patchy signals. Centripetal enhancement was found in six cases using contrast-enhanced imaging. Flaky patches of contrast enhancement were seen in the lesions.

CONCLUSION: The CT and MRI features of most of the hepatic angiosarcomas in the present study were relatively characteristic: the border of the mass was indistinct, the density was heterogeneous, and haemorrhage was frequently seen, with secondary calcification in a few cases, whereas enhanced imaging showed typical centripetal heterogeneous enhancement. In addition, highly malignant angiosarcoma could not be enhanced.

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Introduction

Hepatic angiosarcoma is the most common interstitial malignancy of the liver, accounting for <1% of all primary liver tumours.^{1,2} It is highly invasive and presents with a poor prognosis. The majority of untreated patients die within 6 months,³ and most patients die within a year, even after surgical resection.^{4,5}

Hepatic angiosarcoma is primarily composed of vessels or lymphatic endothelial cells; therefore, it has abundant

* Guarantor and correspondent: R.-N. Wang, Minimally Invasive Center, Tumour hospital, Sun Yat-Sen University, Guangzhou 510060, China. Tel.: +862087343272.

** Guarantor and correspondent: X. Yu, Key Laboratory for Biorheological Science and Technology of Ministry of Education (Chongqing University), Chongqing University Cancer Hospital & Chongqing Cancer Institute & Chongqing Cancer Hospital, Chongqing, 400044, China. Tel.: +862365075632.

E-mail addresses: 87785027@qq.com, wangruoning8@163.com (R.-N. Wang).

blood vessels, and haemorrhage can occur spontaneously. Invasive biopsy can easily lead to bleeding. Non-invasive imaging studies are conducive to diagnosis.⁶

Previous studies have applied the imaging methods of ultrasound, abdominal computed tomography (CT), or magnetic resonance imaging (MRI).^{6–8} Most reports include only a few cases,^{9–11} and even fewer include >10 cases.^{6,12} In the present study, the CT and MRI findings of 19 cases of hepatic angiosarcoma as confirmed at histopathology were analysed retrospectively to summarise the characteristic imaging signs of this condition. The present study was undertaken to improve the understanding of this disease.

Methods and materials

Clinical data

The clinical and imaging data of 19 patients with hepatic angiosarcoma across three medical centres were analysed retrospectively. As the study was a retrospective study, ethics committee approval was not required.

All patients underwent preoperative abdominal unenhanced and contrast-enhanced CT (11 cases) or MRI (eight cases). All patients underwent surgical resection or surgical biopsy of their histopathologically confirmed hepatic angiosarcoma. The median age of the patients was 53 (17–71) years old, and the male: female ratio was 8: 11. The median time from onset to treatment was 1 month (0–108 months). The lesions of five patients were found using the B-ultrasound of a physical examination, and one patient experienced post-injury pain. The remaining nine patients experienced pain or fullness/discomfort in the upper abdomen. One patient presented with a history of vinyl chloride exposure. One case showed postoperative recurrence 29 months after surgery for hepatic haemangioendothelioma. Three cases were complicated by cirrhosis. No jaundice was found on physical examination. The laboratory tests showed a positive result for hepatitis B virus (HBV) infection in three cases, significantly elevated alpha-fetoprotein (AFP) in three cases, elevated carcinoembryonic antigen (CEA) and carbohydrate antigen-199 (CA-199) in two cases, liver function damage in five cases, varying degrees of abnormal coagulation indicators in 12 cases (most were prolonged prothrombin time and increased proportion of prothrombin time), and decreased platelet count in five cases.

CT

CT was performed in the supine position using a Philips Brilliance 64-slice CT system, with a section thickness of 5 mm, intersection gap of 5 mm, pitch of 0.9, tube voltage of 120 kV, and iohexol (350 mg iodine/ml) was used as the enhanced contrast agent at a dose of 1.5 ml/kg. The contrast agent was injected at a flow rate of 3 ml/s through the cubital vein with a high-pressure syringe. The scanning delay times were 30, 50, and 160 seconds for the arterial, portal, and delay phases, respectively. The images were reconstructed without gaps using standard algorithms.

