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ORIGINAL RESEARCH

The Clinicopathological and Imaging Characteristics of Primary Hepatic Carcinosarcoma and a Review of the Literature

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Purpose: To improve the understanding of hepatic carcinosarcoma (HCS) by analyzing radiological imaging data and clinicopathological features.

Materials and Methods: A retrospective analysis was performed on four patients with HCS confirmed immunohistochemically. The analysis included three males and one female, aged 29 to 64 years. Four patients underwent computed tomography (CT) scans, and one underwent magnetic resonance imaging (MRI) scans simultaneously.

Results: Three patients had a history of hepatitis B, cirrhosis or fibrosis, and two patients had schistosomiasis. Two cases tested positive for elevated serum carbohydrate antigen (CA) 19–9. The maximum diameters of the lesions ranged from 7.8 to 9.0cm. Pathologically, the carcinomatous and sarcomatous elements in two patients could not be classified, one of the patients had cholangiocellular carcinoma (CCC) and undifferentiated sarcoma, the other had hepatocellular carcinoma (HCC) and undifferentiated pleomorphic sarcoma (UPS). All tumors showed heterogeneous density/intensity, accompanied by vast cystic changes and necrosis, with two cases having cystic septations. Capsule formation was not identified. The margins of the radiological images showed irregular ring enhancement. One case presented continuous progressive enhancement, one case with "fast in fast washout" and two cases with "fast in late washout". Lymphonodus metastasis, satellite nodules, vascular embolism, and organ invasion (hepatic flexure of the colon) were identified.

Conclusion: HCS is a rare, high-grade malignancy with poor prognosis. The preoperative diagnosis is expected to improve by carefully analyzing the imaging features of the patients in combination with their clinical characteristics. Radical resection and postoperative chemoradiotherapy can improve the survival rate of patients.

Keywords: hepatic carcinosarcoma, imaging, computed tomography, magnetic resonance imaging

Introduction

In 2000, the World Health Organization (WHO) defined HCS as a malignant tumor of the liver that contains both epithelial and mesenchymal differentiation with no distinct transitional zone between them.[1] HCS is rare, with high degree of malignancy and poor prognosis, associated with a high frequency of early metastasis and recurrence. HCS has mainly been reported in case studies analyzing clinicopathological features and treatment methods, with only more than 20 previous literatures incorporating imaging representation. The purpose of this study is to analyze the radiological imaging and clinicopathological features of four cases of HCS from

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Hunan Provincial People's Hospital, and to review previous literatures, so as to improve the diagnosis of HCS and provide a basis for clinical diagnosis.

Materials and Methods

Subjects

Four patients admitted to the hospital from March 2012 to March 2018 were diagnosed with HCS by surgical pathology (Table 1). The patients included three males and one female, with an average age of 49-year-old (rang, 29–64 years). All patients reported dull pain, three intermittent and one persistent, in the upper abdomen. Three patients had a history of hepatitis B, cirrhosis or fibrosis, and two patients had a history of schistosomiasis. Two cases tested positive for CA19-9, four displayed normal levels of alpha-fetoprotein (AFP), and three displayed normal levels for carcinoembryonic antigen (CEA) (Case 3 was not detected). Follow-up data were obtained by telephone. This study was approved and compliant with the Hunan Provincial People's Hospital's medical ethics committee.

Image Acquisition

All patients who underwent CT and MRI examination in supine position had no history of allergies to the contrast agent. The scanning range was from the level of the diaphragmatic apex to the anterior superior iliac spine.

CT Protocol

Cases 1 and 4 were scanned by Philips Brilliance 16 CT machine (Netherlands). Case 2 was scanned by Philips Brilliance iCT (Netherlands). Case 3 was scanned by Neusoft NeuViz 64i CT (Shenyang, China). The imaging parameters were as follows: tube voltage 120 KV, tube current 165–375 mA, reconstructed slice thickness 5mm.

MRI Protocol

Case 1 was also scanned by Siemens Magnetom Trio A Tim System 3.0t MR scanner (Germany) with a torso coil. The main image sequences are as follows: noncontrast enhanced scan, axial gradient echo (GR) with fat-suppression T1-weighted imaging (T1WI): repetition time (TR) 3.4ms, echo time (TE) 1.2ms, slice thickness 2.5mm, matrix 256×136, field of view (FOV) 320×210mm; spin echo (SE) with fat-suppression T2-weighted imaging (T2WI): TR 3652.1ms, TE 83.0ms, slice thickness 5mm, matrix 640×416, FOV 320×210mm; T1WI in-phase: TR 5.5ms, TE 2.5ms, slice thickness 2.5mm, matrix 256×136, FOV 320×210mm; T1WI out-phase: TR 5.5ms, TE 3.7ms, slice thickness 2.5mm, matrix 256×136, FOV 320×210mm; Coronal SE T2WI: TR 2000.0ms, TE 95.0ms, slice thickness 4mm, matrix 320×320, FOV 320×210mm. Dynamic enhanced sequences, axial GR T1WI, TR 3.4ms, TE 1.2ms, slice thickness 2.5mm, matrix 256×136, FOV 256×136mm; enhanced coronal GR T1WI: TR 3.0ms, TE 1.2ms, slice thickness 2mm, matrix 256×256, FOV 320×210mm.

