

Intrahepatic mass-forming cholangiocarcinoma growing in a giant hepatic hemangioma

A case report

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Abstract

Rationale: Hepatic hemangioma (HH) is a common benign tumor with a high number of normal or abnormal blood vessels. Intrahepatic cholangiocarcinoma (ICC) is a relatively common malignant primary hepatic carcinoma (10%–15%) with high incidence rate and high fatality, yet low discovery rate in the early stages. Ultrasonography (US), computed tomography, and magnetic resonance imaging (MRI) are frequently used and indispensable imaging techniques for the diagnosis of hepatic lesions. It is possible to differentiate a liver lesion from HH with high accuracy owing to their different patterns and hemodynamic characteristics.

Patient concerns: A 59-year-old Asian woman was referred to hospital for a hepatic mass, which was 9.0 × 6.5 cm in size. The patient was tested positive for hepatitis B antigen but negative for serum alpha-fetoprotein and carbohydrate antigen 199 and had a slightly elevated carcinoembryonic antigen level (3.56 ng/ml).

Diagnosis: Liver US and MRI were performed. Grey-scale US revealed a huge heterogeneous mass on the right lobe with a point and line-like blood flow signal on Doppler US. Dynamic contrast-enhanced MRI showed heterogeneous annular nodular enhancement in the arterial phase. An initial diagnosis of HH was made based on the clinical history and imaging results; however, histopathologic examination of the liver lesions revealed modest to severe atypical hyperplasia of intrahepatic bile duct epithelium, cancerization, and mid to high differentiated mass-forming type cholangiocarcinoma combined with focal organized hemangioma.

Interventions: The intrahepatic mass-forming cholangiocarcinoma (IMCC) lesion was considered a focal organization of hemangioma during operation and was surgically removed. No routine chemotherapy was performed after the operation.

Outcomes: The IMCC recurred 23 months after surgery, with elevated serum CA19-9 and CA125. Liver damage was evident, and the patient developed jaundice. The patient was discharged without active treatment and died in 4 months.

Lessons: Although preoperative imaging of focal hepatic lesions is indispensable, intraoperative frozen section analysis and histopathological examination remain essential for definitive diagnosis. This is particularly important for high-risk patients and those with suspected malignancy.

Abbreviations: AFP = alpha-fetoprotein, CA19-9 = carbohydrate antigen 199, CEUS = contrast-enhanced ultrasound, HBV = hepatitis B virus, HH = hepatic hemangioma, ICC = intrahepatic cholangiocarcinoma, IMCC = intrahepatic mass-forming cholangiocarcinoma, MRI = magnetic resonance imaging, US = ultrasonography.

Keywords: CA199, intrahepatic mass-forming cholangiocarcinoma, liver hemangioma, magnetic resonance imaging, misdiagnosis, nodule in nodule, recur, ultrasonography

Editor: N/A.

Informed written consent was obtained from the patient for publication of this case report and accompanying images.

The authors have no conflicts of interest to disclose.

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1. Introduction

The origin, etiology, pathology, and treatments differ between liver hemangioma and intrahepatic cholangiocarcinoma (ICC).^[1,2] Intrahepatic mass-forming cholangiocarcinoma (IMCC) is the most common pathological classification subtype of ICC.^[3] Hepatic trematode, intrahepatic bile duct stones, hepatitis B virus (HBV) infection, and age are risk factors for ICC.^[4,5] Medical imaging plays an important role in the diagnosis of ICC. Although hemangioma and IMCC could be accurately diagnosed and distinguished based on imaging examinations, histopathology remains the gold standard for definitive diagnosis. However, IMCC that grows inside a hemangioma may lack the typical imaging features. In this study, we describe a case of IMCC that grew inside and mimicked the presentation of a hemangioma. This study reviewed the imaging features of this tumor and analyzed several causes of misdiagnosis to further improve the understanding of these observations.

