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ABOUT COVER

Editorial Board of World Journal of Gastrointestinal Oncology, Gaetano Piccolo, MD, PhD, Doctor, Department of Health Sciences, University of Milan, San Paolo Hospital, Via Antonio di Rudini 8, Milan 20142, Lombardy, Italy. gpiccolo1983@gmail.com

AIMS AND SCOPE

The primary aim of World Journal of Gastrointestinal Oncology (WJGO, World J Gastrointest Oncol) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, etc.

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CASE REPORT

Rare and lacking typical clinical symptoms of liver tumors: Four case reports

Yun Zhao, Yu-Kun Bie, Guang-Ya Zhang, Yi-Bin Feng, Feng Wang

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Abstract

BACKGROUND

Rare liver tumors (RLTs) have an extremely low likelihood of forming, and some have been recorded only in isolated cases. The lack of normal clinical symptoms in RLTs makes preoperative diagnosis extremely challenging, which results in frequent misinterpretation. The present case report helps enhance our ability to recognize and treat uncommon liver tumor disorders.

CASE SUMMARY

We describe four distinct examples of rare liver tumor diseases. These cases were all true cases with no conventional clinical signs or imaging findings. In all patients, hepatic occupancy was discovered on physical examination, which raised the preoperative suspicion of hepatic cancer. All tumors were surgically removed, and postoperative histology and immunohistochemistry were performed to confirm the diagnosis. The first patient had primary hepatic fibrosarcoma. The second case involved a primary hepatic neuroendocrine tumors. These two patients had malignant liver tumors, and both had extremely satisfactory surgical outcomes. The third case involved focal hepatic steatosis, and the fourth case involved a single necrotic nodule in the liver. These two patients had benign liver tumors, but they had already undergone surgery and did not require any postoperative care.

CONCLUSION

The number of patients with RLTs is small, and the clinical and imaging results are vague. Preoperative diagnosis is challenging, and patients are sometimes mistakenly diagnosed with liver cancer, which leads to unnecessary surgical therapy in certain individuals.

Key Words: Liver tumor; Primary hepatic fibrosarcoma; Primary hepatic neuroendocrine tumor; Focal hepatic steatosis; Solitary necrotic nodule of the liver; Lack of typical clinical symptoms; Case report



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Core Tip: To exclude rare liver tumors in patients with atypical liver tumors, imaging should be performed multiple times before surgery. If necessary, preoperative positron emission tomography/computed tomography may be performed to persuade the patient to undergo a liver puncture biopsy. If there is still no evidence of cancer in the patient, then liver surgery should be avoided, and short-term follow-up may be considered.

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INTRODUCTION

Rare liver tumors (RLTs) are primary benign and malignant tumors that occur with a low incidence and very rare clinical occurrence, in addition to common benign and malignant tumors, such as primary hepatocellular carcinoma, cholangiocarcinoma, liver cysts, liver abscesses, and hepatic cavernous hemangiomas. Primary hepatic fibrosarcoma (PHF) is a rare and extremely malignant tumor that originates from hepatic fibroblasts[1]. According to the United States Surveillance, Epidemiology, and End Results Cancer Data Bank, of the 54709 cases of primary hepatic malignancy, only two patients were diagnosed with PHF. Primary hepatic neuroendocrine tumors (PHNETs) are rare neuroendocrine tumors (NETs) that account for 0.3% of all NETs and 0.11% of primary liver tumors[2,3]. Although the global prevalence of non-alcoholic fatty liver disease is 25.24%[4], little is known about focal hepatic steatosis (FHS) compared to diffuse hepatic steatosis. Single necrotic nodule in the liver (SNNL) is a rare benign tumor of the liver, and few cases of SNNL have been reported in the national and international literature. SNNL was first described by Shepherd and Lee in 1983 [5]. These four cases of liver tumors and their rarity make preoperative and differential diagnoses very difficult, and there are no treatment guidelines for this type of disease. The aim of these case reports is to increase the attention of hepatobiliary surgeons, increase their experience in the diagnosis and treatment of rare diseases, reduce misdiagnosis and avoid inappropriate treatment.