MRI

All patients were imaged using the 1.5 T MRI system (Siemens Avanto). Body coils were used. Sagittal T2-weighted imaging (WI) was acquired using a fat-suppressed fast spin-echo sequence: 3,765.5 ms repetition time (TR)/88 ms echo time (TE), 36×31 cm field of view, 320×240 matrix, 3 mm thickness. Axial T1WI was acquired using 110 ms TR/4.76 ms TE, 6 mm section thickness, 320×240 image matrix, 36×31 cm field of view. Axial view T2WI was acquired using 4,000 ms TR/142.5 ms TE, 5 mm section thickness, 4 excitations, 38×38 cm field of view, and 256×224–512×446 matrix.

Gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) was intravenously injected for fat-suppressed T1-weighted transverse imaging. The dose was 0.1 mmol/kg per patient, and the injection rate was 2 ml/s with 4.4 ms TR/2 ms TE, 3 mm section thickness, 320×195 image matrix, 38×31 cm field of view. The scanning delay times were 18, 45, and 120 seconds for the arterial, portal, and delay phases, respectively.

Image analysis

Three radiologists with >15 years of experience in abdominal imaging diagnosis analysed all of the CT and MRI signs, including main lesions, subfoci, attenuation, and changes, lesion boundaries, internal components, signal intensity on MRI, and enhancement methods. The region of interest (ROI) was selected based on the findings of each image sequence to avoid regions of bleeding, necrosis, and cystic degeneration.

Histopathological analyses

Samples underwent conventional fixation, decalcification, haematoxylin and eosin (H&E) staining, and light microscopy. The typing of all cases was determined via immunohistochemistry. Three senior doctors specialising in abdominal pathological diagnosis read the results.

Results

General results and follow-up

Of the 19 cases examined in this study, 11 underwent surgical resection or preoperative chemotherapy and surgical resection, and eight underwent biopsy because surgical resection could not be performed. One case sought treatment due to traumatic pain, and metastases were found in the liver, spleen, lung, and heart; two cases were initially diagnosed with spleen angiosarcoma; one case presented with lung metastasis 6 months after surgery; one case showed multiple liver metastases in the residual liver, with lung metastases 1 year and 7 months after right hepatectomy; one case showed breast metastasis 4 years after liver lobectomy; and one case showed bone metastasis of the cervical spine 3 years after surgery. Three patients died after diagnosis (one died of multiple organ failure) after a

range of 8–39 months. Three cases with short-term prognoses after the treatment showed no progression according to the postoperative imaging data. The remaining five cases were lost to follow-up.

Imaging findings

The lesions of 11 cases were located in the right lobe of the liver (peripheral lesions were found in three); the lesions of seven cases were located in the left lobe of the liver (peripheral lesions were found in one); and the lesions of one case included multiple lesions in the left and right lobes of the liver, spleen, and right atrium. In all cases, the maximum diameter of the main lesion was >3 cm, and the largest was 13×18 cm, with an average maximum diameter of 9.1 cm. The size of one liver lesion was 2.9×3.6 cm, and the size of one spleen lesion was 7.3×9 cm. The boundaries of the lesions were unclear in 13 cases (68%), and 17 cases (89.4%) showed heterogeneous density/signals, of which seven cases had spotted or flaky haemorrhage lesions.

CT findings

CT examination was performed for 11 cases. The lesion size, boundary, internal density, unenhanced and enhanced three-phase CT attenuation values, and enhancement methods are shown in Table 1. Contrast-enhanced CT was performed for six cases (6/11, 54.5%) with centripetal heterogeneous filling (Fig 1), and the results showed no significant enhancement in two cases (18.2%), mild-to-moderate heterogeneous enhancement in two cases (18.2%), and annular enhancement in one case.

MRI findings

MRI examination was performed for eight cases. The lesion size, boundary, internal signal, enhancement methods, and other data are shown in Table 2. All lesions showed heterogeneous signals, including heterogeneous hypointense T1WI signals and homogeneous or heterogeneous hyperintense T2WI signals, with higher hyperintense spot or patchy signals of haemorrhage lesions. Centripetal enhancement was found in six cases using contrast-enhanced scanning; the filling of the contrast agent in the lesions was incomplete in the shape of flaky patches (Figs 2–4); heterogeneous and continuous enhancement was shown in one case; and annular enhancement with spot filling of the contrast agent was observed in one case.

