Gastrointestinal

A case of pseudoglandular hepatocellular carcinoma: The usefulness of a multimodal approach

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A B S T R A C T

Hepatocellular carcinoma (HCC) mainly composed of the pseudoglandular pattern is very rare. We present a case of pseudoglandular HCC that was hyperechoic on ultrasound, with strongly high signal intensity on T2-weighted imaging and weak arterial contrast enhancement. Computed tomography hepatic arteriography showed corona enhancement. Radiologists should keep in mind this combination of multimodal radiological findings for pseudoglandular HCC.

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Introduction

Hepatocellular carcinomas (HCCs) are classified into trabecular, pseudoglandular, compact, and scirrhouss types [1]. Among them, HCC mainly composed of the pseudoglandular pattern is very rare [2,3]. We describe herein the radiological findings from a pseudoglandular-type case of HCC.

Case report

A 72-year-old man was referred to our hospital for further examination of the diagnosis of early gastric cancer. During preoperative workup, a hepatic mass was incidentally identified. Laboratory data were normal: white blood cells, 3840/μL (normal 3300-8600); red blood cells, 433 × 10⁴/μL (normal

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hemoglobin, 13.7 g/dL (normal 13.7-16.8); platelets, 18.6 × 10^4/μL (normal 15.8-34.8); total bilirubin, 0.6 mg/dL (normal 0.4-1.5); aspartate aminotransferase, 23 U/L (normal 13-30); alanine aminotransferase, 29 U/L (normal 10-42); alkaline phosphatase, 280 U/L (normal 106-322); γ-glutamyltransferase, 23 U/L (normal 13-64); albumin, 4.6 g/dL (normal 4.1-5.1); and prothrombin time-international ratio, 1.02 (normal 0.90-1.10). Tests for hepatitis B virus surface antigen and antibodies against hepatitis C virus were negative. Hepatitis B core antibody was positive. Serum tumor markers were also in the normal range: carcinoembryonic antigen, 1.2 ng/mL (normal <3.2 ng/mL); carbohydrate antigen 19-9, 6.8 U/mL (normal <37 U/mL); alpha-fetoprotein, 3.6 ng/mL (normal <6.2 ng/mL); and proteins induced by the absence of vitamin K, 21 mAU/mL (normal <40 mAU/mL). The patient drank occasionally and had no history of alcohol abuse.

Ultrasound demonstrated a homogeneous echogenic mass with posterior enhancement in segment 2 and 3 measuring 3.2 cm in diameter (Fig. 1A) without Doppler flow (Fig. 1B). Computed tomography (CT) examination was performed using a 64-MDCT scanner (Toshiba Medical Systems, Tokyo, Japan). After precontrast images through the liver were obtained, 1.62 mL/kg of a nonionic iodinated contrast agent (Iopamiron 370; Bayer, Osaka, Japan) was injected with a fixed duration of 30 seconds at a variable injection rate by an automated power injector. Two continuous arterial phases were scanned with a bolus-triggered technique (monitoring frequency from 10 seconds after contrast injection, 1 second; trigger threshold, an increase of 100 HU in the descending aorta; and delay from trigger to initiation of scan, 15 seconds). The portal venous and delayed phases were acquired at 60 seconds and at 240 seconds, respectively. CT showed a low-density result in the precontrast phase, and isoattenuation to slight hypoattenuation in both the arterial (Fig. 1C) and delayed phases (Fig. 1D). Signs of liver cirrhosis such as nodular liver contour, atrophy of the right hepatic lobe and medial segment of the left hepatic lobe, and enlarged caudate and lateral left hepatic lobe were not seen (Fig. 1E). Vascular invasion was not observed.

