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A patient with liver cirrhosis and hepatic lesions

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Summary We report an unusual case of a cirrhotic patient with two different types of hepatic lesions: Eventually, the patient was diagnosed with hepatocellular carcinoma and hepatic splenosis. Possible diagnostic strategies and the differentiation between these two entities are discussed.

Keywords Hepatocellular carcinoma · HCC · Hepatic splenosis · Liver tumor · Liver cancer

Introduction

Imaging of a cirrhotic patient with hepatitis C and elevated alpha-fetoprotein revealed unusual findings.

Case presentation

A 70-year-old man was referred to the hepatology department because of active hepatitis C virus (HCV) infection and signs of cirrhosis on ultrasonography. The patient reported no history of severe diseases or major operations except an emergency splenectomy 45 years ago after a splenic gunshot injury. Because of cirrhosis (Child–Pugh class B8) and elevated alpha-fetoprotein (198.6 ng/mL), a gadoxetate-enhanced magnetic resonance imaging (MRI) of the liver was conducted, unfortunately with suboptimally triggered contrast phases. MRI showed signs of decompensated liver cirrhosis, including mild ascites and spontaneous portosystemic shunts, and four hepatic lesions, e.g., one in segment VIII with a maximum diameter of 3.4 cm, appearing variably hyperintense with central hypointensity in the arterial phase and hypointense in the portal venous and hepatobiliary phase. A detailed description of the different lesion is given in Table 1. After multidisciplinary tumor board evaluation, an ultrasound-guided biopsy was obtained from a lesion with arterial hypervascularization in segment IV. Histology revealed spleen tissue, leading to the diagnosis of hepatic splenosis.

Given that alpha-fetoprotein was elevated and other lesions, especially the one in segment VIII, were highly suspicious of hepatocellular carcinoma (HCC) but were not accessible for a biopsy, a multidetector computed tomography (CT) staging scan of chest and abdomen (Fig. 1) and another MRI were performed.

The CT confirmed the hepatic lesions, with those in segment VIII and III being suspicious of HCC. It also revealed pulmonary nodules up to 6 mm (likely granulomas), and fractures of two thoracic vertebrae (either osteoporosis- or malignancy-related). The MRI confirmed the diagnosis of multifocal hepatocellular carcinoma beyond Milan criteria in decompensated liver cirrhosis. The typical HCC lesions in segment VIII and II were stable in size, while the third lesion in segment III increased from 1.3 cm to 1.5 cm. A detailed description of the different lesions is given in Table 1.

Given the contraindications for surgery and locoregional therapies (i.e., decompensated liver cirrhosis, suspected osseous metastases), systemic therapy

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Table 1 Lesions and their characteristics in different MRI/CT scans

Lesion number	Final diagnosis	Location	MRI 1		CT		MRI 2		Radiological appearance
			Size	LI-RADS	Size	LI-RADS	Size	LI-RADS	
1	Splenosis	Next to segments II/III and IV	2.9 cm	2	3.1 cm	2	3.1 cm	1	Sharply marginated extrahepatic lesion adjacent to the umbilical fissure, between segment II/III and IV. The lesion shows arterial phase hyperenhancement (APHE) with an increase of enhancement in the portal venous phase, along with washout in the transitional and hepatobiliary phase. The lesion shows patchy APHE in the 2nd MRI scan
2	Splenosis	Between left liver lobe and stomach	3.9 cm	2	3.9 cm	3	3.8 cm	2	Poorly marginated lesion dorsal to the left lateral segment and medial to the lesser gastric curvature. On MRI, the lesion appears clearly extrahepatic, while on CT, the extrahepatic origin cannot be determined with great confidence. The lesion shows slight APHE, is isodense/isointense on the portal venous phase and hypointense on the transitional and hepatobiliary phase. On both MRI scans, the enhancement appears patchy both in the arterial and portal venous phase
3	HCC	Segment VIII	3.4 cm	NC	3.7 cm	5	3.6 cm	5	Sharply marginated lesion in segment VIII, with APHE and portal venous washout on CT, as well as washout in the transitional phase on MRI 2. Due to suboptimal contrast timing, the lesion has to be classified LI-RADS NC on MRI 1. The lesion has areas of necrosis and a capsule appearance on MRI
4	HCC	Segment II	2.8 cm	NC	2.3 cm	4	2.1 cm	5	Partly sharply, partly poorly marginated lesion adjacent to the umbilical fissure in segment II, with APHE on CT and MRI 2, with portal venous washout which is further increased in the transitional and hepatobiliary phase
5	Probable HCC	Segment III	1.3 cm	NC	1.4 cm	4	1.5 cm	4	Sharply marginated lesion close to the dorsal rim of segment III, with APHE and portal venous washout and a capsule appearance on MRI