CASE PRESENTATION

Chief complaints

Case 1: A 64-year-old male patient whose body mass index (BMI) was 22.1. A computed tomography (CT) scan revealed intrahepatic occupation for 18 months.

Case 2: A 40-year-old male patient with a BMI of 22.0. A liver tumor was detected via CT examination during the treatment of a right ureteral stone.

Case 3: A 63-year-old male patient with a BMI of 26.0. CT examination revealed liver occupancy for 5 months.

Case 4: A 60-year-old female patient with a BMI of 25.2. Ultrasound examination revealed liver occupancy for 6 days.

History of present illness

Case 1: There were no symptoms of abdominal pain or bloating during the course of the disease.

Case 2: The hepatic tumor was solid mass that appeared as an infected-like lesion on CT, which led to a lack of attention at the first visit. Two weeks later, a follow-up enhanced CT of the epigastric region revealed the same lesion, but the tumor was considered a neoplastic lesion. There were no clinical symptoms, such as fever, jaundice or abdominal pain, during the course of the disease.

Case 3: There were no symptoms of abdominal pain or bloating during the course of the disease.

Case 4: She had no abdominal pain or distension.

History of past illness

Case 1: He had a history of "hepatitis B virus (HBV) carrier" and "right lung middle lobe squamous cell carcinoma resection".

Case 2: There was no previous history of hepatitis or alcohol consumption.



Case 3: He denied a history of hepatitis and no smoking or alcohol habits.

Case 4: She had a history of hypertension for one year, was hospitalized for conservative treatment of hypertensive cerebral hemorrhage, and underwent surgery for left kidney stones in 2019.

Personal and family history

Case 1: He was not addicted to smoking or alcohol and denied a family history of cancer.

Case 2: There was no alcohol consumption.

Case 3: The patient had a family history of liver disease and liver cancer.

Case 4: She denied any family history of liver disease or liver cancer.

Physical examination

Case 1: Physical examination revealed negative abdominal signs.

Case 2: Physical examination revealed that vital signs were normal, there was no vellowing of the skin or sclera, and the results of the abdominal examination were negative for all signs.

Case 3: The results of the physical examination revealed normal vital signs and negative abdominal signs.

Case 4: Physical examination revealed that vital signs were normal, and abdominal signs were negative.

Laboratory examinations

Case 1: The laboratory test results revealed a platelet count of $60 \times 10^{\circ}/L$ (reference range, $125-350 \times 10^{\circ}/L$), and blood cell morphology in which platelets were easily observed (average 5.4/oil microscope). The high-sensitivity HBV deoxyribonucleic acid assay revealed a titer of 48.6 IU/mL (reference range, < 20 IU/mL). The infection series found a hepatitis B surface antigen (HBsAg) of 88.76 IU/mL (reference range, 0-0.05 IU/mL). Tumor marker levels, hepatic fibrosis indices, liver function and other laboratory test results were normal.

Case 2: The laboratory findings revealed c-reactive protein of 13.76 mg/L (reference range, < 10.0 mg/L) and procalcitonin of 0.136 ng/mL (reference range, 0-0.052 ng/mL). The biochemical indices revealed normal bilirubin, alanine aminotransferase of 750.0 U/L (reference range, 0-50 U/L), and azelaic aminotransferase of 750.0 U/L (reference range, 17-59 U/L). Tumor marker levels and routine blood tests were normal.

Case 3: The laboratory test results were as follows: Hepatitis B series: HBsAg, 44.28 IU/mL (reference range, 0-0.05 IU/ mL); hepatitis B E antibody, 9.75 PEIU/mL (reference range, 0-0.4 PEIU/mL); and hepatitis B core antibody, 93.03 PEIU/ mL (reference range, 0–0.7 PEIU/mL). The results of the quantitative HBV nucleic acid assay revealed a titer of 1.55^{E+04} IU/mL (reference range, < 200 IU/mL). Carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), and carbohydrate antigen 19-9 (CA19-9) levels were within the normal range. Liver function, liver fibrosis indices, coagulation series and other laboratory tests were normal.

