Letter to the Editor

Diffused primary hepatic angiosarcoma: a case description

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Introduction

As a mesenchymal tumor originating from liver sinusoidal endothelial cells, primary hepatic angiosarcoma (PHA) is an extremely rare malignant neoplasm accounting for 1.5–2% of primary malignant liver tumors (1). Despite its rarity, PHA is the most common hepatic mesenchymal tumor, with a significantly worse prognosis than hepatocellular carcinoma (HCC) (1). Although the exact pathogenesis of the disease is unknown, chemicals such as vinyl chloride, colloidal thorium dioxide, androgenic steroids, and phenylhydrazine have been linked to the development of PHA (2). Due to the absence of typical clinical and imaging manifestations, highly aggressive behavior, low radical resection rate, and insensitivity to chemoradiotherapy, PHA has the characteristics of a high mortality rate and a poor prognosis (3). Here, we present a case of PHA and describe its findings according to contrast-enhanced ultrasound (CEUS) and abdominal magnetic resonance imaging (MRI).

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 58-year-old male patient was referred to our hospital with edema of both lower limbs and jaundice. An abdominal MRI conducted in the local hospital revealed diffusely distributed multiple lesions in the liver. Laboratory testing yielded the following abnormal results: red blood cell (RBC) 2.87×10^{12}/L, hemoglobin (HGB) 102 g/L, platelets (PLT) 76×10^{9}/L, which were below the normal respective ranges; prothrombin time (PT) 18.8 s prolonging more than 3 s; aspartate aminotransferase (AST) 77 U/L, alanine aminotransferase (ALT) 69 U/L, gamma-glutamyl transpeptidase (GGT) 949 U/L, pre-albumin (PA) 10.70 mg/dL, total bile acid (TBA) 28 μmol/L, total bilirubin (TBIL) 75.1 μmol/L, direct bilirubin (DBIL) 29.0 μmol/L, which were diversely increased and indicated abnormal liver function. Tumor markers such as α-fetoprotein (AFP), cancer antigen 19-9 (CA199), and carcinoembryonic antigen (CEA) were all within normal limits.

To clarify the cause of liver damage, abdominal ultrasound and CEUS were carried out. Abdominal ultrasound revealed a perivascular hyperechoic nodule in the liver S7 segment (about 2.61 cm × 1.57 cm × 1.77 cm in size), which increased our suspicion of hepatic hemangioma (*Figure 1*). CEUS revealed diffusely distributed multiple nodules that showed synchronized enhancement and extinction with peripheral liver tissue in the arterial phase, portal phase, and delayed phase. Although inhomogeneous enhancement of the nodules was observed, fast extinction of focus in the delayed phase was not detected. The above findings did not resemble the typical malignant tumor manifestation of quick wash-in and quick wash-out with low enhancement, but corresponded to the benign manifestation of quick wash-in and equal wash-out with equal enhancement. Based on these findings, diffused hepatic benign lesions were considered (*Figure 2*).

Considering that ultrasonography is somewhat subjective, MRI-enhanced scanning was repeated. The liver was full, with a smooth surface and heterogeneous signals.

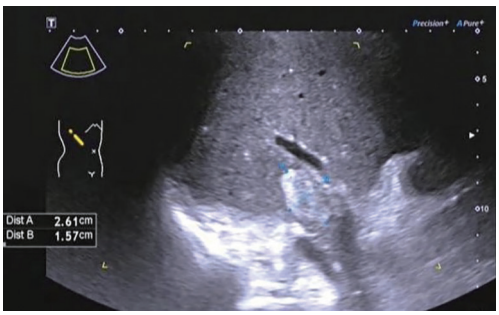

Figure 1 Abdominal ultrasound revealed a perivascular hyperechoic nodule in the 7th segment of the liver.

Diffuse long T1 and long T2 signals were seen, and T2-weighted signals were more clearly shown, which varied in size and morphology, with a roundish or irregular shape. In the arterial phase, obvious heterogeneous enhancement was observed, with a lace-like edge and thin strip or small round low signals in the center. The lesions were still significantly enhanced with high signals and a reduced range of low signals within them in the portal phase. In the delayed phase, iso-signal lesions and multiple thin strips of low signals between lesions were observed. The whole liver showed uniform signals 5 minutes after the contrast agent injection. The findings above led us to make a diagnosis of diffuse angiogenic tumors for which malignancy was not excluded (*Figure 3*).

To further clarify the diagnosis, the patient underwent ultrasound-guided liver biopsy after a complete assessment. The histological results showed mild dysplasia in the hepatic sinusoids and cluster distribution of vascular endothelial cells with hyperchromatic nuclei. The relevant immunohistochemical results were as follows: CD34 (vas+), Ki-67 (10%+), ERG (+), and CD31 (vascular endothelium+). Based on the combination of the histological and immunohistochemical results, we made a diagnosis of PHA (*Figure 4*).

