Primary hepatic lymphoma mimicking acute hepatitis

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INTRODUCTION

Primary hepatic lymphoma is a rare extranodal form of lymphoma. It may initially present as hepatic dysfunction resembling acute hepatitis, and clinical diagnosis of the disease could be delayed and complicated, occasionally progressing to fulminant hepatic failure. Here we report the featured radiologic findings of primary hepatic lymphoma on serial follow-up of ultrasonographic and computed tomography (CT) examinations.

CASE

Case 1

A 57-year-old woman visited the emergency department at our hospital with generalized edema which developed a month previously. Her clinical history did not include any specific disease, and her family history was unremarkable. On physical examination, there was no abnormal finding except splenomegaly. The initial results of laboratory investigations were as follows: serum total bilirubin level of 3.0 mg/dL (normal range: 0.2-1.2 mg/dL), direct bilirubin level of 1.5 mg/dL (normal range: 0-0.4 mg/dL), aspartate aminotransferase (AST) of 54 U/L (normal range: 0-37 U/L), alanine aminotransferase (ALT) of 10 U/L (normal range: 0-40 U/L), gamma-glutamyl transpeptidase (γGT) of 177 U/L (normal range: 11-43 U/L), alkaline phosphatase (ALP) of 240 U/L (normal range: 42-98 U/L), and lactate dehydrogenase (LDH) by 842 U/L (normal range: 211-423 U/L). Prothrombin time (PT) and activated partial thrombin time (aPTT) were initially within normal range. On peripheral blood cell count, all of the blood cell counts declined: red blood cell count of 3.12×10⁶/mL (normal range: 4.2-6.3×10⁶/mL), white blood cell count of 1.5×10³/mL (normal range: 4-10×10³/mL), and platelet count of 80×10³/mL (normal range: 130-400×10³/mL). The test for peripheral blood cell morphology also showed normocytic, normochromic anemia, leukopenia, and thrombocytopenia. Serological tests for hepatitis A, B and C viruses, EBV, and CMV were all negative.

Initial abdominal CT demonstrated hepatosplenomegaly, edematous wall thickening of the gallbladder, and effusion in the pleural and pericardial spaces. The initial diagnosis was acute hepatic failure with unknown cause. There was no evidence of lymphadenopathy in the abdomen (Fig. 1A). On the abdominal ultrasonography (US) performed 3 days after the CT study, the echogenicity of the liver parenchyma was mildly coarse, supporting the CT diagnosis of parenchymal disease (Fig. 1B).
On the 10th hospitalized day, the laboratory evaluation showed deteriorating hepatic function: the international normalized ratio (INR) of PT was elongated to 1.81. The levels of total and direct bilirubin were also elevated to 27 and 16 mg/dL, respectively. As the next step, US-guided liver biopsy was performed using an automatic biopsy gun (Tru-cut, TSK laboratory, Japan). Two pieces of specimen were obtained, and histopathology showed numerous lymphocytes infiltrating into the periportal space and hepatic sinusoid. On high-power field of microscopy, variably sized, hyperchromic nuclei with mitotic activity in the lymphocytes were seen. The results of immunochemical profiles of this specimen revealed B cell lineage. The final pathologic diagnosis was diffuse large B-cell type of non-Hodgkin's lymphoma.

The patient refused to receive any treatment for the lymphoma and expired 27 days after initially being hospitalized due to hepatic failure.

Case 2

A 59-year-old man visited the gastroenterology department at our hospital with abdominal bloating. His clinical history did not reveal any specific disease, and his family history was also unremarkable. On physical examination, no abnormality was found, and the results of laboratory investigations were also normal. Initial abdominal US demonstrated mild coarseness of the liver without any focal lesion (Fig. 2A).

Five days after the initial abdominal US, he revisited the emergency department with newly developed symptoms including high fever over 39.5°C, general weakness, cough and sputum. On physical examination performed on his second visit, mild hepatomegaly and tenderness on the right upper quadrant were identified. There were no palpable lymph nodes. The laboratory evaluation showed deteriorated hepatic function: AST of 200 U/L, ALT of 20 U/L, γGT of 223 U/L, ALP of 477 U/L, LDH of 1,060 U/L. The levels of total and direct bilirubin were highly elevated to 27 and 16 mg/dL, respectively. On peripheral blood cell count, all of the blood cell counts declined: red blood cell count of 3.31×10⁶/mL, white blood cell count of 5.5×10³/mL, and platelet count of 110×10³/mL. Serological tests for hepatitis A, B and C viruses, Epstein-Barr virus and cytomegalovirus were all negative. Abdominopelvic CT scans taken at the emergency department showed hepatosplenomegaly with collapsed gallbladder, suggestive of acute hepatitis.