Histopathological characteristics

The border between the tumour and the surrounding tissue was unclear, showing multiple areas of necrosis. The neoplastic cells were arranged in solid and fissure-like structures, and the vascular cavity-like structure was formed locally, which infiltrated into normal liver tissue with massive haemorrhage. The tumour cells of well-differentiated angiosarcoma were well differentiated, with rare mitoses and no obvious cellular atypia, and the blood vessel branches interacted with each other to form a

Table 1
The CT features of hepatic angiosarcoma

Case	Age	Sex	Location	Size (cm)	Coagulation function	Boundary	Density	CT unenhanced scans (HU)	A (HU)	V (HU)	D (HU)	Enhancement pattern	Differentiation	Cirrhosis
1	52	F	B	5.1 × 4.3	Abnormal	Rough	Uneven	47	48	59	82	Heterogeneous	Moderate	
2	65	M	L	10.2 × 9.7	Abnormal	Rough	Uneven	63	64	66	65	Non	Low	Yes
3	58	M	R	6.7 × 4.8	Normal	Rough	Uneven	39	56	61	67	Centripetal, heterogeneous	Moderate	
4	33	M	R	8.5 × 6.2	Abnormal	Rough	Uneven	43	46	55	69	Centripetal, heterogeneous	High	
5	53	F	R	17 × 12	Abnormal	Smooth	Uneven	43	44	59	75	Centripetal, heterogeneous	Moderate	Yes
6	69	F	L	6.0 × 5.6	Abnormal	Rough	Uneven	50	51	53	59	Centripetal, heterogeneous	High	
7	17	F	R	8.30 × 6.1	Normal	Smooth	Uneven	49	49	70	84	Centripetal, heterogeneous	Moderate	
8	53	F	R	18 × 13.0	Normal	Rough	Uneven	39	39	41	42	Non	Low	
9	71	F	L	3.6 × 2.9	Abnormal	Smooth	Uneven	33	60	72	69	Rim	Moderate	
10	53	M	R	8.9 × 7.7	Abnormal	Rough	Uneven	40	59	61	63	Centripetal, heterogeneous	Moderate	Yes
11	58	F	R	4.8 × 3.0	Abnormal	Rough	Uneven	54	60	72	69	Heterogeneous	Low	

R, right; L, left; B, both right and left; A, arterial phase; V, venous phase; D, delayed phase; HU, Hounsfield Units.