Discussion

PHA is characterized by a high death rate and a dire prognosis. According to retrospective research and systematic reviews (2,3), patients with a diagnosis of PHA have a median overall survival (OS) of around 6 months. Significantly, Mangla (1) conducted the first database study of demographics and treatment outcomes specifically for PHA patients in 2022, revealing that the median OS of PHA was 1.9 months, which is more credible.

Although there are a variety of imaging presentations of PHA, most of the documented cases have reported localized mass type, which is prone to hemorrhage and necrosis when the masses are large; on the contrary, the diffuse type is rare. Regardless of the type, PHA is not easily distinguished from hemangioma and HCC on imaging. On ultrasonography, PHA mostly appears as single or multiple occupying lesions, which may be hyperechoic, hypoechoic, or mixed echo, with clear or indistinct borders and no obvious envelope. Larger cases of PHA may comprise mixed cystic and solid lesions, and most examples lack abundant blood flow. CEUS has not been thoroughly studied for the diagnosis of PHA. The characteristic manifestations may include rapid high enhancement in the arterial phase, low enhancement in the portal phase, and low enhancement in the delayed phase. Besides, larger tumors may have internal multiple non-enhancing areas. These manifestations are consistent with the ultrasonographic findings of hypervascular lesions. After reviewing the findings of CEUS imaging in this case, enhancement was detected from the fourth second onwards, which is earlier than the enhancement in hemangioma and HCC. We think this may be a feature of hepatic angiosarcoma.

In this case, the abdominal ultrasound revealed a perivascular hyperechoic nodule, which was more likely to lead to a diagnosis of hepatic hemangioma. CEUS showed the manifestation of hypervascular lesions, including quick wash-in, equal wash-out, and equal enhancement, indicating the possibility of benign tumors. However, the typical manifestation of hepatic hemangioma is that the contrast medium around the mass shows nodular enhancement and gradually fills from the periphery to the center in the arterial phase and portal phase, and lesions still show high enhancement or equal enhancement in the delayed phase, that is, “quick wash-in and slow wash-out with high enhancement” (4). The characteristic manifestation of hepatic carcinoma is rapid filling in the arterial phase with high enhancement and rapid subsidence in the portal phase with low enhancement, that is, “quick wash-in and quick wash-out” (5). The main reason for the misdiagnosis, in this case, is that the case is a diffuse type of PHA with total liver involvement, resulting in the lack of normal liver tissue for comparison in imaging diagnosis, which affected the observation of routine ultrasound and CEUS, and finally influenced diagnosis.

Contrast-enhanced computed tomography (CT) can help diagnose PHA, which can show ring enhancement and no internal enhancement in the arterial phase, and continuous