Contrast Agent Parameter

CT

Non-ionic contrast agent iodohyanol (350mgI/mL, 100mL, Shanghai General Electric Pharmaceutical Co., Ltd, Shanghai, China) was used in CT scan, and was injected intravenously through the anterior cubital vein by dual cylinder high-pressure injector (Ulrich, Germany). Case 1 underwent dual-phase scanning (triphase scanning was performed in MRI), others underwent triphase. The dose of contrast agent was about 70–110mL (1.5mL/kg), and the flow rate was 3.0–4.0mL/s. After injection of contrast agent, the arterial phase (AP) and portal vein phase (PP) and equilibrium phase (EP) scanning were performed at a delay of 25–30s, 60–65s and 120s, respectively.

MRI

Dimeglumine gadopentetate (12mL, Guangzhou Kangchen Pharmaceutical Co., Ltd, Guangzhou, China) was intravenously injected through the anterior cubital vein by dual cylinder high-pressure injector, with triphase scanning. The dose of contrast agent was about 20–24mL

Table 1 Clinical Data of Four Patients with Hepatic Carcinosarcoma

Case NO.	Age (y)	Gender	HBV	Cirrhosis	Schistosomiasis	CA19-9	AFP	CEA
1	63	F	-	-	+	183.21	8.17	1.77
2	29	M	+	+	+	2.64	5.64	0.78
3	42	M	+	+	-	42.27	18.05	NA
4	62	M	+	Fibrosis	-	9.58	2.77	1.12

Abbreviations: y, years; +, present/positive; –, absent/negative; NA, not available; HBV, hepatitis B virus; CA19-9, carbohydrate antigen 19–9 (0–35U/mL); AFP, alpha-fetoprotein (0–20.00ng/mL); CEA, carcinoembryomic antigen (0–5.00ng/mL).

(0.4mL/kg), and the flow rate was 2.0~3.0mL/s. Contrast enhanced images were obtained with a scanning delay of 20~25s (AP) and 60–65s (PP) and 120s (EP) after the start of contrast agent injection.

Image Analysis

One attending radiologist and the associate professor read the images independently, and the resulting quantitative data were averaged. If the qualitative data were inconsistent, the two radiologists read the image again and reached a verbal consensus. Main parameters include: lesion site (accurate to segment), number (single or multiple), size (maximum diameter, accurate to one decimal point), shape (round, oval, irregular or lobulated), margin (clear or unclear, capsule or not), density/signal (homogeneous or heterogeneous, calcification, hemorrhage, cystic/necrosis), enhanced images (enhanced mode, degree), adjacent tissues and metastasis (invasion of adjacent viscera, vascular embolus, lymph node, metastasis).

Pathological Evaluation

According to the definition of WHO, HCS is a malignant tumor in which the components of carcinomatous and sarcomatous are closely mixed. Pathologically, morphological findings of hematoxylin-eosin (HE) stained sections and marker analysis of carcinomatous and sarcomatous are required.[2] Four patients with surgically resected specimens underwent routine HE staining and immunohistochemical examination, including: the epithelial marker cytokeratin (CK-P); mesenchymal marker Vimentin (Vim); angiogenic marker cadherin 34 (CD34); Hepatocyte markers: phosphatidylinositol proteoglycan 3(gly-3), cellular marker for proliferation ki-67, Hepa-1; bile duct cell markers CK7 and CK19.

Literature Review

Since WHO redefined HCS in 2000, the time period of literature retrieval was from 2000 to 2020. In the Pubmed database, utilized search terms were ((("liver"[MeSH Terms], OR "liver"[All Fields]), OR hepatic[All Fields]), AND ("carcinosarcoma"[MeSH Terms], OR "carcinosarcoma"[All Fields])), AND ("2000"[Date - Create]: "2020"[Date - Create]). A total of 34 English full-text documents were found, including 59 cases.[2–35] Among them, there were 24 related to image representation.[2,3,7–11,13,14,17,19–24,26–33]

Results

Surgical Method

All patients underwent laparotomy or segectomy. Case 1 hepatic segments (S) 4b-5 resection, partial resection of duodenum and colon; the left lateral lobectomy performed in Case 2 and 3, and the lymph node dissection was performed in Case 2. Case 4 underwent S5-6 resection. No tumor tissue was found at the cutting edge of any of the pathological specimens.

Image Features

CT Findings

On unenhanced scan, four cases of lesions showed heterogeneous hypodense (low density at the edge and lower at the center), and the edges of the enhanced images showed irregular ring enhancement, among which 2 cases (Case 2 and 4) had septations (Figure 1), and the septations were also intensified, while the lower density at the center was not strengthened. All cases had moderate enhancement in AP, and Case 4 had attenuation in PP and EP, in Case 2 and 3 (Figure 2), the PP continued to strengthen, then attenuation in EP, showed "fast in fast washout" or "fast in late washout"; Case 1 continued to strengthen in PP. Case 1 had the tumor that invasion of colonic hepatic flexure; there were multiple lymph node metastases (hepatic duodenal ligament, perirenal and retroperitoneal), the largest of which was about 6cm in diameter; Case 4 had carcinomatous emboli of portal vein and right hepatic vein branch. Abdominal effusion was not found in all patients. Due to insufficient understanding of HCS, Case 1 was misdiagnosed with a liver abscess, and Cases 2 to 4 were misdiagnosed with HCC.

MRI Findings

Case 1 underwent simultaneous triphase enhanced MRI scanning. Due to the misdiagnosis of hepatic abscess, the patient had undergone puncture and drainage before the MRI examination, and scattered gas accumulation was observed in the lesion. The inhomogeneous hypointense in fat-suppression T1WI, and fat-suppression T2WI was mixed high signals with multiple patchy low signals in the center. No fat signal was found in the in-phase and out-phase. The AP of the enhancement scan was obviously inhomogeneous enhanced, and the PP and EP showed continuously progressive enhancement, with the enhancement range gradually increasing (Figure 3). The coronal enhanced image could clearly show the tumor invading the colonic hepatic flexure (Figure 3F).