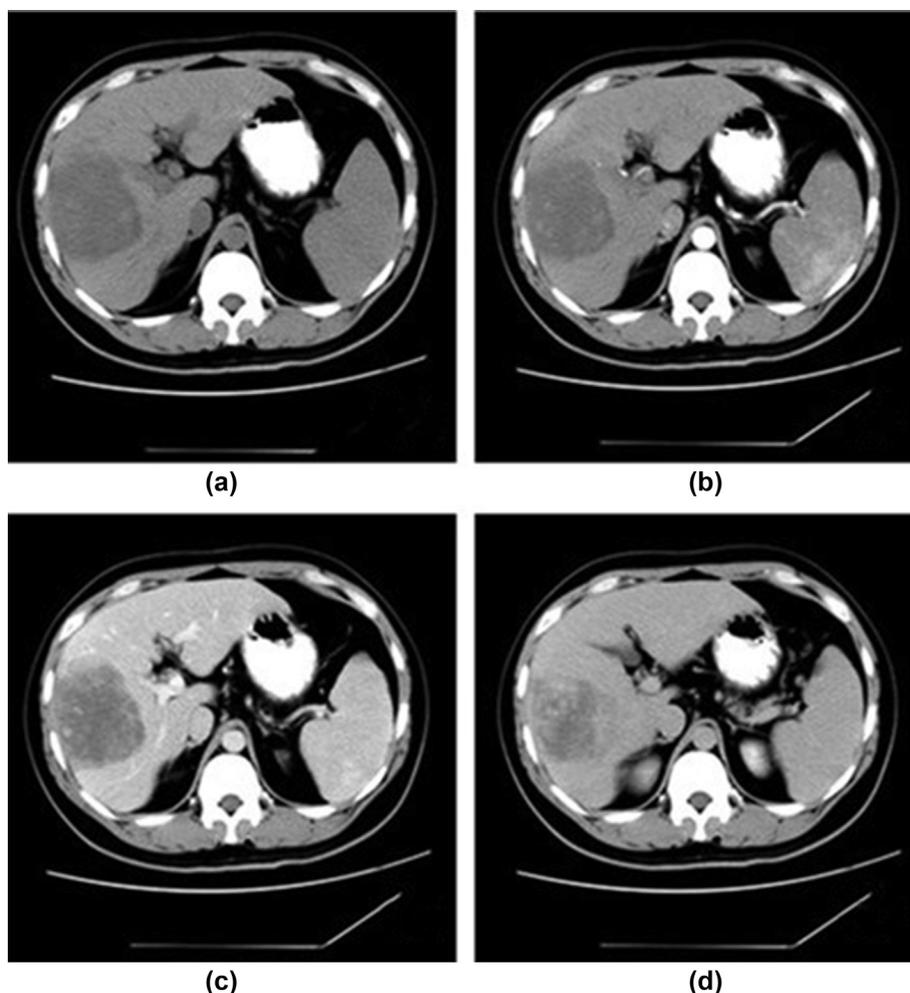


Figure 1 A 33-year-old male patient with right hepatic haemangiosarcoma. (a) Unenhanced CT image shows a lobulate mass with an indistinct boundary in the right lobe. (b–d) Enhanced CT images of the arterial, venous, and delay phases showed a heterogeneous centripetal enhancement of the mass, and the contrast agent did not completely fill in the lesion at the end.

relatively complete network. The vascular network formed by the tumour cells of poorly differentiated angiosarcoma had poor continuity or did not form the luminal structures, with a distribution of a large area of blood, obvious cellular atypia, and pathological mitoses.

Discussion

Hepatic angiosarcoma is a rare and aggressive tumour, with only approximately 200 confirmed cases each year

worldwide¹³; however, it is the most common mesenchymal malignancy of the liver.¹ The biological behaviour of this tumour is highly invasive; therefore, the diagnosis in most cases is confirmed during the advanced stage. In the current study, most patients were treated within 6 months. Extrahepatic metastases were found in three cases at the initial diagnosis in which one patient presented with cardiac metastases. Surgical resection was performed for 11 patients, and eight patients did not undergo surgical resection because of extrahepatic metastases or large

Table 2
The MRI features of hepatic angiosarcoma

No	Age	Sex	Location	Size	Coagulation indicators	Boundary	Signal on T1WI	Signal on T2WI	Enhancement	Cirrhosis
1	36	M	R	10.3 × 7.9	Abnormal	Irregular	Uneven low	Uneven high	Centripetal heterogeneous filling	Yes
2	71	F	L	11.1 × 7.6	Abnormal	Irregular	Uneven low	Uneven high	Centripetal heterogeneous filling	No
3	68	F	L	5.7 × 4.1	Abnormal	Irregular	Uneven low	Uneven high	Centripetal heterogeneous filling	No
4	30	F	L	4.5 × 3.3	Normal	Irregular	Uneven low	Uneven high	Rim	No
5	48	M	B	10.4 × 8.0	Normal	Irregular	Uneven low	Uneven high	Centripetal heterogeneous filling	No
6	62	F	R	9.6 × 7.7	Abnormal	Regular	Uneven low	Uneven high	Centripetal heterogeneous filling	No
7	45	M	R	16.4 × 12.7	Abnormal	Regular	Low	Uneven high	Centripetal heterogeneous filling	No
8	52	M	R	8.3 × 5.0	Normal	Regular	Low	Uneven high	Heterogeneous	No

R, right; L, left; B, both right and left.