Follow-up abdominal US performed 9 days after the initial study revealed a further decrease in the background echogenicity of the hepatic parenchyma as well as hepatomegaly. The gallbladder was collapsed and accompanied by diffuse wall thickening (Fig. 2B). Eight days later, the hepatic echogenicity had become coarser and hepatosplenomegaly was markedly aggravated. Moreover, the gallbladder wall was more thickened and the amount of ascites was increased (Fig. 2C, Fig. 2D). The changes observed on serial US and CT imaging resembled those observed in progressively worsening acute hepatitis, leading to the diagnosis of idiopathic fulminant hepatopathy.

As the next step, US-guided liver biopsy was performed using an automatic biopsy gun. Two pieces of specimen were obtained,
and the histopathology demonstrated numerous lymphocytes mainly infiltrating into the periportal space. On the high-power field of microscopy, lymphocytes with nuclei of variable size and mitotic activity were seen. The result of immunohistochemical profiles of this specimen revealed peripheral T-cell lymphoma. However, the special stain for γδ T-cell receptor was negative, and the final pathologic diagnosis of peripheral T-cell lymphoma was reached.

The disease was not responsive to chemotherapy using cyclophosphamide hydroxydoxorubicin, vincristine and prednisolone (CHOP), and rapidly progressed to multiple organ failure with severe sepsis and pancytopenia. The patient eventually expired three weeks after admission.

DISCUSSION

Hepatic involvement of non-Hodgkin’s lymphoma can be divided into primary hepatic lymphoma, secondary involvement of systemic lymphoma, and hepatosplenic T-cell lymphoma. Secondary involvement is the most common form of lymphoma in the liver, appearing in 16-40% of non-Hodgkin’s lymphoma. Primary hepatic lymphoma is defined as a lymphoma that is limited to the liver, without extrahepatic involvement. Most primary hepatic lymphoma originates from B cell lineage, with only few cases of T-cell lineage reported in the literature. Hepatosplenic T-cell lymphoma is a very rare variant of mature T-cell lymphoma independently classified by the 2008 WHO classification. For the differential diagnosis, a liver biopsy should be performed along with immuno-

Figure 2. Initial hepatic ultrasonography of a 59-year-old man shows normal parenchyma echogenicity of the liver (A). On the 9th day from the initial ultrasonography, decreased background echogenicity of the hepatic parenchyma with diffuse periportal tracking (arrow) are noted (B). On the 17th day, ascites is seen in the perihepatic space (arrow), and the parenchymal echogenicity is coarser than in the previous study (C). The thickened gall bladder is completely collapsed (D).
hypoechoic lesions. However, these typical liver signs are also present in the course of primary hepatic lymphoma. The characteristic findings of hepatic lymphoma include the presence of multiple hypoechoic nodules in the liver and sometimes in the spleen, which may be difficult to differentiate from those seen in patients with hepatitis. In these cases, the role of laboratory tests and liver biopsy is essential to provide a definitive diagnosis. It should be noted that liver biopsy may be required to confirm the diagnosis of primary hepatic lymphoma.

In conclusion, the characteristic radiologic findings of primary hepatic lymphoma may be similar to those of acute parenchymal disease although aggressive progression of the disease is usually observed on follow-up imaging. Therefore, primary hepatic lymphoma should be included in the differential diagnosis, and liver biopsy should be considered.

SUMMARY

Primary hepatic lymphoma is a rare manifestation of lymphoma. Clinical diagnosis of the disease could be delayed and complicated since it may mimic acute hepatitis. The radiologic findings of primary hepatic lymphoma may be similar to those of acute parenchymal liver disease although aggressive progression of the disease is usually observed on follow-up imaging. Therefore, primary hepatic lymphoma should be included in the differential diagnosis of acute hepatopathy that demonstrates a severe and aggressive course. Liver biopsy should be considered to confirm its diagnosis.

Conflicts of Interest

The authors have no conflicts to disclose.

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