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CASE REPORT

Contrast-enhanced ultrasound in diagnosis of primary hepatic angiosarcoma

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Abstract Primary hepatic angiosarcoma (PHA) is a rare malignant tumor that occurs mainly in the elderly, with almost no specific symptoms or tumor markers. Information on the imaging characteristics of this tumor is limited due to its rarity. Therefore, it is difficult to diagnose PHA. So far, its definite diagnosis depends on histopathologic examination combined with immunohistochemical results. Patients with PHA have a poor prognosis in spite of surgical resection of this tumor. In this case report, we present a 72-year-old woman with PHA, focusing on the imaging features of this tumor, especially its enhancement pattern on contrast-enhanced ultrasound images. Contrast-enhanced ultrasound provided helpful information for diagnosis.

Keywords Contrast-enhanced ultrasound · Primary hepatic angiosarcoma · Diagnosis

Introduction

In adults, angiosarcomas account for about 2% of all soft tissue sarcomas [1]. Angiosarcomas generally originate from skin, breast, bone, soft tissues, or viscera. Skin and breast are the most common locations [2]. Primary hepatic angiosarcoma (PHA) is rare, representing about 1–2% of all primary hepatic tumors [1–3]. Clinical manifestations and laboratory tests are non-specific for the diagnosis of PHA. Therefore, imaging findings of this rare tumor are important for its recognition. The appearance of PHA on computed tomography (CT) and magnetic resonance imaging (MRI) has been reported in a few cases [4–6]. Sonographic findings, particularly contrast-enhanced ultrasound imaging features of PHA, are relatively scarce [7, 8]. The purpose of this case report was to describe CEUS findings of PHA.

Case presentation

A 72-year-old woman complained about right upper quadrant pain, nausea, and dizziness. She then underwent an abdominal ultrasound examination. Grey-scale ultrasound image demonstrated a heterogeneous mass at the inferior segment of the right posterior liver lobe. The mass was about 6.4 × 4.7 cm in size with an irregular shape and unclear margin (Fig. 1a). The inside of the mass showed a mixed pattern with a solid and cystic appearance. At the left lateral liver lobe, a hypoechoic nodule measuring 0.6 cm was noted (Fig. 1b). It was well-circumscribed with a regular shape. Color Doppler showed sparse blood signals in the larger mass (Fig. 1c). For further diagnosis, the patient agreed to undergo contrast-enhanced ultrasound (CEUS). A 1.2-ml contrast agent (SonoVue) suspension was injected through her cubital vein followed by a 5-ml saline flush. An iU22 ultrasound system (Royal Philips, The Netherlands) equipped with a C5-1 (1–5 MHz) transducer was used for the examination. The mechanical index setting was 0.05 for CEUS. Taking normal liver parenchyma as a reference, the periphery of the larger mass was hyperenhanced like an irregular bright, thick ring in the arterial phase (Fig. 2a). In the portal phase, the peripheral enhancement washed out gradually, appearing slightly hyperenhanced (Fig. 2b). In the late phase, the mass presented

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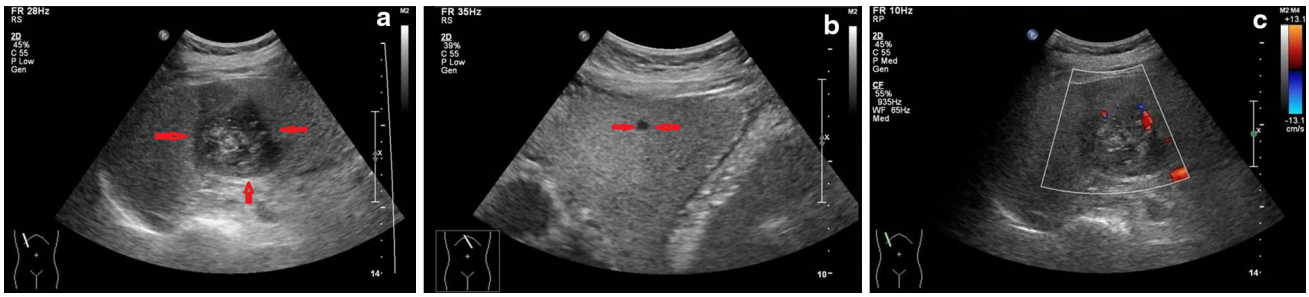

Fig. 1 B-mode and color Doppler ultrasound images. **a** A 6.4 × 4.7-cm hypoechogenic mass occupying the inferior segment of the right posterior liver lobe. **b** A 0.6-cm hypoechogenic nodule located at the left lateral liver lobe. **c** Color Doppler showed sparse blood signals of the larger mass at the right liver lobe