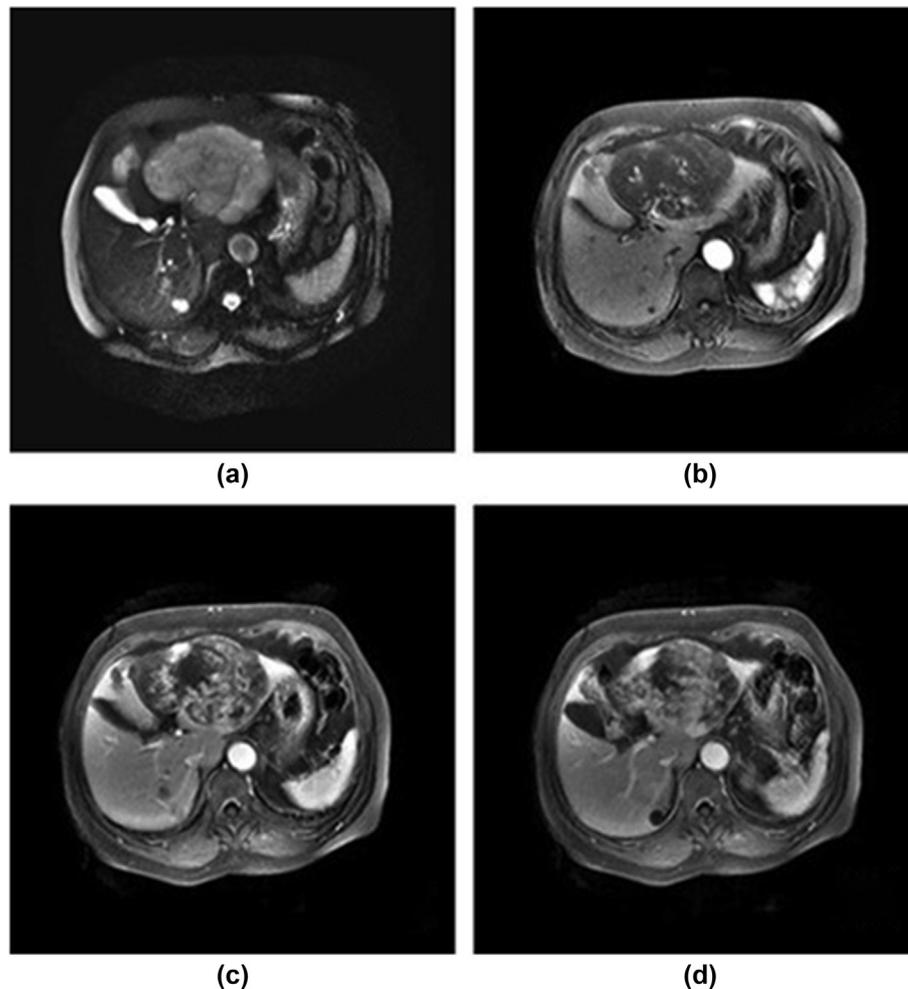


Figure 2 A 71-year-old female patient with hepatic angiosarcoma in the left lobe. (a) T2WI lipid-suppressing sequence on MRI showed the lobulate, heterogeneous, and hyperintense signals of a mass with an indistinct boundary in the left lobe. (b–d) Enhanced MRI of the arterial, venous, and delay phases showed a heterogeneous centripetal enhancement of the mass, and the contrast agent did not completely fill in the lesion at the end.

tumour size (>15 cm). Postoperative recurrence or metastasis occurred in eight cases after surgical resection (3–51 months). Of these patients, one survived for >4 years after surgery; therefore, a small number of patients can survive for a long time after surgery.¹⁴

The pathogenesis of hepatic angiosarcoma is uncertain. Previous exposure to carcinogens, such as cerium (IV) oxide, vinyl chloride, and arsenic has been widely considered as a risk factor^{15,16}; however, only one patient in this study showed a clear history of exposure. Hepatic angiosarcoma is closely related to hepatic fibrosis and hepatic cirrhosis.¹² Hepatic cirrhosis was observed in 42% of the biopsy specimens. In the present study, four cases (21%) showed a cirrhosis base. The prevalence of angiosarcoma in males was significantly higher than that in females (3–4:1), which might be related to the greater chance of chemical exposure in the work environment of males.¹⁷ The ratio of the incidence between males and females in the present study (0.72:1) might be related to the small size of the sample.