Case 4: The laboratory test results were unremarkable, and the CEA, AFP and CA19-9 levels were all within the normal range.

Imaging examinations

Case 1: Magnetic resonance imaging (MRI) enhancement of the upper abdomen revealed a 4.1 cm × 3.0 cm mass occupying the lower segment of the right posterior lobe of the liver, which suggested a neoplastic lesion with possible metastasis, and a primary hepatocellular carcinoma to be drained (Figure 1).

Case 2: MRI enhancement examination of the upper abdomen suggested the presence of a neoplastic lesion (malignant possibility), which was accompanied by a reduced signal in the hepatobiliary phase of the adjacent liver parenchyma (Figure 2).

Case 3: Upper abdominal CT enhancement revealed a hepatic S5 subperitoneal strengthening nodule, which was considered a tumorigenic lesion, and did not exclude the possibility of hepatocellular carcinoma. The surface of the liver was not smooth, and the patient was referred to the clinic to exclude cirrhosis. MRI enhancement of the upper abdomen revealed a subperitoneal nodular shadow of liver S5, which indicated a tumor lesion (possible liver cancer) (Figure 3).

Case 4: CT enhancement examination of the upper abdomen revealed point-like and small patchy enhancement foci in the upper right anterior lobe and lower right posterior lobe in the arterial phase, and rounded low-density shadows were observed in the upper right anterior lobe and lower right posterior lobe in the venous phase, with clear boundaries. The size of the larger foci was approximately 2.2 cm × 2.0 cm, and the range of enhancement in the foci of the upper right anterior lobe and lower right posterior lobe was slightly enlarged in the delayed phase. For lesions in the upper part of the right anterior lobe and lower part of the right posterior lobe of the liver, the possibility of neoplastic lesions and inflammatory lesions to be excluded should be considered, and MRI examination should be recommended. MRI enhancement of the upper abdomen revealed equal and slightly long T1 and equal and slightly long T2 signals were



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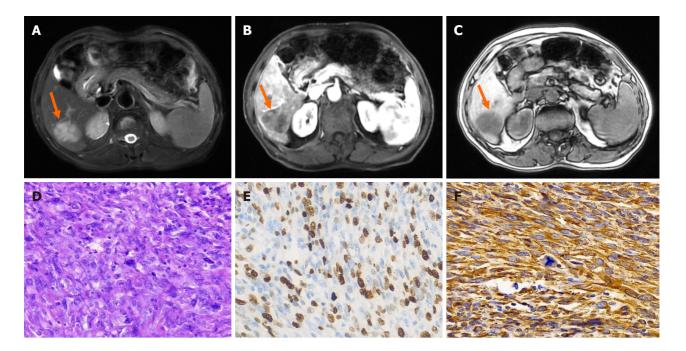


Figure 1 Magnetic resonance imaging and pathological results of primary hepatic fibrosarcoma. A: Magnetic resonance imaging (MRI) T2 weighted imaging of the compressed fat sequence revealed high signal density (arrow); B: MRI revealed mild heterogeneity with modestly distinct margins during the arterial phase (arrow); C: The lesion in the hepatobiliary phase showed low signal intensity (arrow); D: Hematoxylin and eosin staining 400 ×; E: Ki-67 positivity rate of approximately 60%, immunohistochemical staining 400 ×; F: Vimin (+), immunohistochemical staining 400 ×.

observed in the S6 and S8 segments of the liver, with a slightly high signal on diffusion weighted imaging (DWI) and a high apparent diffusion coefficient. Foci in the S8 segment showed progressive irregular enhancement of the edges, foci in the S6 segment showed ring enhancement, and foci in the hepatobiliary stage exhibited a low signal (Figure 4). Alterations in the S6 and S8 segments of the liver suggest a neoplastic lesion (possible myofibroblastoma), and puncture examination should be performed if necessary.