435-555); hemoglobin, 13.7 g/dL (normal 13.7-16.8); platelets, 18.6 × 10^4/μL (normal 15.8-34.8); total bilirubin, 0.6 mg/dL (normal 0.4-1.5); aspartate aminotransferase, 23 U/L (normal 13-30); alanine aminotransferase, 29 U/L (normal 10-42); alkaline phosphatase, 280 U/L (normal 106-322); γ-glutamyltransferase, 23 U/L (normal 13-64); albumin, 4.6 g/dL (normal 4.1-5.1); and prothrombin time-international ratio, 1.02 (normal 0.90-1.10). Tests for hepatitis B virus surface antigen and antibodies against hepatitis C virus were negative. Hepatitis B core antibody was positive. Serum tumor markers were also in the normal range: carcinoembryonic antigen, 1.2 ng/mL (normal <3.2 ng/mL); carbohydrate antigen 19-9, 6.8 U/mL (normal <37 U/mL); alpha-fetoprotein, 3.6 ng/mL (normal <6.2 ng/mL); and proteins induced by the absence of vitamin K, 21 mAU/mL (normal <40 mAU/mL). The patient drank occasionally and had no history of alcohol abuse.

Ultrasound demonstrated a homogeneous echogenic mass with posterior enhancement in segment 2 and 3 measuring 3.2 cm in diameter (Fig. 1A) without Doppler flow (Fig. 1B). Color Doppler ultrasound demonstrated no visible internal vascular flow (B). The liver tumor (arrow) showed slight hypoattenuation on the axial CT with arterial phase (C) of the dynamic contrast study and hypoattenuation on the delayed phase (D). Axial CT with portal venous phase image demonstrated normal appearance of the liver contour without vascular invasion of the tumor (E). The lesion showed no signal drop-off on the out-of-phase of the axial MR image (F) compared with in-phase image (G). 3D-isotropic axial T2-weighted fast spin echo (volume isotropic fast spin echo acquisition, VISTA) (FA90 TR/TE 465/110) demonstrated a strongly high-signal mass (H). The tumor showed hypointense on the precontrast image (I), hypointense on the arterial phase (J), hypointense on the portal venous phase without capsule (K), and hypointense on the hepatobiliary phase (20 minutes after contrast injection) (L) of the gadoxetic acid-enhanced axial images with fat suppression. Biopsy needle (arrowhead) was observed within the tumor on the ultrasound-guided biopsy (M). The tumor showed weak enhancement on the first phase (N) of the CTHA and subsequent rim enhancement, so-called corona enhancement (arrowheads), on the second phase (O). The additional lesion in segment 8 showed hyperintense on the arterial phase of the gadoxetic acid-enhanced axial image with fat suppression (P) and hypointense on hepatobiliary phase (Q). Microscopic examination revealed HCC growing in a pseudoglandular pattern with rich fluid content (R). 3D, three-dimensional; CT, computed tomography; HCC, hepatocellular carcinoma; MR, magnetic resonance.
gradient echo imaging showed hypointensity without a signal drop-off on out-of-phase imaging (Fig. 1F) compared with in-phase image (Fig. 1G), and T2-weighted fast spin echo imaging showed extreme hyperintensity (Fig. 1H). Gadoxetic acid-enhanced dynamic magnetic resonance imaging (MRI) revealed hypointense lesion in the pre- (Fig. 1I) and postcontrast phases including arterial (Fig. 1J), portal venous (Fig. 1K), and hepatobiliary phases (Fig. 1L). Capsular formation was not obviously identified. At this point, a liver biopsy was performed (Fig. 1M), and pathology revealed atypical hepatocytes indicating a hepatocellular lesion, but further diagnosis was difficult. We performed angiography-assisted CT including CT during arterial portography and CT hepatic arteriography. The CT during hepatic arteriography data acquisition began 7 seconds (first phase) and 30 seconds (second phase) after the initiation of a transcatheter hepatic arterial injection of nonionic contrast material. Computed tomography arterial portography disclosed a portal perfusion defect, and CTHA showed slight hyperattenuation on the first phase (Fig. 1N), and corona-like rim enhancement in the second phase (Fig. 1O). An additional tiny nodule, 7 mm in diameter, was also detected in segment 8 on the gadoxetic acid-enhanced MRI (Fig. 1P and Q). The patient underwent a left lateral segmentectomy (resection of segments 2 and 3) and a partial hepatectomy of segment 8. Histologic examination of the tumor in the segment 2 and 3 showed moderately differentiated hepatocellular carcinoma growing in a pseudoglandular pattern (Fig. 1R). The additional nodule in segment 8 showed well-differentiated HCC, indicating multicentric occurrence. Early gastric cancer was treated by endoscopic mucosal dissection 40 days after the hepatic surgery.