Laboratory tests showed that patients with hepatic angiosarcoma often had elevated levels of alanine

transaminase (ALT) and aspartate transaminase (AST).⁵ Thrombocytopenia and anaemia were common haematological findings. Thrombocytopenia and the vasogenic nature of tumours might lead to liver rupture. The levels of tumour markers, such as AFP, CEA, CA19-9, and CA125, all appeared in the normal range or were only slightly elevated.¹⁸ In the present study, HBV infection was positive in three cases. AFP was significantly elevated in three cases. CEA and CA-199 were elevated in two cases. Liver function was impaired in five cases, and platelet counts were decreased in five cases. The results of a coagulation examination showed varying degrees of abnormalities in 12 (63.16%) cases (most were prolonged prothrombin time and an increased proportion of prothrombin time), which were the most common abnormalities on the laboratory tests. Local or systemic coagulation disorders were related to excessive platelet accumulation in the vascular cavities and sinusoids with poor growth and differentiation.¹⁸

Hepatic angiosarcoma was divided into single mass, mixed massive mass, multiple nodules, and diffuse nodule types based on morphology.¹⁰ In China, a single mass is the

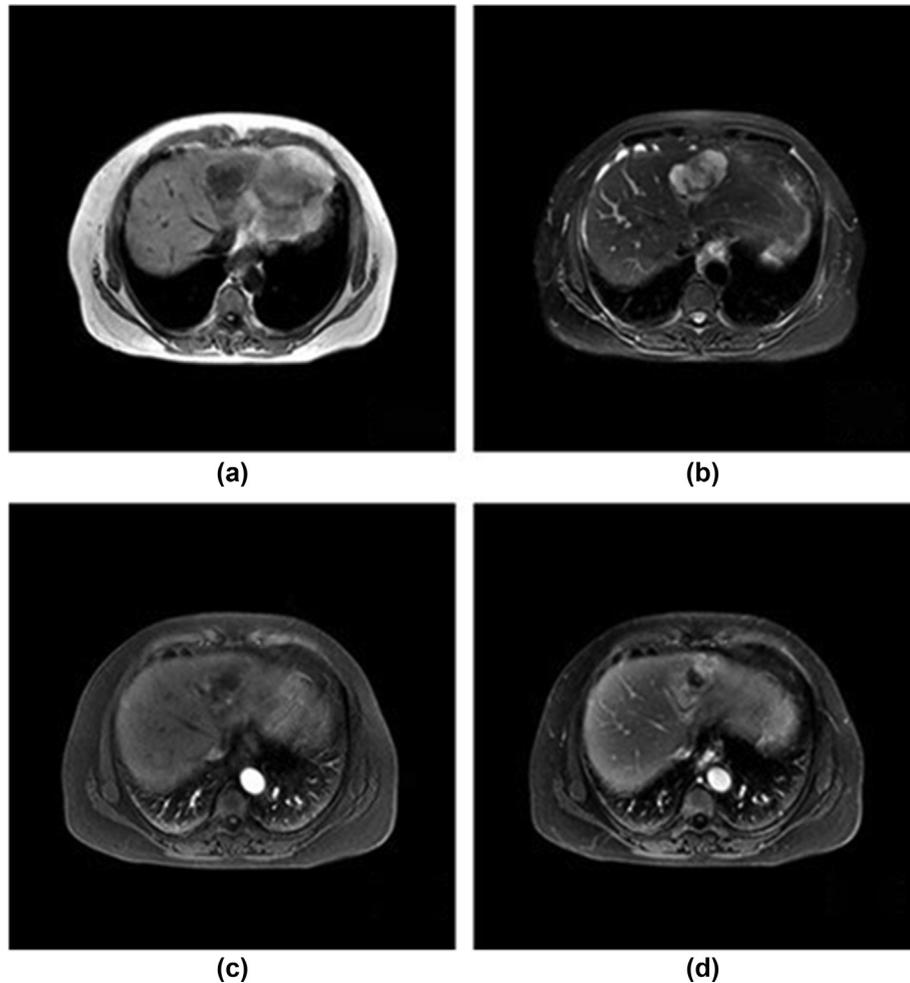


Figure 3 A 36-year-old male patient with right hepatic haemangiosarcoma. (a,b) T1WI and T2WI MRI sequences showed heterogeneous hypointense and hyperintense signals of a mass with an irregular boundary. (c,d) Enhanced MRI of the arterial and venous phases showed heterogeneous centripetal enhancement of the mass, and the contrast agent did not completely fill in the lesion at the end.

