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Atypical Clinical and Imaging Presentation of a Large, Well-differentiated Hepatocellular Carcinoma: A Case Report

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Abstract: Hepatocellular carcinoma is the most common primary neoplasm of the liver that typically occurs in the setting of chronic liver disease. In this case report, we present an atypical case of well-differentiated hepatocellular carcinoma, which was detected in a 43-year-old man with no known symptoms of liver disease. We review the imaging features of the mass, which did not follow typical enhancement characteristics defined by the Liver Imaging Reporting and Data System criteria. The diagnosis was ultimately confirmed by histologic analysis of a surgically resected specimen.

Keywords: atypical HCC, Hepatocellular carcinoma, LI-RADS, well-differentiated HCC

Introduction

Hepatocellular carcinoma (HCC) is the most common primary neoplasm of the liver, which arises from the liver parenchymal cells.[1] Hepatocellular carcinoma usually develops on a background of chronic liver disease, such as cirrhosis or chronic hepatitis B or C. The diagnosis of HCC in patients with these or other high-risk liver diseases relies heavily on diagnostic imaging because high sensitivity and specificity of the Liver Imaging Reporting and Data System (LI-RADS) criteria allows making clinical decisions based on imaging appearance alone.[2,5] However, LI-RADS relies on characteristics that reflect multistep progression of lesions from a dysplastic nodule to a large, dedifferentiated HCC in a step-wise fashion.[3] We report a case of a large, well-differentiated hepatocellular carcinoma, which did not exhibit imaging features expected for its size. The lesion occurred in a young patient with no known liver disease and displayed atypical enhancement characteristics.

Key Points

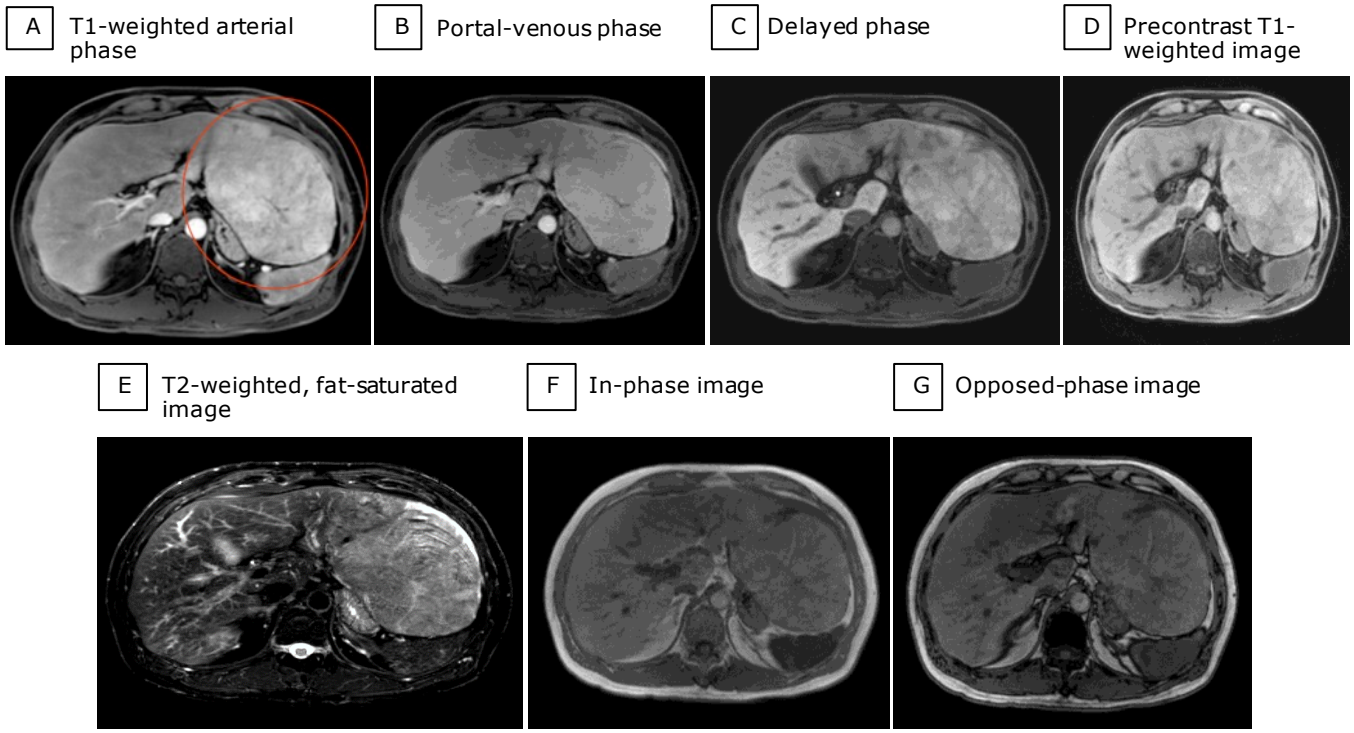
- Large, well-differentiated hepatocellular carcinoma (HCC) may not demonstrate typical enhancement characteristics provided by Liver Imaging Reporting and Data System (LI-RADS) classification.
- Epidemiology and prognosis of atypical HCCs are distinct from those of typical HCCs.