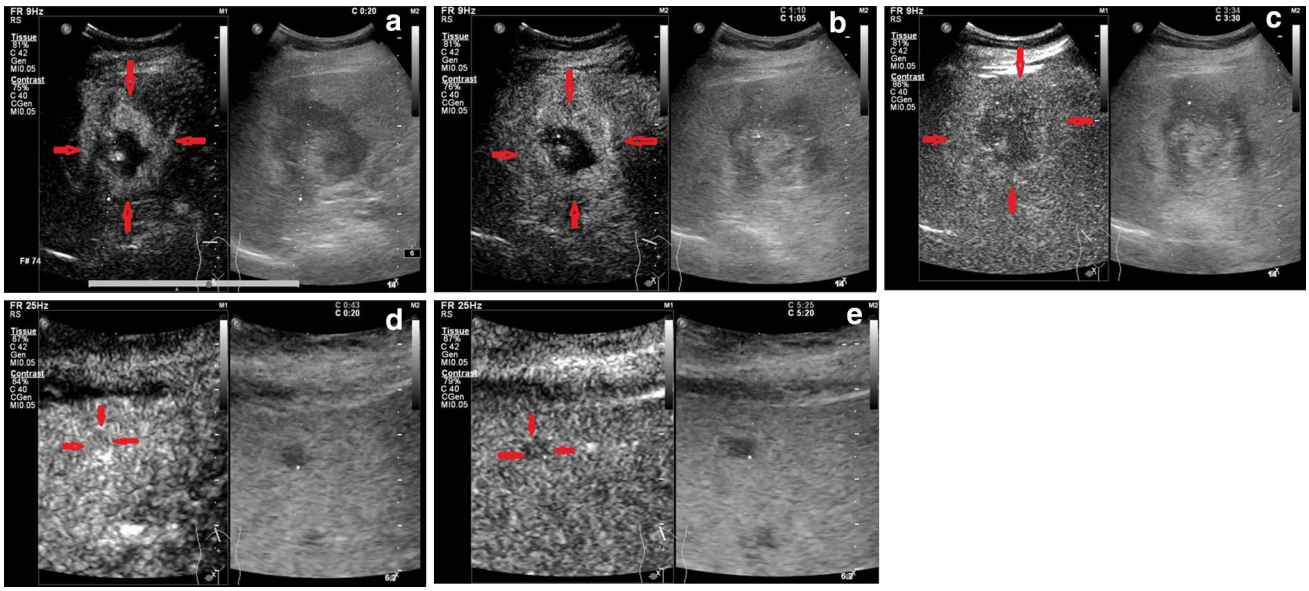

Fig. 2 Contrast-enhanced ultrasound images. **a** The larger mass was hyperenhanced like an irregular bright, thick ring in the arterial phase. **b** The peripheral enhancement of the larger mass washed out gradually, appearing slightly hyperenhanced in the portal phase. **c** In the parenchymal phase, the mass presented hypoenhancement. **d** The smaller nodule at the left lobe was slightly hyperenhanced at 20 s. **e** In the parenchymal phase, the smaller nodule displayed hypoenhancement

hypoenhancement (Fig. 2c). For the above three phases, no enhancement was seen in the central part of the mass (Fig. 2a–c). The smaller nodule at the left lobe was slightly hyperenhanced at the 20 s (Fig. 2d). In the parenchymal phase, it displayed hypoenhancement (Fig. 2e). Therefore, a diagnosis of primary hepatic cell carcinoma accompanied by intrahepatic metastasis was made after CEUS. In addition to ultrasound, the patient underwent contrast-enhanced MRI (CEMRI). This procedure was performed with a 1.5-T MR unit (Siemens Medical Solutions, Avanto, Germany), with gadopentetate dimeglumine (Magnevist, Bayer Schering Pharma AG) as the contrast agent, which was injected into the patient at a dose of 0.2 mmol/kg. CEMRI presented a 7.1 × 4.5-cm mass at the VI segment of the liver. The imaging sequence used was T1-weighed sequence. The peripheral part of the mass showed rim-like enhancement on MRI in the arterial phase (Fig. 3). In the portal and late phases, the peripheral enhancement continued. The center of the mass was non-enhanced the whole time on MRI. Laboratory tests for AFP, CEA, CA19-9, and CA-125 were all negative. Right hepatectomy and left hepatic radiofrequency ablation were performed. During surgery, a mass measuring about 7 cm occupied the VI, VII, and VIII segments of the liver. The larger mass had an integrated capsule, soft grey-yellow texture, and large necrotic areas inside. The small nodule was around 1 × 1 cm at the left lobe. Radiofrequency ablation was performed for the small nodule; therefore, the nature of the nodule was not determined. Immunohistochemical results were positive for CD31, CD34, and ERG, and negative for Factor VIII and EMA (Fig. 4b–f). Combined with the histopathologic appearance (Fig. 4a), hepatic angiosarcoma (grade 3, poorly differentiated) was confirmed.