most common type. The current study found 14 cases of single-mass type (14/19), five cases of massive nodule mixed type (5/19), and four cases of the lesions with surrounding subfoci. Because these cases were often associated with intratumoural haemorrhage, unenhanced CT of the lesions showed homogeneous or heterogeneous hypointense with hyperintense haemorrhagic lesions. Some lesions of long disease duration can present with haematoma and calcification. Eggshell-like calcification at the edge of the lesion was observed in one case of the current study. Because the tumour has no capsule, its cells can easily invade the normal liver tissue and cause significant reactive fibrosis, usually with an indistinct and unsmooth lesion boundary. The CT attenuation values of the unenhanced CT of the 11 lesions in this study ranged from 33–63 HU, which might be because of the volume effect caused by the different proportions of the parenchymal area to the cystic degeneration, necrosis, and haemorrhage area of the tumours. Enhanced CT examinations were typically characterised by annular enhancement of the arterial phase, no internal enhancement, and continuous centripetal filling during the venous and delay phases; however, the final

enhancement remained heterogeneous and flake-like, instead of the homogeneous and complete centripetal filling for the haemangiomas. In this study, 64% of all cases of highly differentiated hepatic angiosarcoma exhibited this kind of enhancement. If the histopathology revealed poorly differentiated angiosarcoma, enhancement was not obvious (2/11) or was heterogeneous (1/11) for all scan phases. In the present study, the two cases of poorly differentiated angiosarcoma showed a discontinuous vascular network in the tumour tissue under a microscope, and some areas showed no vascular network formation. Only the individual tumour cells floating in the blood were observed. Angiosarcomas with lower degrees of malignancy show better continuity of the neovascular network and more similar enhancement to haemangioma with homogeneous centripetal filling and the final enhancement of the entire lesion; however, all cases of angiosarcoma in the present study with different degrees of differentiation showed heterogeneous enhancement. This finding might be because the large diameters of the lesions were complicated with cystic degeneration, necrosis, and areas of bleeding. Therefore, for a liver mass showing a poorly defined border,