APHE arterial phase hyperenhancement, *CT* computed tomography, *HCC* hepatocellular carcinoma, *LI-RADS* Liver Imaging Reporting and Data System, *MRI* magnetic resonance imaging, *NC* non-categorizable

was recommended in multidisciplinary tumor board evaluation. Shortly after the diagnosis had been established, the patient developed a myocardial infarction with ST-segment elevation. He underwent acute coronary angioplasty and multiple drug-eluting stents were placed. Ten days after hospital discharge, treatment with the tyrosine kinase inhibitor lenvatinib (immunotherapy was not approved yet) was initiated. Unfortunately, the patient deceased only a few weeks later.

Discussion

Hepatic splenosis is the ectopic autotransplantation of splenic tissue, appearing as a tumor within or in direct contact with the liver. Usually, this rare condition develops in patients with a history of splenic trauma, spleen rupture, or splenectomy [1]. Diagnosis can be challenging as splenic tissue appears hypervascularized in the arterial phase compared to liver tissue. Hence, hepatic splenosis exhibits a similar appearance as malignancies like HCC and can often not be distinguished with ample certainty [2]. Alpha-fetoprotein can be useful for the distinction, although a normal alpha-fetoprotein level does not rule out HCC. Especially in cirrhotic patients with a relevant risk of developing HCC, a high level of certainty is required to rule out HCC in case of hepatic lesions with arterial hyperenhancement and the diagnosis of hepatic splenosis is usually confirmed by biopsy. If hepatic splenosis is primarily suspected, e.g., in a patient with typical history and without any risk factors for HCC, Tc-99m heat-denatured red blood cell scintigraphy is a noninvasive way to confirm the diagnosis of splenosis [1].

Hepatocellular carcinoma (HCC) is the most frequent malignant liver tumor and usually develops in cirrhosis. HCV infection, which often remains undetected for a long time, is a common etiology for cirrhosis and HCC. In a cirrhotic patient, HCC can be diagnosed by contrast-enhanced MRI or CT scan and without biopsy if imaging quality is optimal and results are typical [3]. Yet, given the insufficient quality of the initial MRI in our case and the atypical appearance of two of the hepatic lesions, the decision to obtain a biopsy was made after multidisciplinary tumor board discussion. Although biopsy results revealed that the tumor in segment IV was hepatic splenosis, the elevated alpha-fetoprotein in addition to multiple hepatic lesions in a cirrhotic patient remained highly suspicious for HCC. As the lesions suspicious of HCC were not accessible for a biopsy, a CT scan and another MRI were performed. Some lesions showed typical radiographic hallmarks of HCC, while others showed a similar pattern like the lesion with histological confirmation of spleen tissue. Af-