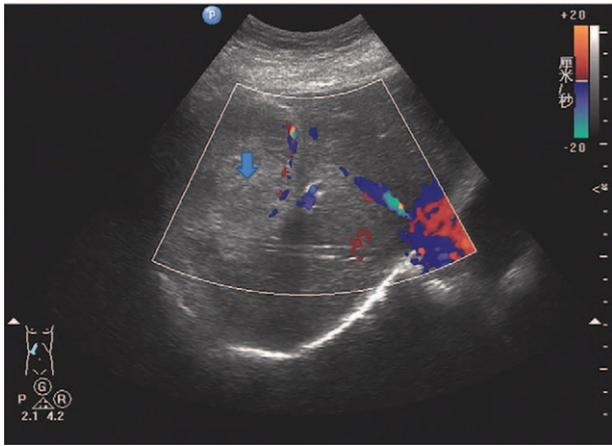


Figure 1. Conventional ultrasound image of hepatic hemangioma with hypoechoic region (arrow) in the right lobe. Intercostal section view.

2. Case presentation

A 59-year-old Asian woman had a hemangioma with a diameter of 3 cm for 5 years. Although the follow-up examinations revealed that the hemangioma gradually increased in size, the patient did not present any abnormal symptoms on physical examinations.

Laboratory tests showed that liver function test results were normal. The patient tested negative for serum alpha-fetoprotein (AFP) and CA199 and had slightly increased carcinoembryonic antigen levels (3.56 ng/ml). The patient tested positive for serum HBV surface antigen and negative for hepatitis C virus.

Conventional gray-scale abdominal ultrasound revealed a 9.0 × 6.5-cm, defined, and heterogeneously hyperechoic lesion in the right hepatic lobe. Color Doppler imaging (CDFI) revealed a poor blood flow signal. A blurred, hypoechoic region was identified in the lesion near the right hepatic lobe capsule (Figs. 1 and 2). No obvious abnormality was found in the spleen, pancreas, and gallbladder. Heterogeneous hypointense T1-weighted spin-echo images (T1WI, Fig. 3) and heterogeneous

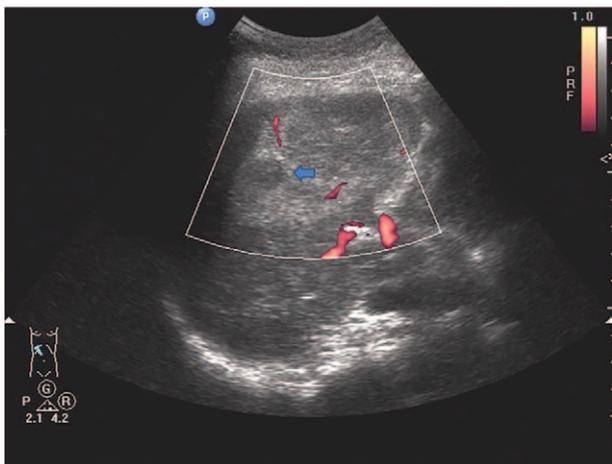


Figure 2. Conventional ultrasound image of hepatic hemangioma with hypoechoic region (arrow) in right lobe. Intercostal section view.

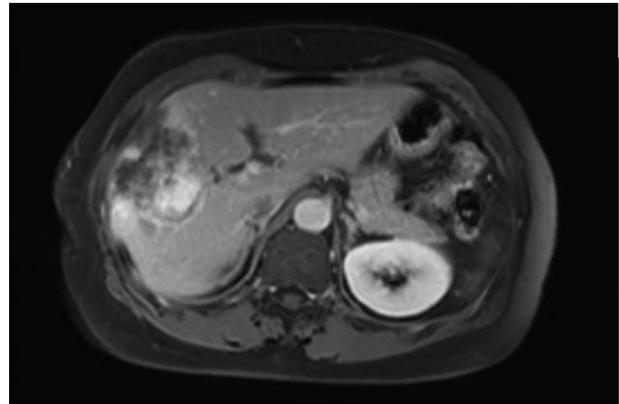


Figure 3. The mass manifested as heterogeneous hypointense on T1W1 and heterogeneous hyperintense on T2W2 with a tuberculiform hyperintense region (arrow) on MRI. MRI=magnetic resonance imaging, T1W1=T1-weighted images, T2W2=T2-weighted images.