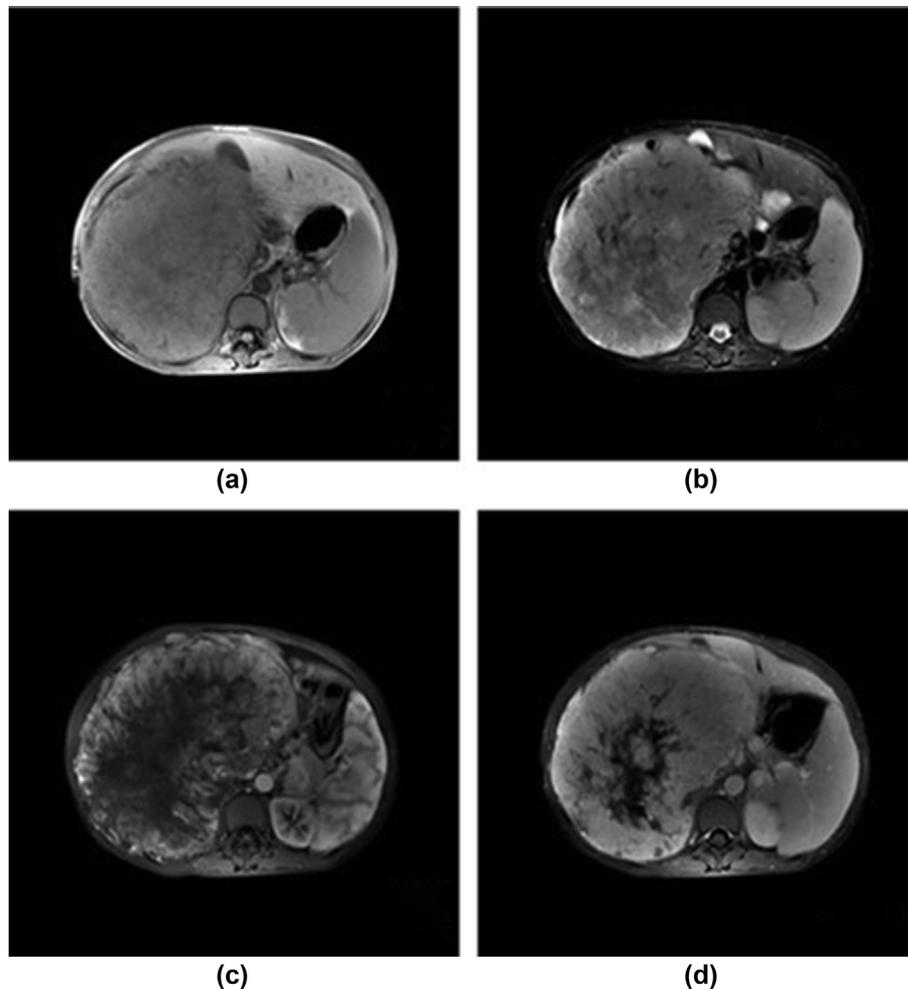


Figure 4 A 45-year-old male patient with a large haemangiosarcoma in the right hepatic lobe. (a,b) T1WI and T2WI MRI sequences showed heterogeneous hypointense and hyperintense signals of a mass with an irregular boundary. (c,d) Enhanced MRI of the arterial and venous phases showed heterogeneous centripetal enhancement of the mass, and the contrast agent did not completely fill in the lesion at the end.

heterogeneous density, accompanied by bleeding on CT, and typical centripetal heterogeneous filling on enhanced scanning, the possibility of angiosarcoma should be considered. In cases without significant enhancement of the mass, poorly differentiated angiosarcoma should be excluded.

MRI can better reveal the internal components of lesions. The lesions of the eight cases receiving MRI examinations in the present study showed heterogeneous signal at T1WI and T2WI, and a hyperintense haemorrhage lesion was observed in three cases (37.5%). The rate of haemorrhage of hepatic angiosarcoma reported in the literature is significantly higher than that of other sarcomas.¹⁰ One study⁶ showed that angiosarcomas with lesions of >3 cm can exhibit characteristic centripetal enhancement. Of the eight cases in the current study, typical heterogeneous centripetal enhancement was observed in the lesions of six cases, whereas spot or patchy enhancement was observed in the remaining two cases; however, the lesions of all of the cases in this study were >3 cm. In the future, the MRI features of hepatic angiosarcoma should be investigated, including more cases with smaller lesions.

In conclusion, the CT and MRI features of most of the hepatic angiosarcomas in this study were relatively characteristic: the border of the mass was indistinct, the density was heterogeneous, and haemorrhage occurred easily, with secondary calcification in a few cases, whereas an enhancing scan showed typical centripetal heterogeneous enhancement. In addition, the highly malignant angiosarcoma could not be enhanced; however, it is difficult to differentiate haemangiomas with smaller and homogeneously enhancing angiosarcomas. In addition, a few angiosarcomas cases enhanced heterogeneously, with rapid early enhancement and a clearly defined boundary, which is difficult to distinguish from hepatocellular carcinoma.

This study has limitations. As a multicentre retrospective analysis, no case in this study had simultaneous CT and MRI examinations; thus, it was impossible to compare the two imaging methods. All of the lesions in this study were >3 cm. The CT and MRI features of small angiosarcoma lesions were not investigated. The number of MRI cases was too small, with no time–intensity curve (TIC); thus, it is impossible to analyse the receiver operating characteristic (ROC) of the angiosarcoma-enhanced curve. Diffusion-

weighted imaging (DWI) sequences were not performed, and quantitative indicators such as the apparent diffusion coefficient (ADC) value are lacking; therefore, a future study investigating the differences in ADC values between angiosarcomas and primary liver cancer is needed.

Acknowledgements

This work was supported by the key specialty construction of the clinical project of FoShan (Fspy3-2015019) and Medical research fund of guangdong province (B2018193), the Medical research project of ChongQin (2016MSXM088).

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