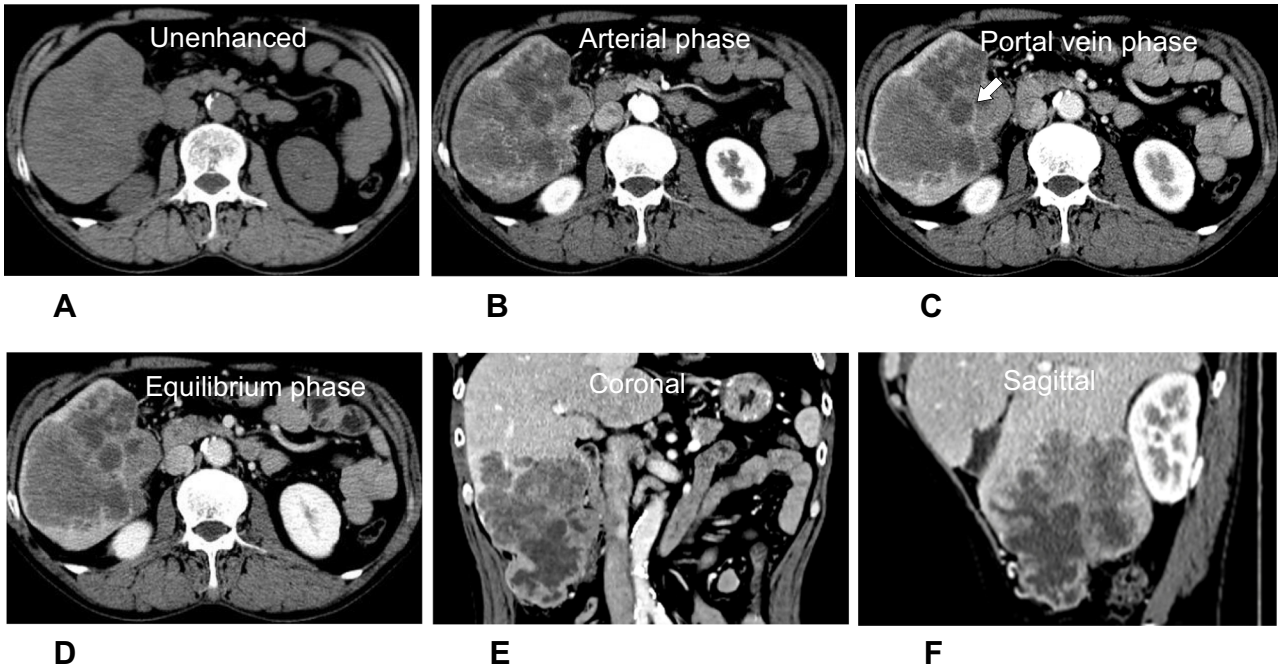

Figure 1 The CT non-enhanced and enhanced images of Case 4. Case 4: 62 years old, male. (**A**) A lobulated mass located in the segments 5–6 of the right liver showed heterogeneous hypodense on non-enhanced CT images with septations inside. (**B** and **D**) On enhanced images, the tumor margin presented irregular ring enhancement with septations reinforced (**C** arrow), moderate enhancement in arterial phase, attenuation in portal vein phase and equilibrium phase. The mass protruded from the liver surface could be seen in coronal (**E**) and sagittal (**F**).