MULTIDISCIPLINARY EXPERT CONSULTATION

Case 1

After discussion with a preoperative multidisciplinary team (MDT), a malignant hepatic tumor was considered with a high possibility of metastasis.

Case 2

After a preoperative MDT discussion, liver cancer was considered highly likely, and laparoscopic hepatic tumor resection was performed.

Case 3

After a preoperative MDT discussion, the possibility of primary liver cancer was not excluded. The patient refused to undergo liver puncture biopsy, and he requested liver tumor resection.

Case 4

The preoperative diagnosis was a high possibility of hepatic myofibroblastoma. The patient refused to undergo puncture biopsy, and hepatic tumor resection was performed.

FINAL DIAGNOSIS

Case 1

Postoperative histopathology revealed an "S6 liver tumor" spindle cell tumor with morphology and immunohistochemistry that suggested a fibrosarcoma (Figure 1). The immunohistochemistry results were as follows: cytokeratin (CK) wide (-), vimin (+), Melan A (-), specific monoclonal antibody against melanoma (-melanoma) (-), smooth muscle actin (-), S-100 (-), signal transducer and activator of transcription 6 (-), CD34 (vascular +), Ki-67 (+, approximately 60% positive) (Figure 1E and F), CK5/6 (-), anaplastic lymphoma kinase (-), electroretinography (ERG) (-), CD117 (-), DOG-1 (-), CK5/6



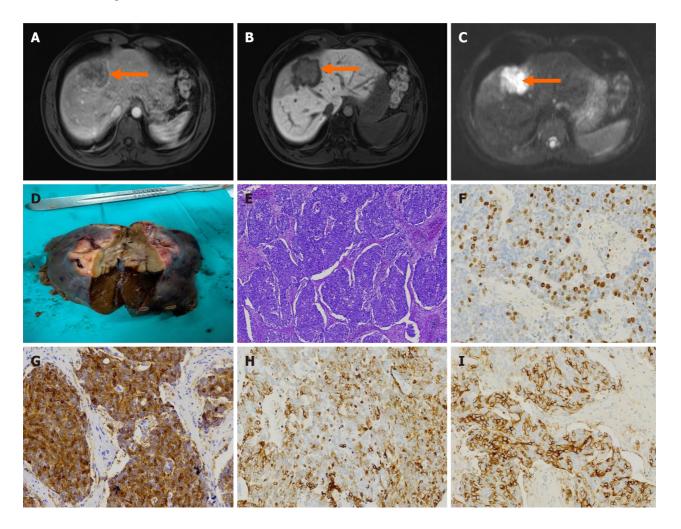


Figure 2 Magnetic resonance imaging, pathological examination, and immunohistochemical results of primary hepatic neuroendocrine tumors. A: The margins of the lesion showed enhancement during the arterial phase of magnetic resonance imaging, with the middle lobe exhibiting a mild septal-like enhancement pattern (arrow); B: The lesion in the hepatobiliary phase exhibited a low and slightly low signal (arrow); C: Diffusion weighted imaging revealed a high signal shadow of the lesion (arrow); D: Tumor pathology specimen; E: Hematoxylin and eosin staining 100 ×; F: Ki-67 positivity rate of approximately 30%, immunohistochemical staining 400 ×; G: synaptophysin cell positivity, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistochemical staining 400 ×; H: Cytokeratin wide cell positive, immunohistoch

(-), ERG (-), CD117 (-), DOG-1 (-), and epithelial membrane antigen (-).