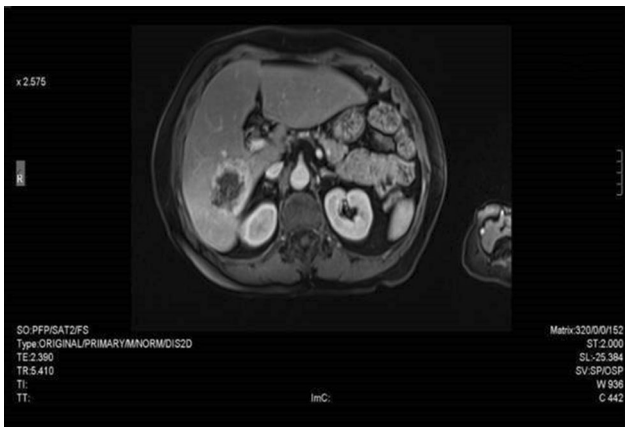

Fig. 3 Enhanced MRI presented a 7.1 × 4.5-cm mass at the VI segment of the liver. The peripheral part of the mass showed rim-like enhancement, while the center of it was non-enhanced on MRI in the arterial phase

Discussion

Primary hepatic angiosarcoma (PHA) is an uncommon mesenchymal malignant tumor. Its pathogenesis is unclear. Etiological factors include exposure to thorium dioxide and vinyl chloride [9]. The median survival with this cancer has been reported to be less than 6 months without therapy [10].

On grey-scale ultrasound image, the large mass was hypoechoic and ill-defined, while the small hypoechoic lesion was well demarcated, in this case. Color Doppler detected a few blood signals in the large mass only. However, these features are non-specific for diagnosing PHA.

As for CEUS characteristics of PHA, only a few cases or series have been described in the literature. One study [7] evaluated four patients with PHA on CEUS. In the arterial and portal phases, tumors demonstrated nodular peripheral enhancement, except for one that displayed diffuse chaotic enhancement. In the late phase, they were all hypoenhanced. Another study by Liang Wang et al. [8] summarized three cases of PHA, focusing on their CEUS features. The three cases presented similar enhancement patterns, characterized by peripheral irregular rim-like enhancement and central non-enhancement in the arterial and portal phases, and hypoenhancement in the late phase. Our case was a large mass accompanied by a small nodule. The enhancement