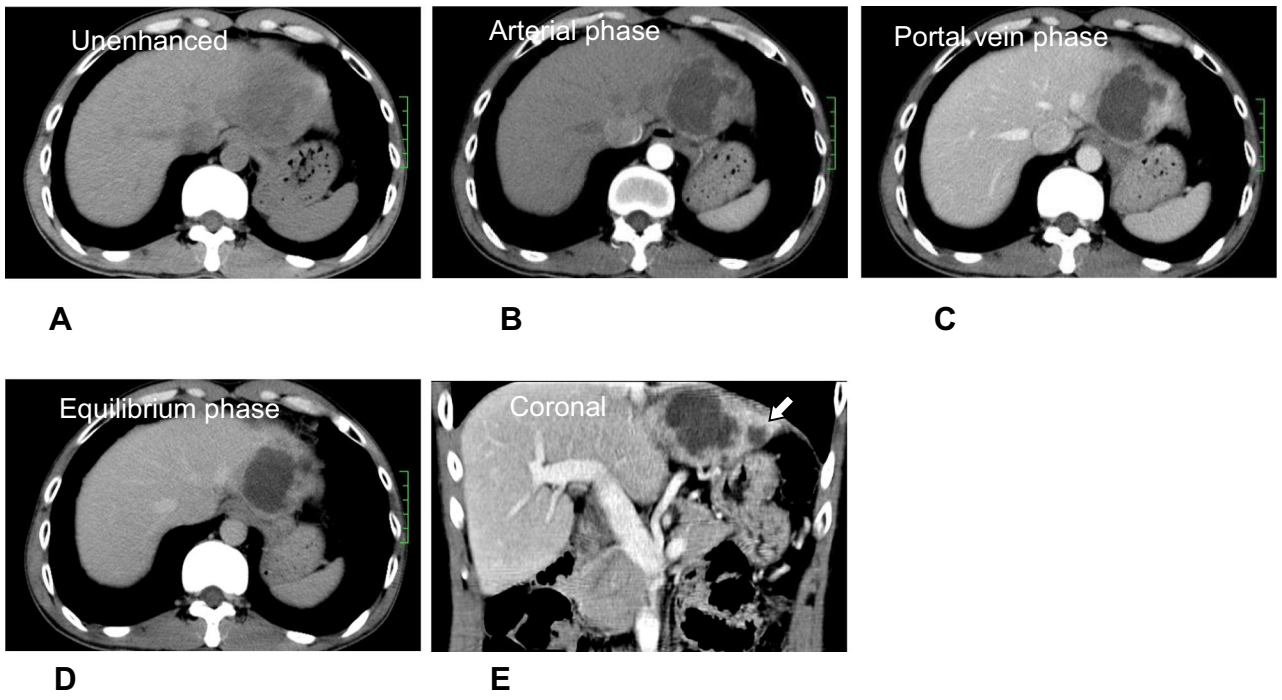

Figure 2 The CT non-enhanced and enhanced images of Case 3. Case 3: 42 years, male. (**A**) There was heterogeneous hypodense lesion in the segments 2–3 of the left liver, which was lobulated and irregular. On enhanced images, the margin showed irregular ring enhancement. The lesion showed moderate enhancement in the arterial phase (**B**) and continued in the portal phase (**C**), but attenuation in the equilibrium phase (**D**). A sub-foci (**E** arrow) was seen around the tumor.

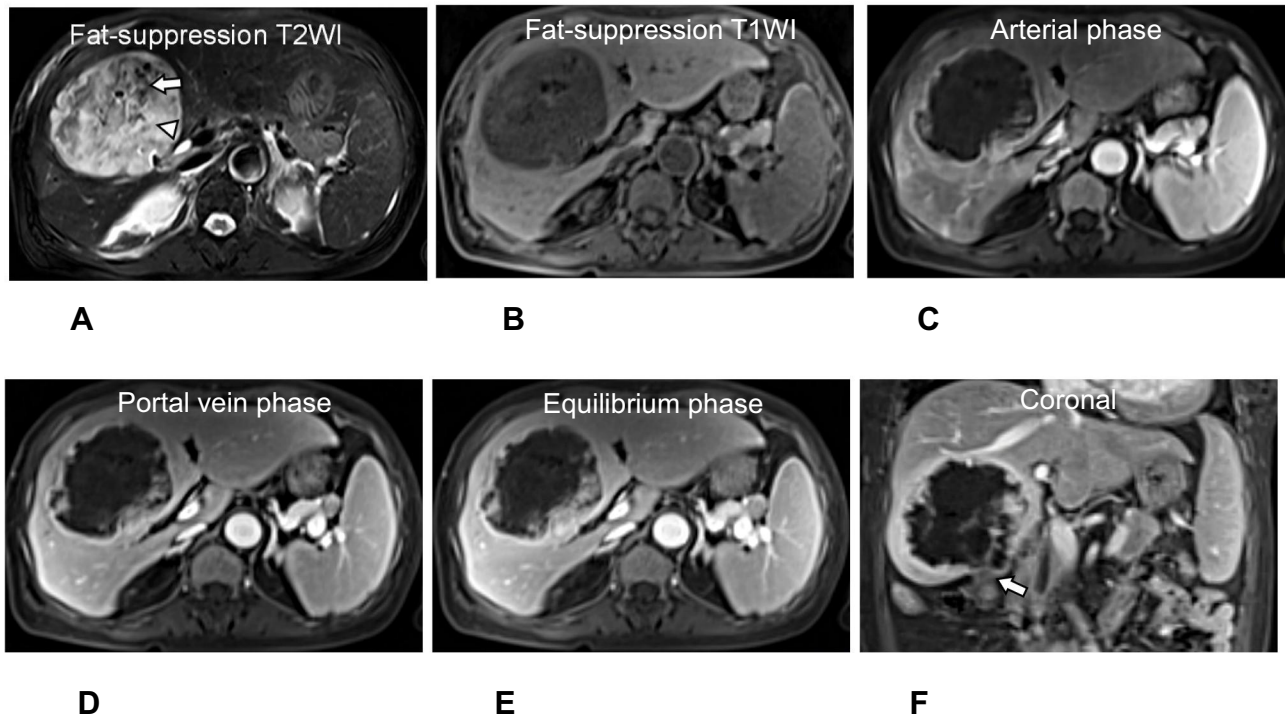

Figure 3 Case 1 with T1WI, T2WI and T1WI-enhanced images. Case 1: 63 years old, female. There was a mass located in the segments S4b-5 with an inhomogeneous hyperintense (**A**, arrowhead) mixed with patchy hypointense (**A**, arrow) in the fat-suppression T2WI, (**B**) inhomogeneous hypointense was in fat-suppression T1WI, and scattered gas accumulation was observed (puncture drainage was performed 5 days before the examination). After enhancement, the mass presented irregular ring enhancement and continuous progressive reinforcement (**C–E**). (**F**) showed the mass invading the colonic hepatic flexure (arrow).

Pathological Results and Follow-Up Data

Four patients each had single primary lesion. One patient had multiple satellite lesions, and two patients had sub-foci around the lesion. In two cases, cancerous legions were located in the left liver, one case in the right liver, and one case involved bilaterally. The mean maximum diameter of the lesions was 8.2cm (range, 7.8–9.0cm). There were three cases with irregular shape and other case with circular shape. The margin of two cases was clear, others were unclear, and three cases were prominent on the liver surface. In Case 2, 8 days after surgery, enlarged lymph nodes were seen in the abdominal cavity (residual metastatic lymph nodes were considered), careful comparison of preoperative images showed increscent; 2 months (m) after surgery intrahepatic metastasis in Case 3; Case 4 died of tumor recurrence 11m after surgery. All of them were not treated with chemoradiotherapy. See Table 2 for details.