Case 2

Postoperative histopathology and immunohistochemistry revealed a malignant tumor, which, combined with immunohistochemistry, was consistent with a high-grade neuroendocrine carcinoma (G3), but no cancerous tissue was observed on the stripped hepatic surface (Figure 2). The immunohistochemistry results were as follows: CK7 (-), CK20 (-), villin (+), CDX2 (-), CK19 (+), CA19-9 (-), hepatocyte (-), glypican-3 (-), GS (-), CD56 (partially +), chromogranin A (-), synaptophysin (+), thyroid transcription factor-1 (-), Ki-67 (+, positivity rate of approximately 30%), CD34 (-), CK wide (+), insulinoma associated protein 1 (+), phosphorylated histone H3 (+, scattered), Rb (-), P53 (+, wild-type), and somatostatin receptor 2A (partial +) (Figure 2F-I).

Case 3

Postoperative pathological diagnosis of the liver and tumor tissue revealed that the structure of the liver lobules in the lesion was discernible, patches of hepatocytes with large vesicular lipoatrophy, some swollen and degenerated hepatocytes, and a few dilatations of capillary bile ducts (containing bile plugs) were observed locally (Figure 3). The immunostaining results were as follows: CK7 (small number of hepatocytes around the confluent area in the lesion +), CK19 (bile ducts +), hepatocyte (+), glypican-3 (-), GS (mottled +), P53 (scattered weak +, suggesting wild-type), CD10 (capillary bile ducts +), CD34 (partial + in the peripheral band of the confluent area in the lesion), D2-40 (lymphatic vessels +), and hepatitis B core antigen (HbcAg) (+), HbcAg (-), HbsAg (a few hepatocytes within the lesion +, peripheral hepatic liver patchy +), and Ki-67 (+, < 5%) (Figure 3E and F). Morphology combined with immunostaining and special stains suggested a benign lesion, which was considered focal steatosis and chronic viral hepatitis B (G1/G2).

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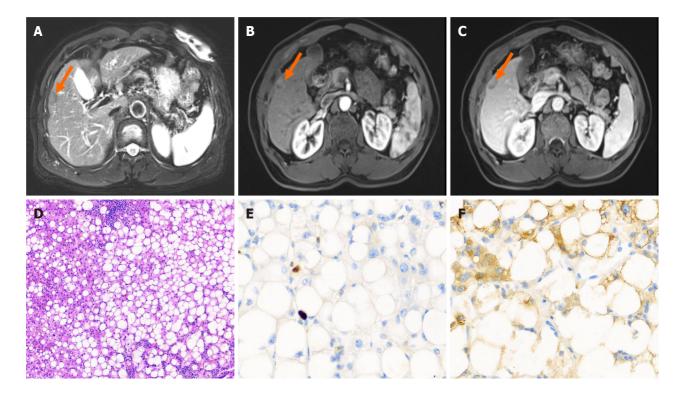


Figure 3 Magnetic resonance imaging, pathological examination and immunohistochemical results of focal hepatic steatosis. A: The lesion in segment S5 is slightly hypointense on the T2-weighted fat-suppressed magnetic resonance imaging (MRI) sequence (arrow); B: The lesion begins to enhance during the arterial phase of MRI (arrow); C: The lesion shows less enhancement in the delayed phase of MRI compared to the adjacent liver parenchyma (arrow); D: Hematoxylin and eosin staining 100 ×; E: Ki-67 (positive, < 5%), immunohistochemical staining 400 ×; F: Hepatocyte (+), immunohistochemical staining 400 ×.

Case 4

Pathological findings were reported 1 week after surgery and included (partial liver tissue) isolated necrotic nodules. Chronic cholecystitis with cholesterol polyp formation (Figure 4). Special stains included antacid stain (-), silver hexamine (-), periodic acid-Schiff preparation with diastase (-), and Gram (-) (Figure 4H and I).

