Abstract

We report the case of a 69-year-old woman with reactive lymphoid hyperplasia (RLH) of the liver. She underwent partial hepatectomy under a preoperative diagnosis of hepatocellular carcinoma; however, histopathological analysis revealed RLH. The liver nodule showed the imaging feature of perinodular enhancement in the arterial dominant phase on contrast-enhanced computed tomography and magnetic resonance imaging, which could be a useful clue for identifying RLH in the liver. Histologically, the perinodular enhancement was compatible with prominent sinusoidal dilatation around the nodule. This dilatation is the cause of the perinodular enhancement, which is useful for the accurate diagnosis of RLH.
INTRODUCTION

Reactive lymphoid hyperplasia (RLH) is a benign condition of unknown etiology and pathogenesis\(^\text{[1]}\). It is common in the gastrointestinal tract, orbit, lung, and skin, but rare in the liver, where it is difficult to differentiate from malignant liver tumors such as hepatocellular carcinoma (HCC) and liver metastases. The liver nodules with perinodular enhancement on contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) have been reported in some papers in the English-language literature\(^\text{[2-7]}\). However, few reports have focused on perinodular enhancement in RLH. Histological analysis revealed prominent sinusoidal dilatation surrounding the liver nodule as the cause of the perinodular enhancement. This imaging feature can aid in the accurate diagnosis of RLH.

Informed consent was obtained from the patient. At our institution, approval of the Institutional Review Board is not required for retrospective case reports.

CASE REPORT

A 69-year-old woman with atrial fibrillation was being followed up at the cardiology department. Abdominal ultrasonography performed to investigate hematuria revealed the incidental finding of a well-defined hypoechoic lesion in Segment 1 of the liver. She had no history of persistent viral infection, autoimmune disease, inflammatory bowel disease or malignant tumors. Her body mass index was 26.7, which means she was overweight, but she had no fatty liver. Blood examination showed that her liver function was normal, and that hepatitis B surface antigen, hepatitis B core antibody, hepatitis C antibody and anti-nuclear antibody were negative. The tumor marker values were α-fetoprotein 4.9 ng/mL, PIVKA-2 31-000 mAU/mL, carcinoembryonic antigen 1.8 ng/mL and carbohydrate antigen 19-9 18.1 U/mL. We considered that the high PIVKA-2 value was due to the warfarin she was taking for atrial fibrillation. Unenhanced CT showed a liver nodule with subtle low attenuation relative to the liver parenchyma. On triple-phase contrast-enhanced CT, the nodule demonstrated perinodular enhancement in the arterial dominant phase, and washout of contrast medium in the equilibrium phase (Figure 1). On unenhanced MRI\(^\text{[8]}\), the nodule showed low signal intensity on T1-weighted imaging and high signal intensity on T2-weighted imaging. The nodule showed high signal intensity on diffusion-weighted imaging (b = 800 m\(^2\)/s, inverted black-and-white gray scale), and low signal intensity on the apparent diffusion coefficient map. On gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced MRI, the nodule showed perinodular enhancement in the arterial dominant phase, washout of contrast medium in the late phase, and low signal intensity in the hepatobiliary phase (Figure 2). Under the preoperative diagnosis of HCC, partial hepatectomy was performed. A section of the resected liver showed a well-circumscribed and yellow-white unencapsulated lesion (15 mm × 10 mm) (Figure 3).

DISCUSSION

RLH is generally thought to be a benign lesion characterized by hyperplastic lymphoid follicles with reactive germinal centers\(^\text{[1]}\). Ota et al\(^\text{[9]}\) and Zen et al\(^\text{[10]}\) reported a reduction in the size of lesions in RLH of the liver; however, the risk of malignant transformation is also reported, namely, the development of malignant lymphomas\(^\text{[10]}\). Although RLH can be found in various organs, including the gastrointestinal tract, orbit, lung and skin, its occurrence in the liver is rare. It occurs predominantly in middle-aged women (mean age, 54.1 years)\(^\text{[3]}\). Although the exact etiology remains unknown, associations have been suggested between the development of hepatic RLH and chronic hepatitis\(^\text{[11]}\), autoimmune disease\(^\text{[5,10,12]}\), and malignant tumor\(^\text{[13]}\). None of these was present in our case.