Table 2 Tumor Characteristics and Follow-Up of 4 Patients with Hepatic Carcinosarcoma

Case NO.	Site	Maximum Diameter	Shape	Margin	Invasion or Metastasis	Follow-Up	Recurrence
1	S4b-5	7.8cm	Oval, Lobulated	Unclear	Colonic Hepatic Flexure	21d/D	–
2	S2-3	8cm	Oval, Lobulated	Unclear	Intrahepatic Satellite Nodules, Lymphatic Metastasis (Hilar, Retroperitoneal, Abdominal)	21m/D	+
3	S2-3	8cm	Irregular, Lobulated	Clear	Intrahepatic Sub-foci	6m/D	+
4	S5-6	9cm	Irregular, Lobulated	Clear	Intrahepatic Sub-foci, Branch of Portal Vein and Right Hepatic Vein Embolus	11m/D	+

Abbreviations: S, segments; d, days; D, dead; NA, not available; m, months; +, present; –, absent.

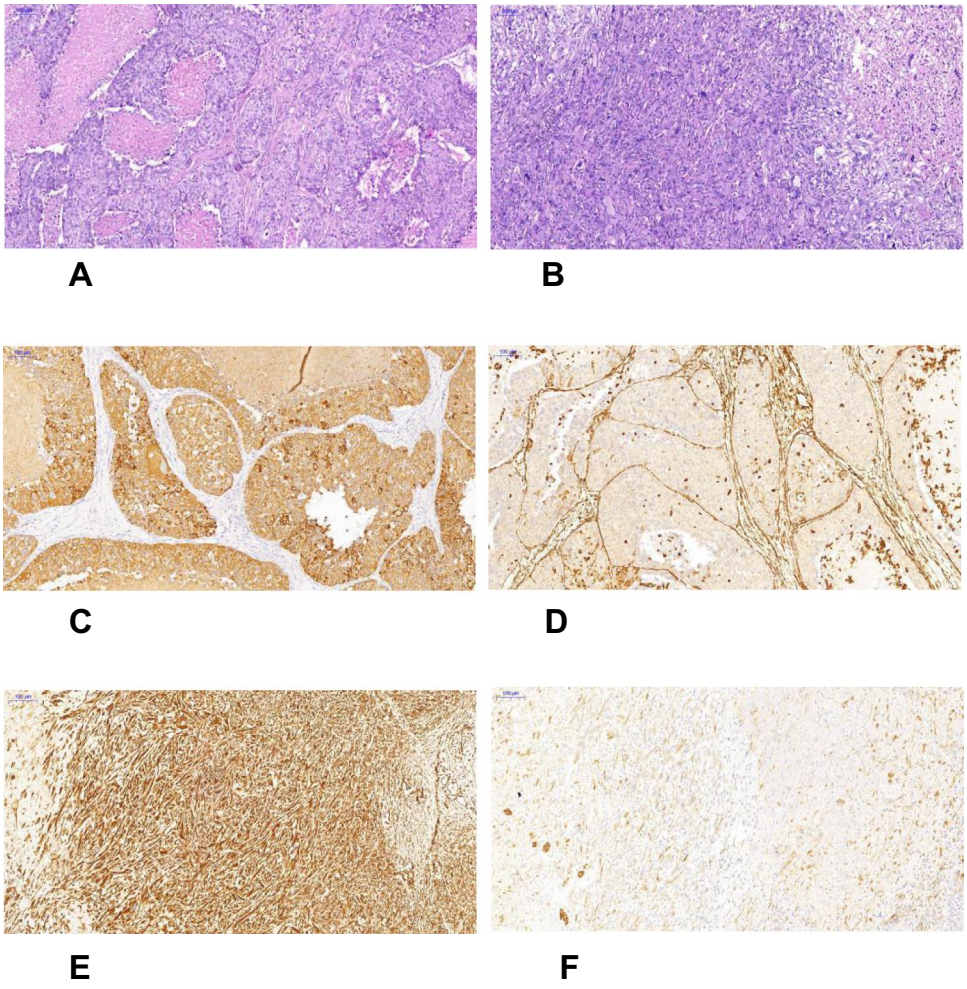

Figure 4 Pathological images of case 4: HE staining and immunohistochemical staining. Case 4: 62 years old, male. Magnification 10×10. Hematoxylin-eosin (HE) staining showed that the carcinomatous component was a poorly differentiated hepatocellular carcinoma, carcinomatous cells with nestlike distribution and obvious atypia, pathological nuclear division was observed, and neoplastic necrosis was found in the center of some nests (**A**). The sarcomatous component was undifferentiated pleomorphic sarcoma, with diffuse distribution of tumor cells, fusiform and epithelioid changes, tumor giant cells and pathological nuclear division, and neoplastic necrosis in some areas (**B**). Immunohistochemical staining: CK-P was positive in the carcinomatous component (**C**) and Vim was negative (**D**); Vim was positive in the sarcomatous component (**E**) and CK-P was negative (**F**).

The maximum diameter of all lesions was greater than 5cm, and there was no capsule formation. One patient had hemorrhage in the mass (Case 1). The surgically resected specimens of four patients were confirmed to be HCS by the routine HE staining and immunohistochemical examination. The components of carcinomatous and sarcomatous in two patients could not be classified. One was poorly differentiated CCC and spindle cells, one was poorly differentiated HCC (Figure 4A) and UPS (Figure 4B). CK-P was positive in the carcinomatous component (Figure 4C) and Vim was negative (Figure 4D); Vim was positive in the sarcomatous component (Figure 4E) and CK-P was negative (Figure 4F). Patients' immunohistochemical indexes and tumor pathological classification are shown in Table 3.