TREATMENT

Case 1

One cycle of hepatic artery perfusion therapy (lopatin 50 mg) + embolization + docetaxel intravenous chemotherapy was given. Three cycles of intravenous chemotherapy, "albumin paclitaxel + nedaplatin", were recommended every 3 weeks. Ten days prior, the liver tumor was enlarged, and laparoscopic liver tumor resection was performed under general anesthesia after further discussion. During the surgery, the surface of the liver was uneven, with blunted edges and nodular cirrhosis, and the liver was enlarged. The liver tumor was located under the peritoneum of the S6 segment of the liver, and the tumor size was approximately 3.8 cm × 3.0 cm, grayish-white, solid, and hard. The S6 segment and the tumor were completely resected.

Case 2

Intraoperatively, a mass approximately 6.0 cm × 5.0 cm in size was observed at the junction of S4, S5, and S8 of the liver, with a crater-like depression in the center and protruding from the hepatic envelope. R0 resection of the tumor was performed. Two weeks after discharge, he underwent intravenous chemotherapy with the 'EP regimen' (etoposide 170 mg D1-3 + cisplatin 40 mg D1-3), which was repeated once every 3 weeks for a total of 6 hospitalized chemotherapy sessions.

Case 3

Laparoscopic hepatic tumor resection and cholecystectomy were performed under general anesthesia. During the surgery, the liver showed nodular cirrhosis, and the tumor was located on the surface of the S5 segment. The tumor was approximately 1.8 cm × 1.2 cm × 1.0 cm in size and grayish yellow with a medium texture. The hepatic S5 segment was routinely resected.

Case 4

Laparoscopic hepatic tumor resection and cholecystectomy were performed under general anesthesia. During the



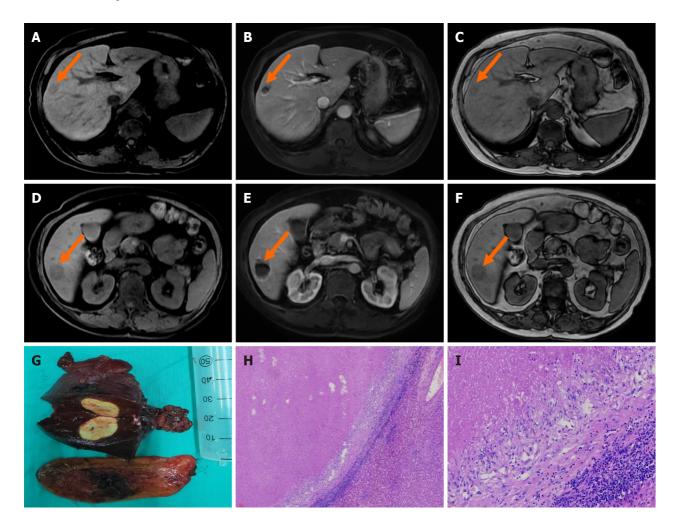


Figure 4 Magnetic resonance imaging, specimen and pathological results of single necrotic nodule in the liver. A: On T1-weighted magnetic resonance imaging (MRI), a nodular isointense to slightly hyperintense signal is observed in segment S8 of the liver (arrow); B: During the arterial phase of MRI, the lesion in segment S8 shows a progressive and irregular peripheral enhancement pattern (arrow); C: In the hepatobiliary phase, the lesion in segment S8 exhibits a hypointense signal (arrow); D: On T1-weighted MRI, a nodular isointense to slightly hyperintense signal is observed in segment S6 of the liver (arrow); E: During the arterial phase of MRI contrast enhancement, the lesion in segment S6 demonstrates a ring-like enhancement (arrow); F: In the hepatobiliary phase, the lesion in segment S6 shows a hypointense signal (arrow); G: Specimens of the tumor in segment S6 of the liver and the gallbladder; H: Hematoxylin and eosin (HE) staining 100 ×; I: HE staining 400 ×.

surgery, no mass was observed on the surface of the liver, and resection of segments S5, S6 and S8 was performed using intraoperative ultrasonic localization. A mass of approximately 3.5 cm × 2.2 cm was observed in segment S6, and a yellow, round, hard and solid mass with a size of approximately 2.2 cm × 2.0 cm was observed in segment S8.