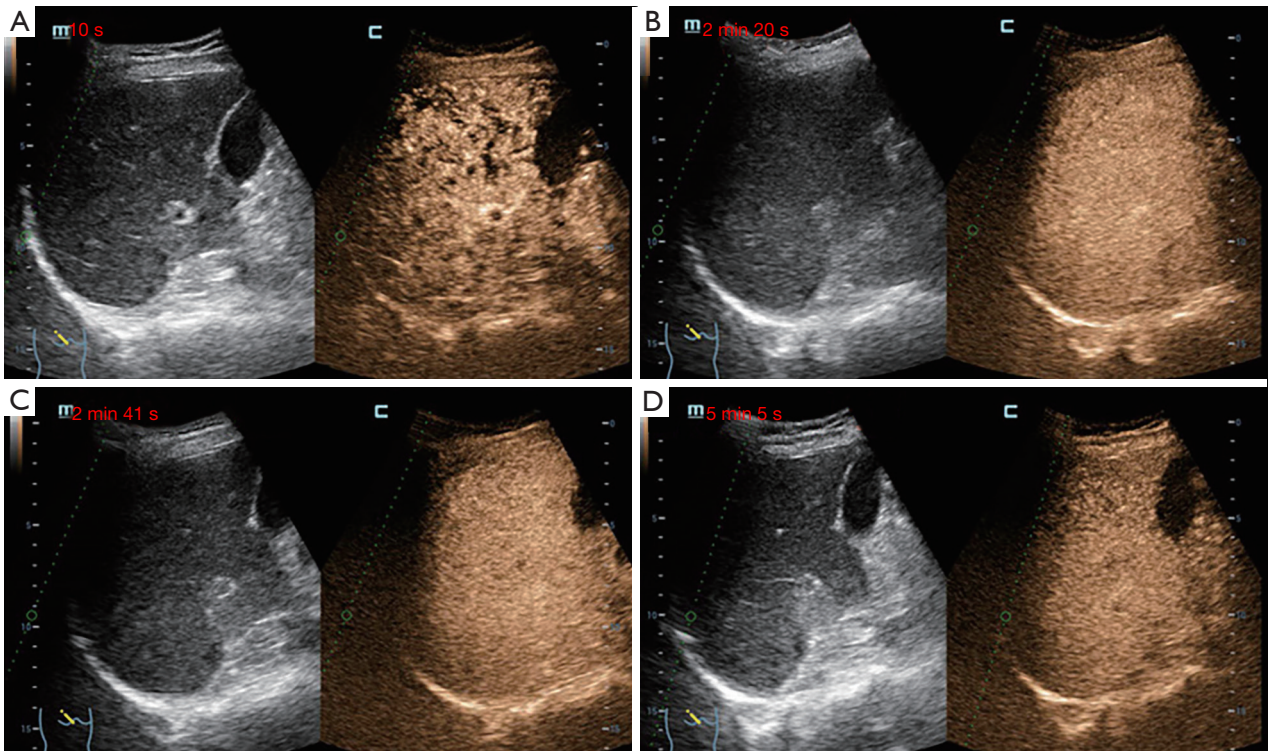

Figure 2 Contrast-enhanced ultrasound. (A) The arterial phase; (B) the portal phase; (C) the delayed phase; (D) 5 minutes later.

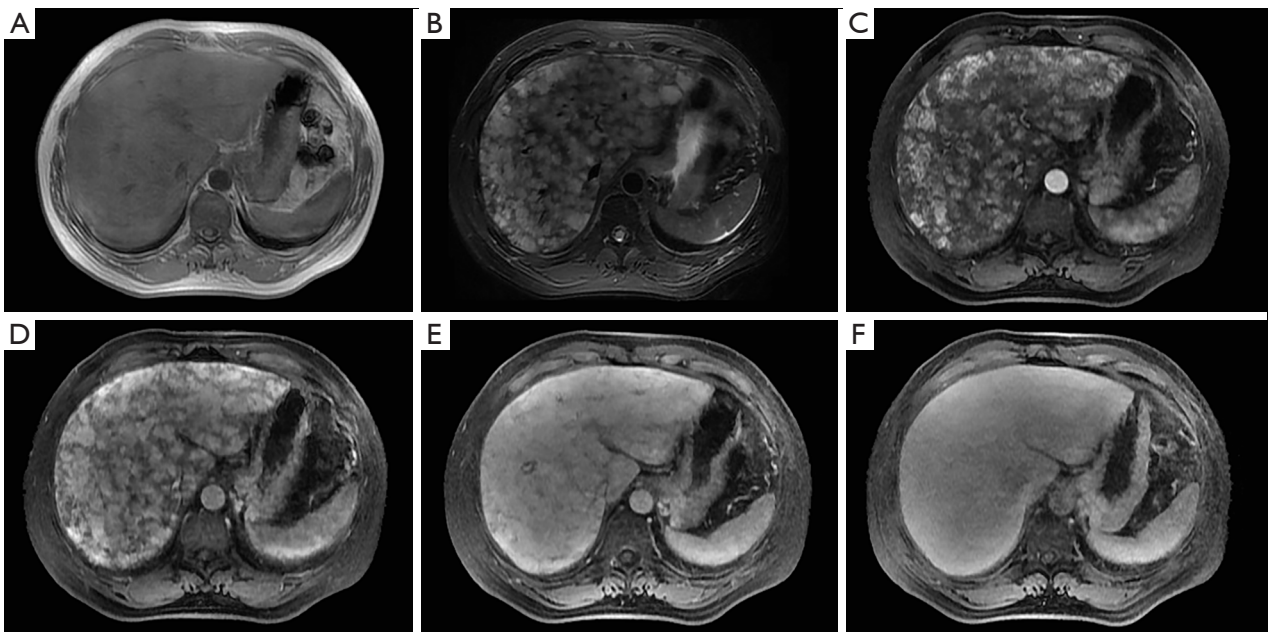

Figure 3 Contrast-enhanced magnetic resonance imaging. (A,B) Diffuse long T1 and long T2 signals. (C) The lesions were heterogeneously enhanced in the arterial phase, with the lace-like edge and thin strip or small round low signals in the center. (D) The lesions were still significantly enhanced with high signals and a reduced range of low signals within them in the portal phase. (E) Iso-signal lesions and multiple thin strips of low signals between lesions in the delayed phase. (F) The whole liver showed uniform signals 5 minutes after the contrast agent injection.