Discussion

The incidence of HCS is low, and the clinicopathological and imaging manifestations, treatment and prognosis are not well understood. Therefore, we conducted a retrospective analysis of the English literature on HCS published in Pubmed since 2000, excluding repeated cases and cases with unknown information. There were a total of 63 cases (including 4 cases in our study). Patients with an average age of 60.4-year-old (range, 29–85 years), 46 (73.0%) cases male, female 17 (27.0%), suggesting that HCS is more common in elderly male patients, case 2 in this study is the youngest of 63 patients (29-year-old) who had been infected with schistosomiasis 10 years before the diagnosis of HCS, no history of similar infection has been mentioned in the previous literature, so the association

Table 3 Immunohistochemical Indexes and Tumor Pathological Classification of the Patients

Case NO.	Components	CK-P	Vim	Gly-3	Hepa-1	Ki-67	CK7	CK19	CD34
1	Carcinoma+ Spindle Cells	+	+	-	-	+,60%	-	-	+
2	CCC+Spindle Cells	+	+	-	-	+, Scattered	+	+	-
3	Carcinoma+ Spindle Cells	+	+	±	-	+,>50%	/	+	+
4	HCC+UPS	+	+	±	-	+,40%	-	/	/

Abbreviations: CCC, cholangiocellular carcinoma; HCC, hepatocellular carcinoma; UPS, undifferentiated pleomorphic sarcoma; CK-P, epithelial marker cytokeratin; Vim, mesenchymal marker Vimentin; Gly-3, phosphatidylinositol proteoglycan 3; Ki-67, cellular marker for proliferation; bile duct cell markers, CK7 and CK19; hepatocyte markers, gly-3, ki-67, Hepa-1; CD34, angiogenic marker cadherin 34; NA, not available; +, present; –, absent.

between them remains to be further studied. Among the 63 patients, 27 (43%) had hepatitis, which chronic hepatitis B virus (HBV) infection and hepatitis C virus (HCV) infection were 24 and 3, respectively. 20 (31.7%) patients were pathologically diagnosed with cirrhosis (17 cases) or fibrosis (3 cases). This shows that the occurrence of HCS and cirrhosis or fibrosis history is not necessarily associated. There were 37 (61.9%) patients with elevated tumor markers (CEA, AFP, CA19-9), among which 22 (34.9%) patients had elevated AFP. Most patients with HCS had elevated tumor markers, but the possibility of HCS could not be ruled out within the normal range.

Based on the analysis of 63 cases with HCS, the author found that the most common carcinomatous component in HCS is HCC (38/63, 60.3%). Including one case[34] with HCC + CCC, and one with HCC + CCC + Adenocarcinoma + neuroendocrine carcinoma.[6] The most common sarcomatous component is the undifferentiated sarcomatous component which is characterized by spindle cells (24/63, 38.1%). Include two or more of sarcomatous element in 11 cases (17.5%). Among them, two cases contained six different components, one contained HCC + neuroendocrine cancer + adenocarcinoma + spindle cells + rhabdomyosarcoma + osteosarcoma,[6] one contained HCC + adenocarcinoma + spindle cells + rhabdomyosarcoma + chondrosarcoma + osteosarcoma.[19] More details in Table 4.

HCS contains sarcomatous component, grows rapidly, and is usually relatively large when symptoms appear. The mean maximum diameter of the tumor in 63 cases was 9.7cm (range, 2.5–25cm), and 5cm or more in 52 (82.5%) cases, all of 4 cases in our study exceeded 5cm. With high malignancy of HCS, among 63 cases, 37 (58.7%) cases had different degrees of intrahepatic metastasis and vascular invasion or tumor embolism formation. Frequently metastatic and violated parts: intrahepatic (14/37, 37.8%), lymphonodus (6/37, 16.2%, porta and retroperitoneal are most common), diaphragm (5/37, 13.5%), peritoneal (4/37, 10.8%), lung (3/37, 8.1%) and adrenal glands (3/37, 8.1%), gallbladder (2/37, 5.4%), gastric wall (2/37, 5.4%), colon (2/37, 5.4%). The portal vein (16/37, 43.2%) is the most easily affected vessel. Among the 63 cases, 37 (58.7%) cases were located in the right liver, 15 for

Table 4 Carcinomatous Components and Sarcomatous Components of 63 Patients with Carcinosarcoma

Carcinomatous Components	Number (Percentage)	Sarcomatous Components	Number (Percentage)
HCC	(38, 60.3%)	Spindle Cells	(24, 38.1%)
Adenocarcinoma	(10, 15.9%)	Osteosarcoma	(13, 20.6%)
CCC	(9, 14.3%)	UPS	(9, 14.3%)
undifferentiated	(5, 7.9%)	Rhabdomyosarcoma	(9, 14.3%)
Cystadenocarcinoma	(1, 1.6%)	Fibrosarcoma	(7, 11.1%)
Two or More	(5, 7.9%)	Chondrosarcoma	(6, 9.5%)
		Leiomyosarcoma	(4, 6.3%)
		UES	(1, 1.6%)
		Two or More	(11, 17.5%)

Abbreviations: HCC, hepatocellular carcinoma; CCC, cholangiocellular carcinoma; UPS, undifferentiated pleomorphic sarcoma; UES, undifferentiated embryonal sarcoma.

left, and 11 involved both the left and right liver, indicating that HCS is more likely occurring in the right liver.