Case Presentation

A 43-year-old man with medical history of type II diabetes was in his usual state of health at the time of an annual physical examination in Taiwan. Although the patient did not have symptoms, computed tomography (CT) of the chest was performed for oncologic screening, given a family history of lung cancer. The imaging revealed a large exophytic mass arising from the left lobe of the partially visualized liver.

Subsequent magnetic resonance imaging (MRI) of the abdomen with gadoxetate disodium (Eovist) contrast demonstrated a 15 x 9 x 12 cm heterogeneously arterially enhancing mass in the left lobe of the liver (Figure 1A). There was no "washout" of contrast in the portal venous phase, and the mass retained gadoxetate disodium contrast in the delayed hepatobiliary phase (Figures 1B, 1C). The mass demonstrated intrinsically heterogeneous signal on T1-weighted images and was mildly hyperintense compared with background liver on T2-weighted images (Figures 1D, 1E). No signal dropout was noted between in-phase and opposed-phase images to suggest intracytoplasmic lipid within the mass (Figures 1F, 1G).

Figure 1. MR Imaging of the Liver in a 43-year-old Man with a Large, Well-differentiated HCC



T1-weighted gadoxetate disodium contrast-enhanced MRI of the abdomen (arterial phase) (A) shows a large exophytic mass arising from the left hepatic lobe (A, red circle). This mass demonstrates heterogeneous arterial hyperenhancement compared with the background liver parenchyma. Portal-venous-phase image (B) shows no "washout" of contrast within the mass. Delayed-phase image (C) demonstrates retained hepatobiliary contrast agent within the mass. Precontrast T1-weighted image (D) shows intrinsically heterogeneous T1 signal within the left hepatic lobe mass. On T2-weighted, fat-saturated image (E), the mass is mildly hyperintense relative to the background liver, with no evidence of a hyperintense central scar. In-phase (F) and opposed-phase (G) images demonstrate no signal dropout on opposed-phase images to suggest intracytoplasmic lipid within the mass.

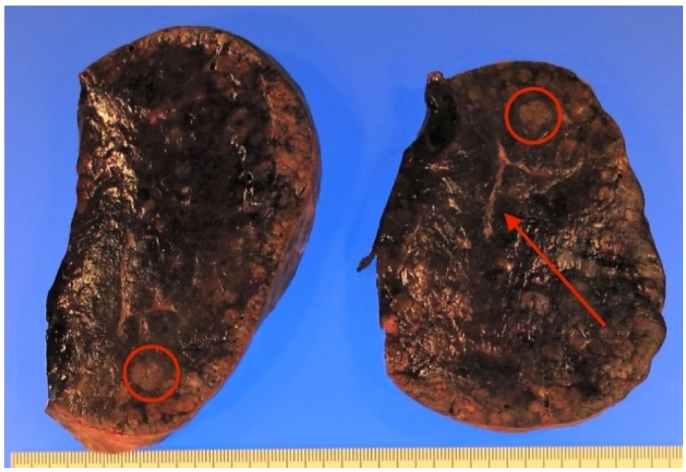
The patient denied history of liver disease and alcohol or drug use and had no evidence of hepatic steatosis or cirrhosis on imaging. Initial laboratory workup revealed an elevated platelet count (468 x 103/μL, reference range 143 - 398 x 103/μL), liver enzymes, α-fetoprotein (AFP), cancer antigen 19-9, and carcinoembryonic antigen within reference range and a hepatitis panel negative for hepatitis virus infection. Given concern for malignant nature of the mass, patient underwent resection of the lesion and partial left hepatic lobectomy.