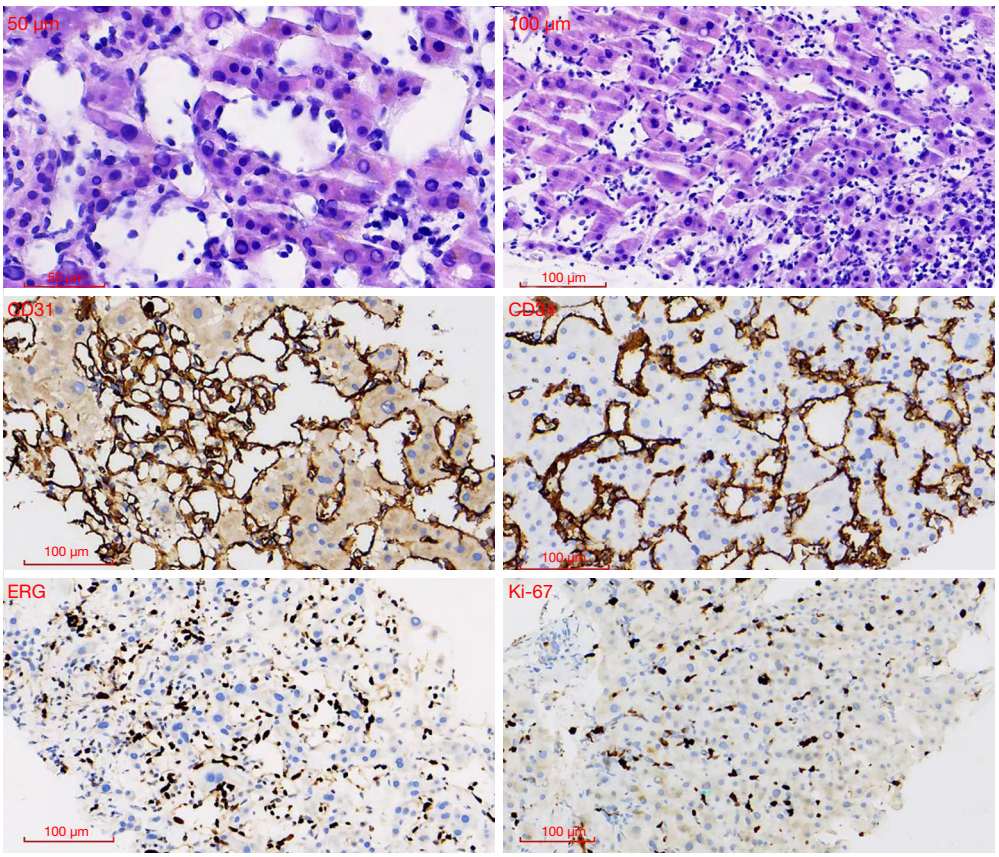

Figure 4 Hematoxylin-eosin staining (the histological result showed mild dysplasia in the hepatic sinusoids and cluster distribution of vascular endothelial cells with hyperchromatic nuclei) and the relevant immunohistochemical results [CD34 (vas+), Ki-67 (10%+), ERG (+), CD31 (vascular endothelium+)].

centripetal filling in the portal phase and delayed phase. However, in our case, CT was not performed on the patient.

MRI is specific for the diagnosis of PHA, the typical manifestations of which include single or multiple nodular and massive low signals on T1-weighted imaging (T1WI) and mixed high signals on T2-weighted imaging (T2WI), fluid-fluid level indicating intra-tumor hemorrhage, and significant irregular enhancement with diversity in the arterial phase. In this case, MRI showed multiple nodular and mass-like long T1 and T2 signals, thin strip or small round low signals in the center of lesions, and fluid-fluid level. Some of the lesions showed persistent enhancement, and the others showed ring enhancement. Eventually, a diagnosis of diffuse angiogenic tumors was considered, of which malignancy was not excluded.

The definitive diagnosis of PHA is based on pathological diagnosis, which needs to be obtained by biopsy or operation. It is necessary to biopsy any liver lesion suspected to be malignant without a history of cirrhosis. Ultrasound-guided needle biopsy bears the risk of hemorrhage, but Koyama *et al.* (6) believe that the success rate of biopsy is 78% without obvious complications and the survival time is longer than that of patients undergoing radical surgery, indicating that liver biopsy for PHA has obvious benefits. The combination treatment of radical resection and targeted therapy is recognized as the most effective treatment strategy for PHA (2). To date, an expert consensus of standard adjuvant chemotherapy regimens of PHA has not been reached. Liver transplantation should not be considered in PHA as it does not increase survival outcomes, regardless of the indication (7). Research found that the probability of accepting surgery in patients with hepatic angiosarcoma was less than 20%, so early diagnosis, timely operation, and personalized adjuvant therapy are critical to improving the survival time and quality of life of

patients (2).

A heightened awareness of PHA should be promoted among sonographers, who may then make a preliminary diagnosis of the focus according to the symptoms. Ultrasound-guided biopsy should be performed promptly to provide the pathological basis for the selection of follow-up treatment and to further assist in clinical diagnosis and treatment.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-219/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee (s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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