In the retrospective analysis of 63 patients, 11 patients were excluded without specific follow-up data. There were 19 patients without metastasis, invasion of adjacent organs or vascular embolism, 11 of them survived during the follow-up period, except 2 patients who were followed up for 28m, respectively, the remaining 9 all exceeded 12m. There were a total of 33 patients with metastasis, invasion or vascular embolism, among which 6 survived. Except 2 patients who were followed up for only 23m, respectively, the remaining 4 all exceeded 12m, and all of them only had portal vein embolism (Table 5). From the above data, we could see that the patients without metastasis, invasion of adjacent organs or vascular embolism have a better prognosis, while patients with portal vein embolism alone have a better prognosis than patients with other organs metastasis or invasion.

Xiang Minglao et al found that in the treatment of 5 patients with HCS, 4 patients died within 6m after palliative hepatectomy and 1 patient survived 21m after radical hepatectomy, so radical resection may be the best treatment for patients with HCS.[35] 3 patients of our study were performed in the radical surgery; however, 3 cases died within a year. The author thinks that it may be related to the facts of metastasis of 3 patients preoperatively, and Xiao et al reported one case of radical hepatic resection with preoperative other tissue without metastasis and invasion. Although the patient in Case 2 had residual lymph nodes after surgery, the survival time of him was longer than that of the other 3 patients. The author considered that it might be because this patient was younger and his own resistance was stronger than that of older ones. Of course, more sample tests are needed. Chemoradiotherapy with doxorubicin and ifosfamide provided a progression-free survival of 12m for a patient with HCS with multiple postoperative lymph node metastases, Daisuke Kurita et al believed that the chemoradiotherapy could prolong the survival of patients with unresectable carcinosarcoma.[29] This is consistent with the retrospective literature analysis. Patients with metastasis or invasion who received postoperative chemoradiotherapy whether dead or alive had longer follow-up period than patients who received only surgical treatment (Table 5). A literature[12] reported a case of HCS undergoing liver transplantation, in which peritoneal and intrahepatic metastasis occurred within 3m after the operation, then the patient died 2m later, Garcez-silva et al believed that liver transplantation might be contraindicated for patients with HCS.

In the retrospective literature, 24 articles[2,3,7–11,13,14,17,19–24,26–33] were involved in the imaging manifestations, including our study of total of 35 patients. Due to the different proportion of carcinomatous components and sarcomatous components in HCS, and their pathological types were not the same, the imaging manifestations were different. However, all the masses showed necrotic cystic changes, the authors were believed that this tumor contains sarcomatous component which grow rapidly; however, the blood supply cannot keep up with it, necrotic cystic degeneration is prone to occur, which make it different from HCC and CCC. There were 4 cases (11.4%) with septations, and septations reinforced. The margins of the mass could be clear or unclear, and 6 patients (17.4%) had fibrous capsule surrounding the mass, among which 4 survived in the follow-up period, with an average time of 23.3m (range, 12–32m). It can be seen that patients with HCS with capsule have a better prognosis, which may be related to the fact that the capsule limits the infiltration of the tumor into the surrounding tissues, while tumors without

Table 5 Follow-Up Data of Patients with or Without Metastasis or Invasion and Metastatic or Invaded Patients with or Without Postoperative Chemoradiotherapy

Patients	Survivals	Mean Survival Time	Deaths	Mean Survival Time	Survival Time Less Than Average
without Metastasis or Invasion	11(57.9%)	18.1m (2–32m)	8(42.1%)	11.7m (5–22m)	4(50%)
With Metastasis or Invasion	6(18.2%)	15.2m (2–30m)	27(81.8%)	6.9m (0.4–37m)	20(74.1%)
with Chemoradiotherapy	3(21.4%)	16m (3–24m)	11(78.6%)	8.9m (1.7–37m)	7(63.7%)
without Chemoradiotherapy	3(15.8%)	14.7m (2–30m)	16(84.2%)	5.5m (0.4–21m)	7(43.8%)

Abbreviation: m, months.

Table 6 Imaging Features of Reported Cases of Hepatic Carcinosarcoma (Describes in Detail with the Dynamic Enhanced Image Performance)

Ref	Enhancement Mode	Calcification	Margin	Capsule	Septum	Involvement /Metastasis	Component	Follow-Up Period
3	F-in-F-W	–	Unclear	–	–	+	Carcinoma+spindle cells	5m/D
8	F-in-F-W	–	Unclear	–	–	+	HCC+spindle cells	1.7m/D
9	F-in-F-W	+	Unclear	–	–	–	CCC+osteosarcoma +chondrosarcoma	22m/D
10	F-in-F-W	–	Clear	+	–	–	HCC+adenocarcinoma +osteosarcoma +chondrosarcoma	19m/A
14	F-in-F-W	–	Unclear	+	–	+	HCC+osteosarcoma+spindle cells	1y/A
17	F-in-L-W	–	Clear	–	–	–	HCC+spindle cells	16m/A
20	F-in-L-W	–	Unclear	–	–	+	Carcinoma+spindle cells	5m/D
	F-in-F-W	–	Unclear	–	–	NA	NA	5m/D
	F-in-F-W	+	Clear	–	–	–	NA	A
24	F-in-L-W	+	Unclear	+	–	+	HCC+osteosarcoma	NA
26	F-in-F-W	–	Clear	–	–	–	HCC+spindle cells	2m/A
	F-in-F-W	+	Unclear	–	–	–	CCC+spindle cells	13m/D
	F-in-F-W	–	Unclear	–	–	+	HCC+spindle cells	8m/D
	F-in-F-W	–	Unclear	–	–	–	HCC+leiomyosarcoma	18m/A
	F-in-F-W	–	Unclear	–	–	–	adenocarcinoma+spindle cells	18m/D
	F-in-F-W	–	Unclear	–	–	+	adenocarcinoma+spindle cells	4m/D
Present	progressivity	–	Unclear	–	–	+	Carcinoma+spindle cells	0.7m/D
	F-in-L-W	–	Unclear	–	+	+	CCC+spindle cells	21m/D
	F-in-L-W	–	Clear	–	–	+	Carcinoma+spindle cells	6m/D
	F-in-F-W	–	Clear	–	+	+	HCC+UPS	11m/D