OUTCOME AND FOLLOW-UP

Case 1

The patient recovered well without postoperative complications and was discharged. After discharge, the patient refused further treatment, such as chemotherapy. After outpatient follow-up for 2 years, the patient experienced no distant complications, tumor recurrence or metastasis.

Case 2

The patient recovered well without postoperative complications and was discharged. Outpatient gastroenteroscopy and positron emission tomography/CT examinations were performed to exclude extrahepatic primary lesions. After one year of outpatient follow-up, the patient experienced no long-term complications, tumor recurrence or metastasis.

Case 3

The patient recovered well without postoperative complications and was discharged. The outpatient follow-up was 22 months, and the patient reported no symptoms or tumor recurrence.



Case 4

The patient recovered well without postoperative complications and was discharged from the hospital. One month later, the patient was followed up in the outpatient clinic, and she reported no symptoms or physical discomfort.

DISCUSSION

Hepatic carcinoma is the sixth most common cancer worldwide in terms of incidence and the fourth leading cause of cancer-related mortality 6]. Although the pathogenesis of hepatic carcinoma is closely associated with inflammation and immune responses in the tumor microenvironment, the specific etiology and pathogenesis of most RLTs is not clear. A review of the literature is necessary to understand the potential causes of RLTs. HF accounts for approximately 1% to 2% of primary malignant tumors of the liver. Pro-related studies have shown that PHF is associated with hypoglycemia, the mechanism of which may involve high insulin-like growth factor II expression[7]. Acquired immune deficiency syndrome may also be a risk factor for hepatic fibrosarcoma^[8]. Relevant studies have indicated that primary benign fibrous tumors are at risk of malignant transformation into fibrosarcoma^[9]. Since Endmonson first reported PHNETs in 1958[10], more than 150 cases have been reported in the English literature [11,12]. Some scholars believe that these tumors are caused by ectopic pancreatic tissue, whereas others believe that they originate from progenitor cells in the intrahepatic bile ducts, but no final consensus has been reached due to their rarity [2,13]. Hepatic steatosis with focal fat deposition leads to FHS. It is a risk factor for FHS promotion in obesity, diabetes, alcoholism, genetic or metabolic disorders, and in chemotherapy-treated cancer patients^[14]. Hepatic steatosis has been reported in up to 47% of cancer patients^[15]. SNNL is prevalent in middle-aged and elderly males, with a prevalence of single nodules and occasional multiple nodules, and lesions are mostly located on the surface of the right lobe of the liver. The etiology of SNNL is primarily related to infection, parasites, hepatic trauma, vascular cirrhosis, and allergic reactions.

RLTs lack typical clinical manifestations and imaging features, and their imaging characteristics were studied retrospectively in these cases. PHF patients had no previous history of hepatitis or cirrhosis, and the AFP assay was normal. On imaging, there was a single solid or cystic solid mass shadow with irregular morphology, large cystic areas appeared when the tumor was large, and the enhancement was not obvious or was weakly inhomogeneous, which was sometimes difficult to differentiate from atypical hepatocellular carcinoma. Yu et al[16] explored the diagnostic value of CT for primary hepatic sarcoma in 12 cases of primary hepatic sarcoma that were diagnosed correctly in only 2 cases using CT preoperatively. According to the 2019 World Health Organization Classification of Neuroendocrine Tumors, NETs are classified as highly, moderately, or poorly differentiated (G1, G2, and G3, respectively). G3, which is a neuroendocrine carcinoma, has a nuclear schizophrenic image of > 20/10 HPF and/or a Ki-67 index > 20%[17]. Nuclear schizophrenia and the Ki-67 index are valuable for assessing the malignancy of PHNETs and its prognosis[18]. Our patient had a Ki-67 index of approximately 30%, which is a poorly differentiated neuroendocrine carcinoma according to the World Health Organization Classification of Neuroendocrine Tumors, which suggests a poorer prognosis. PHNETs may differ in imaging and pathological manifestations according to their grade. The PHNETs showed a single lesion on MRI, with inhomogeneous signals on T1 weighted imaging (WI) and T2WI, enhancement of the margins of the lesion in the arterial phase, and mild enhancement of the middle lobe in a segregated pattern. The lesion in the hepatobiliary phase showed a low or slightly low signal, and the lesion on DWI showed a high signal shadow. Wang et al[19] studied 40 patients with PHNETs and showed that higher tumor grade, AE1/AE3 negativity, and elevated Ki-67 expression correlated with poorer patient survival rates. Although parameters, such as treatment modalities, do not significantly affect overall survival, they are effective in controlling tumor progression and alleviating symptoms.