hyperintense T2-weighted spin-echo images (T2W2, Fig. 4) were obtained on magnetic resonance imaging (MRI) compared to the liver parenchyma. Contrast-enhanced MRI (CEMRI) showed heterogeneous annular and nodular enhancement in the arterial phase (Fig. 5) and uneven filling of contrast agent in the venous phase (Fig. 6).

Based on the imaging results and laboratory examinations, a provisional diagnosis of hepatic hemangioma (HH) was made. The patient underwent a right hepatectomy and a 10 × 8-cm cavernous block was excised from segment IV, V, and VI, which wrapped around a 3.5 × 2.5-cm grey, rigid mass. Furthermore, enlarged common bile duct and inflamed gallbladder were observed. Demarcation between the tumor and liver tissue was clear and no metastasis was found. Frozen sections and histology did not appear to be required due to the clear imaging results and the appearance of the mass.

Pathological results indicated modest to severe atypical hyperplasia of intrahepatic bile duct epithelium, cancerization, mid-high differentiated cholangiocarcinoma, and focal organized hemangioma. The tumor was positive for CK7, CK19, CK8,

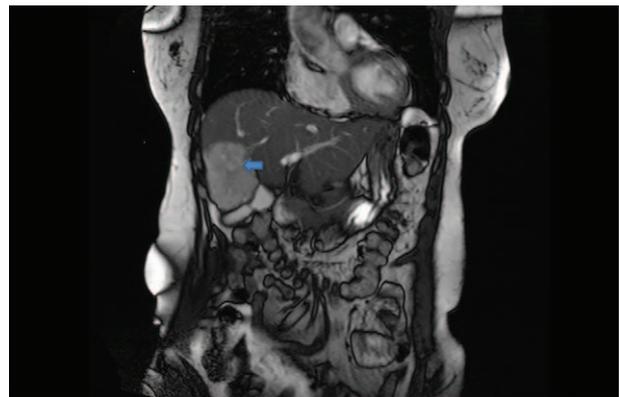


Figure 4. The mass manifested as heterogeneous hypointense on T1W1 and heterogeneous hyperintense on T2W2 with a tuberculiform hyperintense region (arrow) on MRI. MRI=magnetic resonance imaging, T1W1=T1-weighted images, T2W2=T2-weighted images.

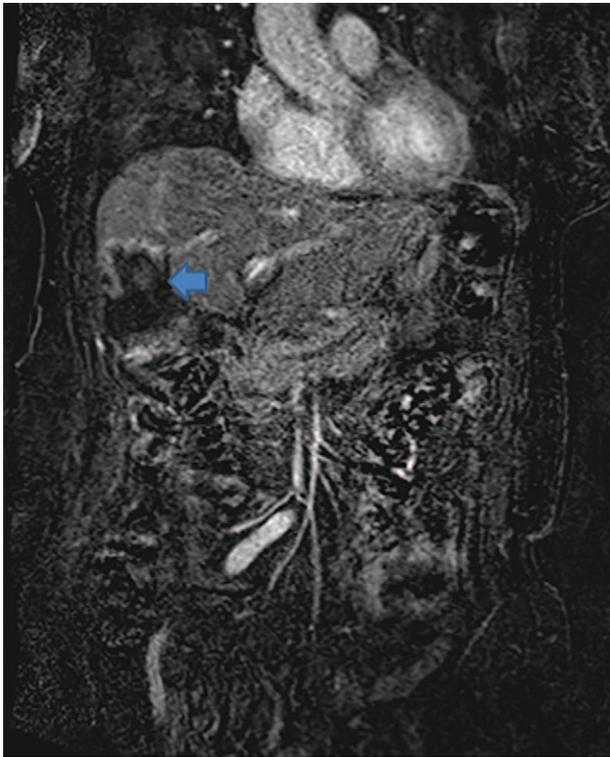


Figure 5. The mass manifested as peripheral, discontinuous, nodular hyperenhancement in the arterial phase with a hyper-enhanced area (arrow) on MRI. MRI=magnetic resonance imaging.