Abbreviations: Ref references, m months, D dead, A alive, + present/positive, – absent/negative, NA not available, F-in-F-W fast in fast washout, F-in-L-W fast in late washout, HCC hepatocellular carcinoma, CCC cholangiocellular carcinoma, UPS undifferentiated pleomorphic sarcoma.

fibrous capsule are more invasive and have a worse prognosis. In all cases, CT plain scan showed inhomogeneous hypodense/T1WI-hypointense, T2WI-hyperintense, and irregular marginal strengthened after enhancement. There were 20 cases describes in detail with the dynamic enhanced image performance (Table 6), except for one case (our study) which showed a continuous progressive enhancement process (this may be related to the higher proportion of the sarcomatous component and the CD34 was positive), and other cases characterized by moderate to clearly enhancement in AP, in PP and EP strengthening continues to decline (14 cases, 70%) or continued in PP and attenuation in EP (5 cases, 25%), characterized by a "fast in fast washout" or "fast in late washout" dynamic enhancement process. If an increased density is found within the mass, it may indicate a chondrosarcoma or osteosarcoma component.[6,9,24,28]

On imaging, HCS presented moderate to clearly irregular marginal enhancement, with large patchy necrosis in the center

of the lesion, which needed to be differentiated from hepatic abscesses. The walls of liver abscesses are often thick and continuously reinforcing, with honeycomb compartments, and edema in the liver parenchyma is often seen around the lesion; but the dynamic enhancement process the former is mainly manifested as "fast in fast washout". Isolated cases of HCS need to be differentiated from UPS, synovial sarcoma, liposarcoma, angiosarcoma, etc. Synovial sarcoma usually occurs in young adults (HCS, in elderly patients); typical liposarcomas contain hypodense/double hypointense adipose tissue; however, peritumor edema and pseudocapsule could be seen in the UPS (pseudocapsule has not been reported in HCS), but preoperative diagnosis is difficult in most cases; Angiosarcoma is characterized by progressive central tp outward or filling in enhancement (HCS, fast in fast washout). HCS need to be differentiated from primary hepatocellular carcinoma, HCC enhancement is often characterized by "fast in fast washout", but the necrosis in it is smaller than that in HCS; Intrahepatic CCC is often characterized by a "slow in slow washout" pattern of enhancement accompanied by distension of the distal bile duct.

The origin of HCS has been a controversial topic, with two main theories. Fayyazi et al speculated that the tumor was derived from a single pluripotent stem cell, which differentiated into epithelial cells and mesenchymal cells.[36] Kubosawa et al supported the theory of the transformation of liver cancer cells into sarcoma cells. The Clonal studies of relatively common carcinosarcomas (such as those of the uterus, lung, breast, and gastrointestinal tract) indicate that they originate from monoclones.[37] Inging-marie Schaefer et al through immunohistochemistry and gene coding analysis of a case concluded that HCS was a tumor with bidirectional morphology but originated from monoclonal.[2] Xin Zhang et al by studying the genes of the components of cancer and sarcoma in 13 patients with HCS found that the changes in the genome were consistent, supporting the idea of the monoclonal origin of HCS.[34] A retrospective analysis was performed on 63 patients with HCS, of which 44 (69.8%) had no history of cirrhosis or hepatic fibrosis, thus supporting the view that hepatocellular sarcoma is a monoclonal tumor.

Limitations

The incidence of HCS was minimal. Searching for the English literatures in the past 20 years, including our study, only 63 patients with HCS were pathologically confirmed, and only 20 patients with complete imaging manifestations were involved, most of which were case reports. In the past 6 years, there were only 4 patients with HCS in our hospital. Their imaging findings and clinicopathology were heterogeneous. Therefore, more cases accumulation and multi-center cooperation are needed to obtain more convincing clinic-photographic feature to improve the diagnosis of HCS.

Conclusion

HCS like other malignant tumors of the liver have no specific clinical manifestations, and many patients only suffer from epigastric pain. HCS is difficult to be diagnosed preoperatively, the prognosis of patients is poor because of its strong invasiveness, easy invasion of adjacent tissues and metastasis to other organs, and radical surgery combined with chemoradiotherapy can help prolong the survival time of patients. Therefore, the careful analysis of the imaging manifestations in combination with the clinical characteristics of the patients is helpful for the clinical surgical treatment, thus improving the survival of the patients.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request with the permission of the Hospital and all authors but not publicly available.

Ethics Approval and Consent to Participate

This study was approved and compliant with the Hunan Provincial People's Hospital's medical ethics committee, while complying with the Declaration of Helsinki. The patients' consent to review their medical records was not required by the ethics committee, the reasons for the waiver are as follows. First of all, this was a retrospective study, in the preoperative informed consent, the patients had been informed that we will dispose of the diseased tissue removed, including pathological and cytological examination, and so on. What is more, the relevant images and pathological data of the patients collected in this study were anonymized or maintained with confidentiality, so as to ensure that the key informations of the participants were not disclosed and to fully protect the privacy of them. Finally, we only analyzed the sample data and there was no risk to the subjects.

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Disclosure

The authors report no conflicts of interest for this work.

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