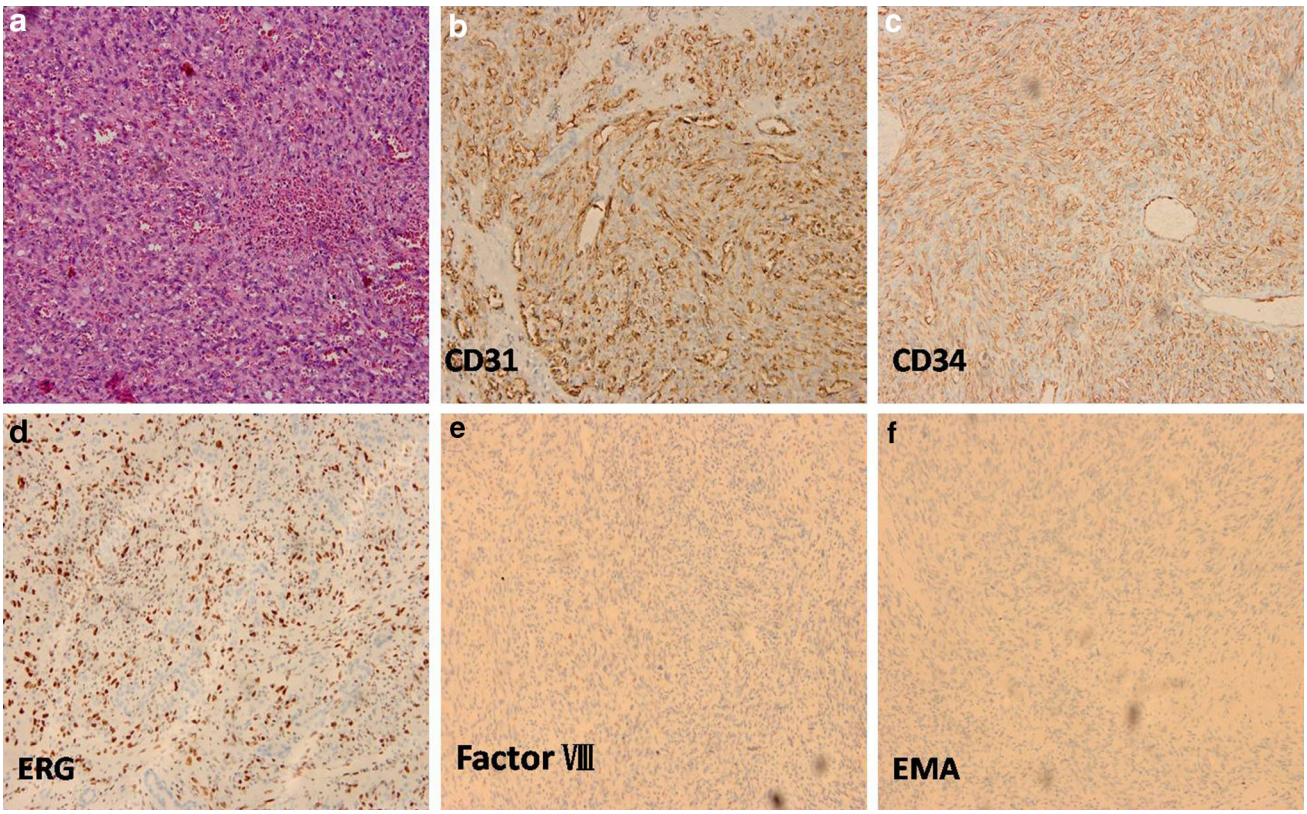

Fig. 4 Primary hepatic angiosarcoma. **a** Photomicrograph (H&E staining; magnification ×200) shows highly atypical cells lining anastomosing sinusoidal channels and papillae, accompanied by hemorrhage and necrosis. **b–f** Immunohistochemical staining (magnification ×200) reveals CD31, CD34, and ERG were all positive, while Factor VIII and EMA were negative, confirming the endothelial origin of the malignant cells

pattern of the large lesion was similar to that in Liang Wang's series, but the small nodule did not have a rim-like or nodular enhancement sign, which may have been due to its small size. Although not typical, the small nodule demonstrated hyperenhancement in the arterial phase and hypoenhancement in the late phase, raising the suspicion of its malignancy. A non-enhancement area in the center of the large mass was a commonly reported CEUS pattern of PHA. However, non-enhancement did not always indicate tumor necrosis, because large-sized blood sinusoids and low blood flow velocity may also be a cause [8, 11].

Biopsy of PHA may cause uncontrolled bleeding due to the vascularity of angiosarcomas [12]. Furthermore, clinical manifestations and laboratory tests are non-specific or even normal in PHA. Its diagnosis is more dependent on imaging. The differential diagnosis mainly includes hemangioma, hepatic cell carcinoma (HCC), and metastasis. With a similar vascular constitution, angiosarcomas may display a nodular centripetal enhancement pattern in the arterial phase, which may be confused with a hemangioma [13, 14]. Nevertheless, hemangiomas always remain hyper- or iso-enhanced in the late phase, while contrast agents often wash out fast in angiosarcomas. As mentioned above, angiosarcomas can have a rim-like hyperenhancement in the arterial phase and hypoenhancement in the late phase, mimicking metastases in the liver. In this situation, the patient's clinical data and laboratory tests are helpful to rule out a primary tumor in another part of the body. Metastasis also tends to wash out faster in the portal and late phases [15]. When it comes to HCCs, small HCCs ($\leq$2 cm) with no obvious necrosis tend to display a fast, homogenous hyperenhancement pattern in the arterial phase and wash out in the portal and late phases [16]. However, poorly differentiated HCCs, or large HCC masses with necrosis, can present an enhancement pattern similar to that of PHA in this case [16]. It is still difficult to differentiate these types of HCCs from PHA by CEUS.

Conclusion

PHA is rare and difficult to diagnose, and CEUS may provide valuable clues in the diagnosis.

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Compliance with ethical standards

Ethical statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from the patient for being included in this case.

Conflict of interest There are no financial or other relations that could lead to a conflict of interest.

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