CK18, CD31, CD34 and negative for Glypican-3, Hepa, AFP, CD10, CK20, TTF-1, and CDX. The tumor was also potentially positive for arginase (Figs. 7–12). Positivity for CK7 and CK19 suggested IMCC. The liver parenchyma was not cirrhotic, and the IMCC was staged at T1M0N0.

Routine follow-up assessments were conducted for the patient after surgery for nearly 2 years. The ICC recurred 2 years after the surgery, with increased serum levels of CA199 (41.07U/ml) and CA125 (184.20U/ml). However, AFP levels remained within the



Figure 6. The mass manifested as uneven filling of contrast agent at the venous phase with hyperenhanced region at same position in Figure 3 (arrow) on contrast-enhanced MRI. MRI=magnetic resonance imaging.

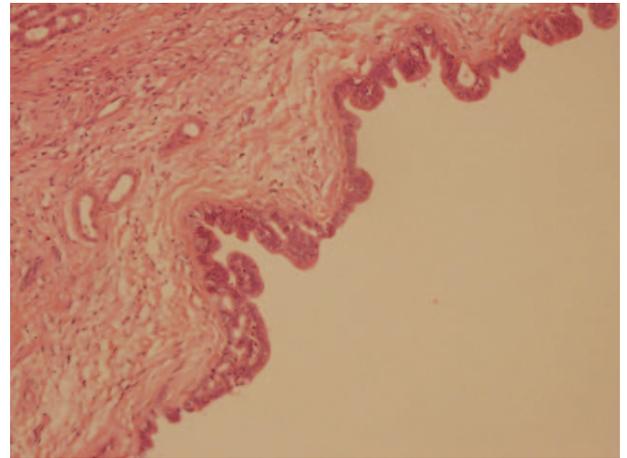


Figure 8. Hematoxylin and eosin staining of liver lesion tissue; IMCC area. IMCC=intrahepatic mass-forming cholangiocarcinoma.

normal range. Following recurrence, the patient was discharged without treatment and died in 4 months.

3. Discussion

ICC growing inside a HH is extremely rare. We have reviewed the literature and to our knowledge, a similar case had not been reported. Atypical hemangioma that mimics mixed hepatocellular and ICC masquerading as acute fatty liver during pregnancy was previously described.^[6,7] Based on the data presented, no histopathological relationship has been reported between HH and ICC.

On gray-scale ultrasound, HH normally appears as a hyper-echoic homogenous mass with well-defined margins and enriched blood signal on CDFI ultrasound.^[8] On MRI, HH typically appears as a well-demarcated, homogenous mass, hypointense on T1-weighted images, hyperintense on T2-weighted images, and shows peripheral nodular enhancement with progressive centripetal homogeneous filling.^[9] Conversely, IMCC appears as an heterogeneous echo lesion with an unclear border on conventional

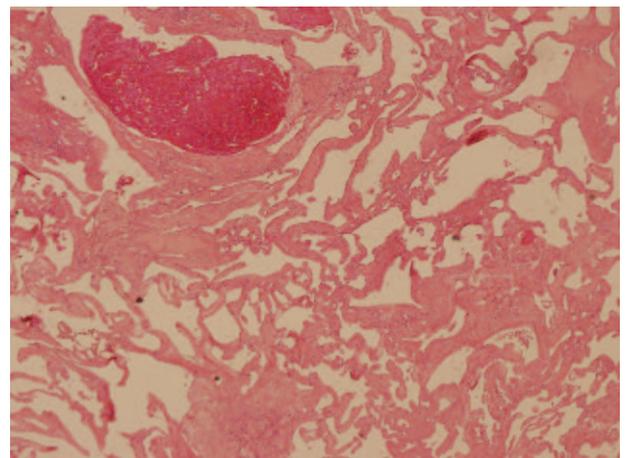


Figure 7. Hematoxylin and eosin staining of liver lesion tissue; hepatic hemangioma.