At the time of the operation, the mass was noted to arise from the left lateral segment, with significant mass effect on the adjacent stomach. The remainder of the liver appeared normal intraoperatively, and an intraoperative ultrasound did not reveal any additional masses within the liver.

Gross specimen examination demonstrated a 785-gram smooth red-brown mass with a pedunculated stalk. Cut section showed a solid, beefy-red parenchyma with numerous ill-defined

nodules and a focal central scar-like area (Figure 2). Microscopically, the mass demonstrated nodular proliferation of hepatocytes with unaccompanied arteries (Figure 3A). No portal areas were seen. Reticulin stain showed thickness of hepatocyte plates and loss of reticulin framework (Figure 3B). The result of histologic analysis revealed well-differentiated hepatocellular carcinoma. Since the tumor resection, the patient has undergone 3 years of annual oncologic and radiologic follow-up with no evidence of recurrent disease.

Figure 2. Macroscopic Examination of the Resected Specimen of a Large Well-differentiated HCC in a 43-year-old Man



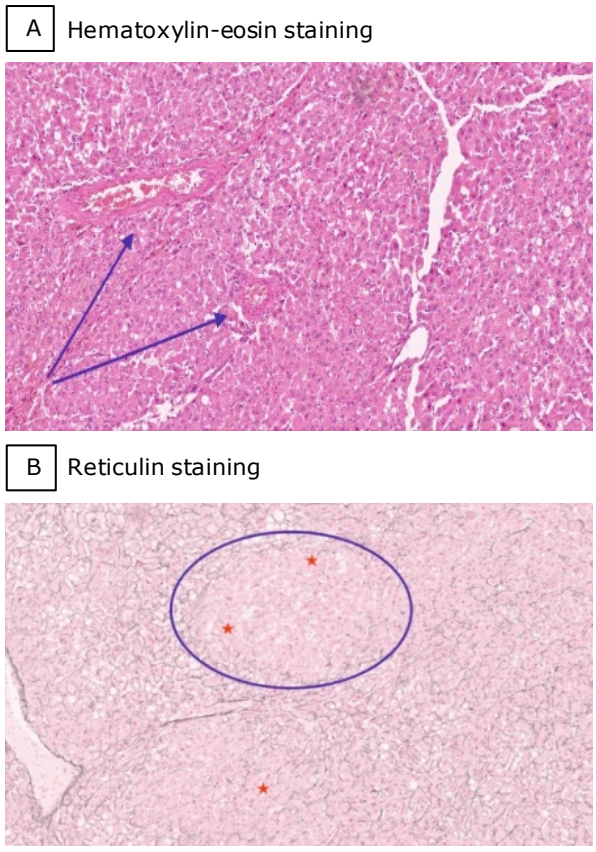
Cross section of the 785-gram left hepatic lobe mass, which measured 15.8 x 11.3 x 6.8 cm. The outer surface of the lesion was uniform and smooth, with a mottled red-brown surface. The cut surface revealed multiple ill-defined nodules (red circles) within the mass. There was a white-tan fibrous central scar-like area (arrow).