Discussion

In this case, the hepatic mass in the segment 2 and 3 was echogenic on ultrasound and strongly hyperintense on T2-weighted imaging. The dynamic contrast study revealed weak and homogeneous arterial enhancement without obvious capsular formation. These findings are not typical for HCC. Thus, biopsy was performed and revealed a hepatocellular lesion. We decided to perform the angiography-assisted CT. Corona enhancement seen on the second phase of CTHA strongly suggested that the tumor was a certain kind of HCC. We could finally make a precise preoperative diagnosis of pseudoglandular HCC based on the findings of the combination of ultrasound, CT, MRI, and angiography-assisted CT. The differential diagnoses of this case included metastasis from gastric cancer, hepatic hemangioma, and primary mucinous cystic neoplasm (MCN) of the liver. Liver metastasis was excluded because the lesion showed strongly hyperintensity on T2-weighted images and did not show ringed enhancement on dynamic contrast study. It is also unlikely for liver metastasis in patient with early gastric cancer. Hemangioma can also show echogenicity and extreme hyperintensity on T2-weighted images; however, it usually shows progressive fill-in after peripheral contrast enhancement or diffusely arterial and prolonged enhancement [4]. Thus, hemangioma was excluded. Finally, MCN can show similar ultrasound findings and T2 elongation but usually appears as a cystic mass with a well-defined thick fibrous capsule, mural nodules, and internal septa [5]. In this case, the tumor showed internal contrast enhancement without a cystic component, which excluded MCN.

Pathologically, pseudoglandular HCC is composed of dilated acinar formation with fluid content. Each acinus is lined with a layer of tumor cells and contains fluid [1] [2]. Most classical HCCs grow in a trabecular pattern, with which pseudoglandular formation is intermingled to some degree; however, for almost all the areas of the tumor to consist of pseudoglandular formation, as seen in our case, is quite rare. Hyperechogenicity on ultrasound is probably due to the reflection of ultrasound waves at the walls of numerous acini, as seen in hemangioma. The markedly high T2 signal corresponds to abundant fluid content in the acini [2,6]. In this case, arterial enhancement was weak on both dynamic CT and CTHA for the size of this tumor since the contrast material distributed only in the sinusoid of the tumor cells, but not in the acini, which contain a large amount of fluid. Although the amount of contrast material distributed in the tumor is relatively small, it drained from the tumor and formed corona enhancement on the second phase of CTHA, which was a key finding in making a correct diagnosis of HCC [7].

With regard to background liver disease, hepatitis B core antibody was positive, indicating past hepatitis virus B infection [8]. However, hepatitis B virus surface antigen and hepatitis C virus were both negative, and tumor markers were all negative. This clinical background, as well as the atypical radiologic findings for HCC, made it difficult to make a diagnosis, but a constellation of multimodality findings, including, of course, liver biopsy results (atypical hepatocytes), convinced us of the diagnosis of pseudoglandular HCC preoperatively.

In conclusion, pseudoglandular HCC was hyperchoic on ultrasound, with markedly high signal intensity on T2-weighted imaging and weak arterial contrast enhancement. CT hepatic arteriography showed corona enhancement. Radiologists should keep in mind this combination of multimodal radiologic findings for pseudoglandular HCC.

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