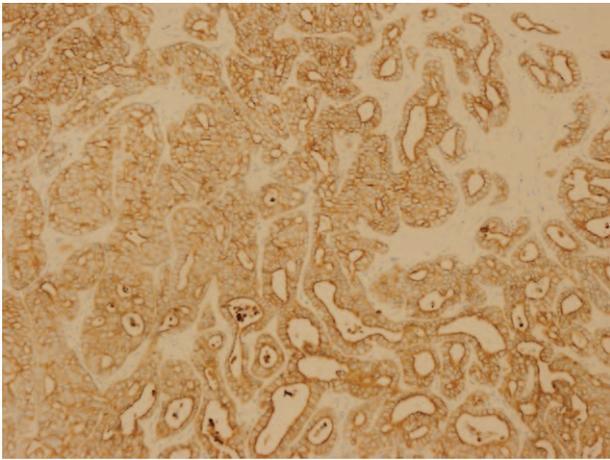


Figure 9. Immunohistochemical staining of ICC. Immunohistochemistry revealed positive labeling of cytokeratin 7.

ultrasound and appears hypointense on T1W1, peripherally hyperintense but internally hypointense on T2W1, and mildly hyper-enhanced peripherally at the arterial phase and following centripetal filling of contrast agent.^[10] After examining the pathological results, we reviewed the images and assessed for the possibility of IMCC. A dim hypoechoic area (Figs. 1 and 2, arrow) was found near the right border on grey-scale ultrasound images. A tuberculiform hyperintense region (Fig. 4, arrow), a hyper-enhanced area (Fig. 5, arrow), and a hyper-enhanced region (Fig. 6, arrow) were observed in the same position on T2W1, and the arterial and the venous phase. However, it is important to note that traditional ultrasound could be affected by respiration, gastrointestinal gas, and the examiner's experience. On spin-echo MRI, both HH and ICC show low signals in T1WI, and the signal for HH might be too high to indicate ICC on T2WI. IMCC could be difficult to distinguish from the background of a giant hemangioma. Nevertheless, both lesions revealed typical features on grey-scale US and spin-echo MRI. Furthermore, the IMCC could be mistaken for thrombosis, fibrosis, and arteriovenous fistula formed in HH, all of which are common pathologic changes in giant HH

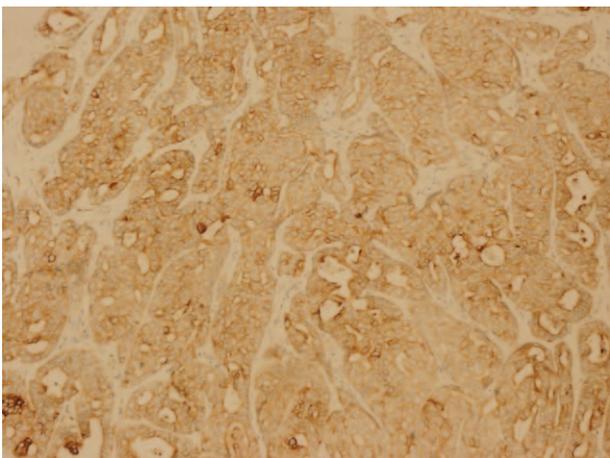


Figure 10. Immunohistochemical staining of ICC. Immunohistochemistry revealed positive labeling of cytokeratin 19.