In some patients, FHS and SNNL are difficult to distinguish from hepatic malignant tumors on imaging, and some patients have a background of hepatitis or cirrhosis. In our two patients, the lesions showed progressive marginal irregular enhancement or ring enhancement on MRI, with a low signal in the hepatobiliary phase, and the degree of late enhancement was lower than the adjacent hepatic parenchyma, which is similar to the manifestation of malignant tumors that are "fast in and fast out". Moreover, the patient refused liver puncture biopsy and requested direct surgical resection. Therefore, the preoperative diagnosis was difficult, and the diagnosis was confirmed only by postoperative histopathology and immunohistochemistry. Shan et al[20] reported that quantitative analysis of contrast-enhanced ultrasound images improved the diagnostic performance of atypical benign FHS and malignant FHS in the context of fatty liver. It is widely recognized that SNNLs are formed via infection and degeneration in the final stage of the natural course of the lesion[21]. According to recent reports, Kondi-Pafiti et al[22] suggested that SNNL was associated with metastatic cancer and that "isolated" necrotic nodules may not occur in isolation; moreover, the possibility of metastatic necrotic neoplastic lesions should be considered in the preoperative diagnosis[23].

For the treatment of RLTs, preoperative MDT should be used to help develop an individualized plan[24]. Hepatic tumor resection remains the primary treatment for patients with difficult preoperative diagnoses and surgical resectability, especially patients who do not wish to undergo hepatic puncture biopsy. The margins of malignant tumors should preferably be larger than 1 cm, and complete resection of the tumor and R0 resection should be ensured to prolong patient survival time^[25]. Case 1 and Case 2 patients were confirmed to have hepatic malignant tumors using histopathological and immunohistochemical examinations, and postoperative chemotherapy was recommended to reduce the recurrence of tumors and prolong their survival time. Case 3 and Case 4 patients were confirmed to have benign hepatic tumors, and no progressive treatment was needed after surgery, with regular follow-up. These two cases were difficult to diagnose preoperatively and could have undergone short-term observation if liver puncture biopsy had been performed preoperatively. However, physicians should respect the patient's choice, and surgical resection is needed for patients with suspected malignant tumors.

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CONCLUSION

RLTs have the common characteristics of being clinically rare, lacking typical symptoms and clinical manifestations. For RLTs, it is difficult to distinguish benign and malignant tumors on imaging, and it is difficult to diagnose preoperatively. When we diagnose and treat liver tumors, we consider the type of RLT as much as possible preoperatively, and we cannot completely rely on postoperative pathological examination and immunohistochemistry to confirm the diagnosis. Comprehensive clinical data combined with detailed imaging and tumor puncture biopsy are used to improve the preoperative diagnosis and avoid overtreatment of benign liver tumors. Moreover, individualized treatment plans for rare malignant tumors of the liver have been developed to maximize the prognosis of patients.

FOOTNOTES

Author contributions: Zhao Y designed the study and wrote the article; Bie YK was responsible for the imaging data and data analysis; Zhang GY was responsible for the pathology data and analysis; Feng YB performed the surgeries and treatment plan; Wang F was responsible for patient management and signing of the consent for treatment and research; all of the authors read and approved the final version of the manuscript to be published.

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