Discussion

The hepatocellular carcinoma (HCC) presented in this case report was atypical in both its clinical and imaging characteristics. Clinically, the patient had no known underlying liver disease that would predispose him to developing hepatocellular carcinoma. The patient reported no drug or alcohol use. The results of a thorough laboratory workup for viral hepatitis were negative, and imaging revealed no evidence of underlying steatohepatitis or cirrhosis.

Radiologically, this well-differentiated HCC did not follow typical enhancement characteristics expected for a classic HCC. Gadoxetate disodium contrast, which was used in this case, acts as a nonspecific extracellular contrast agent in the arterial and the portal venous phases, with hepatocyte-specific uptake in delayed phases.[4] A classic HCC of the size observed in this case would be expected to demonstrate arterial phase hyperenhancement, nonperipheral "washout" of

Figure 3. Histologic Examination of the Resected Specimen of a Large Well-differentiated HCC in a 43-year-old Man



A and B Photomicrographs of the left hepatic lobe mass. Hematoxylin-eosin staining (A) demonstrates nodules of hepatocellular proliferation and unpaired arteries (A, arrows) with no accompanying portal areas. Reticulin stain (B) shows patchy loss of reticulin framework (B, circled area) and thickness of hepatocyte plates (B, stars)

contrast in the portal venous phase, and an enhancing "capsule."[2,5] A classic large HCC would also be expected to become dedifferentiated and no longer retain the hepatocyte-specific contrast.[4] Yet, the observed lesion demonstrated atypical enhancement characteristics for an HCC of this size, as it lacked portal venous "washout" while retaining gadoxetate disodium contrast in delayed phases.

Given the imaging features of this mass, another candidate tumor for differential diagnosis was focal nodular hyperplasia (FNH). A benign hepatic tumor that develops in response to local vascular abnormalities, an FNH typically presents as a homogeneously arterially enhancing mass that is uniformly isointense compared with background liver on T1-weighted images and mildly hyperintense on T2-weighted images. On portal-venous phase images, FNH is isointense compared with background liver, with a central scar that is hyperintense on T2-weighted images and demonstrates delayed enhancement.[4] Given the arterial phase enhancement and retention of gadoxetate disodium contrast on the delayed hepatobiliary phase images, FNH remained a distinct possibility at the time of imaging interpretation. However, the intrinsic T1 signal and arterial enhancement in the observed case were more heterogeneous than expected for a typical FNH. Therefore, the possibility of atypical well-differentiated HCC was also suggested. Ultimately, histologic analysis confirmed the diagnosis of HCC. The diffuse positivity for glutamine synthetase, thickness of hepatocyte plates, and loss of reticulin framework supported the diagnosis.

The atypical imaging features in this case with findings of well-differentiated HCC on histologic analysis indicated that the lesion did not follow the classic progression from a dysplastic nodule in a cirrhotic liver to a large, dedifferentiated HCC. A study conducted by Okuno et al[3] suggested that large (> 3cm), well-differentiated HCCs might be a distinct subtype of HCC with different clinical presentation and unclear causes. Okuno et al[3] found that patients with atypical HCC were less likely to have underlying cirrhosis, vascular invasion, or elevated AFP, which might contribute to better prognosis in these patients. While the underlying causes of these atypical HCCs remain unclear, a possible connection with nonalcoholic fatty liver disease or malignant degeneration of hepatic adenomas was suggested.[3] Our case report supports observations[3] proposing that both the clinical and the imaging characteristics of a large, well-differentiated HCC might be different from those demonstrated by a classic HCC. Further investigation is needed to understand the cause(s) of these atypical HCCs. Radiologists and pathologists should be aware of these hepatic tumors when evaluating hepatic masses. Specifically, when applying LI-RADS criteria to newly discovered liver masses, radiologists should recall that, while serving as a useful diagnostic tool in patients with cirrhosis or other high-risk liver diseases, these criteria were not intended to be applicable to diagnosis of all liver masses.[5]

Author Contributions

Conceptualization, V.S. and M.L.J; Writing – original draft preparation, M.L.J.; Review and editing, M.L.J., Y.G., B.V.N. and V.S.; Supervision, V.S. All authors agree to be 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 authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Disclosures

None to report.

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