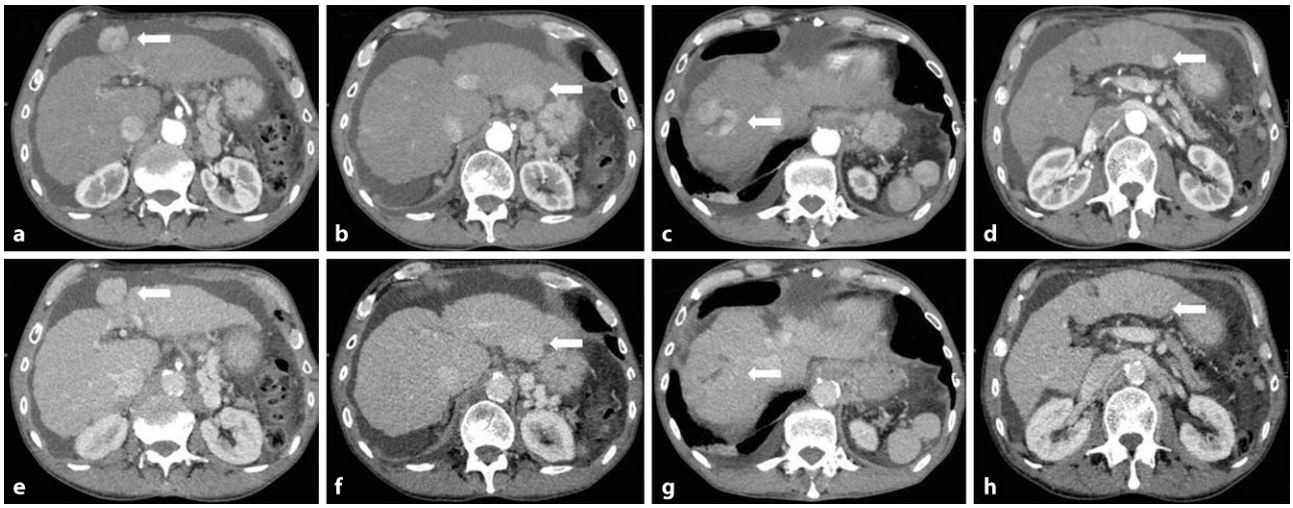

Fig. 1 Computed tomography (CT) scan of the chest and abdomen: **a**–**d** abdominal images of the arterial phase, **e**–**h** matching images of the portal venous phase. Lesions ventral of segment II/IV (**a** and **e**) and between left liver lobe and stomach (**b** and **f**) appear hyperdense in arterial phase and isodense–moderately hyperdense in the portal venous phase. Lesions in segment VIII (**c** and **g**) and segment III (**d** and **h**) show hyperenhancement in the arterial phase and wash-out in the portal venous phase

ter re-evaluation in multidisciplinary tumor board, the diagnosis of multifocal HCC and hepatic splenosis was made without further biopsy. A Tc-99m heat-denatured red blood cell scintigraphy was not performed since splenosis was already confirmed by histology and other lesions showed typical features of HCC on imaging.

Liver transplantation is recommended in patients with decompensated liver cirrhosis and multifocal HCC, if the tumor extent is within certain criteria. Most centers have adopted the Milan criteria, which consider transplantation in a patient with a single tumor ≤ 5 cm or up to 3 tumors with the largest being ≤ 3 cm, but without macrovascular invasion or extrahepatic spread [4]. More recent models extended these criteria and also incorporated surrogate markers of tumor biology, such as alpha-fetoprotein [5, 6].

Transarterial chemoembolization (TACE) is recommended for the treatment of unresectable, multifocal HCC beyond transplant criteria, or for bridging/downstaging prior to liver transplantation. However, TACE cannot be recommended for patients with decompensated liver cirrhosis or a poor performance status (2 or higher). In optimally selected patients with preserved liver function (Child–Pugh stage ≤ B7), who are asymptomatic and without vascular invasion or extrahepatic spread, a median survival of 3–4 years can be achieved by TACE [3].

Systemic therapy is the treatment of choice for patients with advanced stage HCC, but may also be used in earlier stages if surgery or locoregional therapies are contraindicated [3]. Sorafenib and lenvatinb were recently replaced as standard of care in front-line by the combination of atezolizumab plus bevacizumab [7, 8], which recently succeeded in the IMbrave150 phase III trial [9].

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Conflict of interest T. Meischl and D. Tamandl and declare that they have no competing interests. M. Pinter is an investigator for Bayer, BMS, Lilly, and Roche; he received speaker honoraria from Bayer, BMS, Eisai, Lilly, and MSD; he is a consultant for Bayer, BMS, Ipsen, Eisai, Lilly, MSD, and Roche; he received travel support from Bayer and BMS.

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