It is difficult to distinguish between RLH of the liver and malignant liver tumors such as HCC and liver metastases on the basis of the imaging findings\(^\text{[14]}\). In the present case, the imaging feature of perinodular enhancement was evident in the arterial dominant phase on contrast-enhanced CT and MRI. Perinodular enhancement has previously been described in some papers in the English-language literature\(^\text{[2-7]}\), and may be a useful aid for identifying RLH in the liver. However, few reports have focused on perinodular enhancement in RLH of the liver. Among other tumors of the liver, hypervascular HCCs show ring enhancement with central necrosis in three phases on triple-phase contrast-enhanced CT or MRI. Therefore,
perinodular enhancement in the arterial dominant phase may enable differentiation of liver RLH from malignant liver tumors. In addition, Osame et al. (16) and Yoshida et al. (7) observed vessels coursing through a liver lesion (vessel-penetrating sign) on CT, and suggested that this finding may enable malignancy to be excluded.

Histological analysis revealed that the nodule was well-demarcated, with massive infiltration of mature lymphoid cells, forming lymphoid follicles of various sizes with germinal centers, and with prominent sinusoidal dilatation surrounding the nodule. We consider that the sinusoidal dilatation was the cause of the perinodular enhancement in the present study.
Abdominal ultrasonography revealed the incidental finding of a well-defined hypoechoic lesion in Segment 1 of the liver.

Differential diagnosis
A liver tumor such as hepatocellular carcinoma (HCC) and liver metastasis was suspected.

Laboratory diagnosis
The tumor marker values were α-fetoprotein 4.9 ng/mL, PIVKA-2 31-000 mAU/mL, carcinoembryonic antigen 1.8 ng/mL and carbohydrate antigen 19-9 18.1 U/mL, and we considered that the high PIVKA-2 value was due to the warfarin she was taking for atrial fibrillation.

Imaging diagnosis
Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) showed perinodular enhancement in the arterial dominant phase, and washout of contrast medium in the late phase.

Treatment
Under the preoperative diagnosis of HCC, a partial hepatectomy was performed.

Pathological diagnosis
Histopathology confirmed RLH of the liver, characterized by massive infiltration of mature lymphoid cells, forming lymphoid follicles of various sizes, with germinal centers.

Related reports
Some English-language literature has reported that RLH in the liver demonstrated perinodular enhancement on contrast-enhanced CT and magnetic resonance imaging (MRI).

Term explanation
RLH is a benign condition of unknown etiology and pathogenesis. It is common in the gastrointestinal tract, orbit, lung, and skin, but rare in the liver, where it is difficult to differentiate from malignant liver tumors such as HCC and liver metastases.

Experiences and lessons
The liver nodule showed the imaging feature of perinodular enhancement in the arterial dominant phase on contrast-enhanced CT and MRI.

Figure 4 Histological findings. A: The nodule is well demarcated and comprises a massive infiltration of mature lymphoid cells, forming lymphoid follicles of various sizes with germinal centers (HE staining, low magnification); B: Prominent sinusoidal dilatation (double-headed arrow) seen around the nodule (HE staining, high magnification) is the likely cause of the perinodular enhancement observed on the contrast-enhanced imaging examinations; C, D: Immunohistochemical staining is positive for CD10, and is negative for Bcl-2. These results exclude follicular lymphoma. HE: Hematoxylin and eosin.

COMMENTS
Case characteristics
A 69-year-old woman with atrial fibrillation was being followed up at the cardiology department.

Clinical diagnosis
Abdominal ultrasonography revealed the incidental finding of a well-defined hypoechogenic lesion in Segment 1 of the liver.

Differential diagnosis
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arterial dominant phase on contrast-enhanced CT and MRI, which could be a useful clue for identifying RLH in the liver.

**Peer-review**

In a middle-aged female patient, RLH should be considered in the differential diagnosis of a small liver nodule that displays perinodular enhancement in the arterial dominant phase on contrast-enhanced CT and MRI.

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