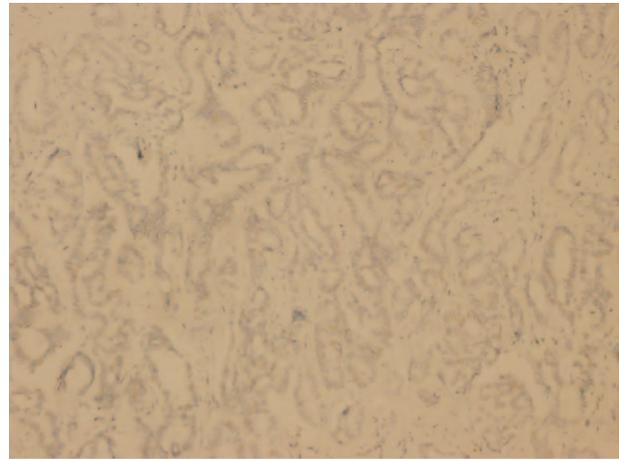


Figure 11. Immunohistochemical staining of ICC. The section was negative for Glypican-3, thus ruling out hepatocellular carcinoma.

that could result in heterogeneous appearance of the entire block. Enhanced pattern using contrast-enhanced MRI might be influenced by the same complications. Due to the slow diffusion of MRI contrast agents between the fibrous tissue and the blood vessels as well as the reduced rate of removal through the blood vessels, CEMRI manifests itself as “fast forward but slow exit,” and the degree of enhancement at the portal and delay phase could become less obvious. The literature suggests that targets that appear on 10-minute hepatobiliary phase could be a potential predictor for differentiating mass-forming ICC on gadoteric acid-enhanced MRI.^[11]

In this report, we reviewed some of the potential causes of IMCC misdiagnosis based on imaging presentation alone. It is difficult to confirm IMCC that grows within a giant HH using a traditional US and MRI approach. Compared with MRI, contrast-enhanced ultrasound (CEUS) provides dynamic real-time imaging with high spatial and temporal differentiation. Studies have shown that CEUS detects benign and malignant liver lesions with an accuracy that is comparable with that of contrast-enhanced computed tomography and CEMRI.^[12,13] It is possible

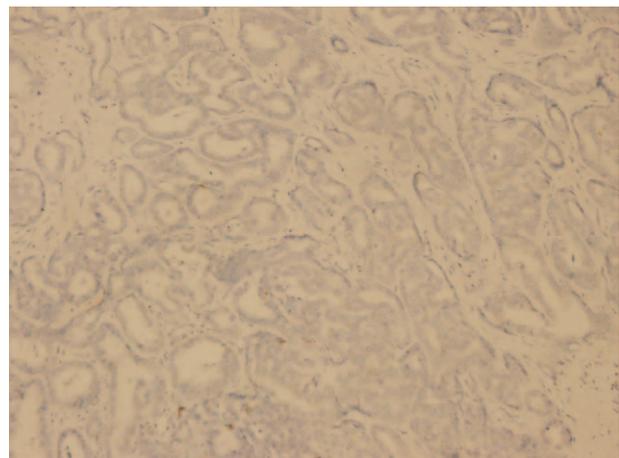


Figure 12. Immunohistochemical staining of ICC. The section was negative for Hepa, thus ruling out hepatocellular carcinoma.

that abnormal perfusion of IMCC could be observed in the tumor using CEUS. Therefore, the inclusion of CEUS as part of the examination could assist in the diagnosis of IMCC in the future.

Here, we report a case of IMCC growing inside a giant hemangioma in an HBV carrier. The IMCC was malignant, difficult to differentiate from hemangioma, and could be misdiagnosed if examinations only relied on standard preoperative imaging. In this case, histopathological examination proved to be irreplaceable, and medical professionals should remain vigilant when examining patients with high-risk factors.

Author contributions

Supervision: Yan Luo, Wenwu Ling.

Visualization: Wenwu Ling.

Writing – original draft: Mengqi Zhou.

Writing – review and editing: Mengqi Zhou.

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