Case Report

Reactive Lymphoid Hyperplasia of the Liver Incidentally Found in a 55-Year-Old Woman with a History of Ulcerative Colitis

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Reactive lymphoid hyperplasia (RLH), also known as pseudolymphoma or nodular lymphoid lesion [1, 2], is a benign disease that occurs in various organs, such as the lungs, the orbits, the skin, and the gastrointestinal tract, however rarely occurring in the liver [1]. RLH is characterized by the proliferation of non-neoplastic polyclonal lymphocytes that form follicles with reactive germinal centers [2]. The first reported case of the RLH of the liver was by Snover et al. in 1981 [3]. The true pathogenesis is unknown, but its occurrence is thought to be associated with reactive immune phenomenon to various immune stimulators, such as chronic viral hepatitis, autoimmune disease, and malignant tumor [2, 3]. No cases occurring in patients with inflammatory bowel disease have been reported to date. We present a case of RLH of the liver in a patient with ulcerative colitis (UC).

1. Introduction

A 55-year-old woman with a seventeen-year history of UC presented with sudden but manageable localized right lower abdominal pain and went to an outpatient clinic. Oral sitafloxacin hydrate was prescribed with a presumed diagnosis of acute appendicitis. The pain did not improve, and the patient presented again to the emergency. Ultrasonography (US) and abdominal computed tomography (CT) ruled out appendicitis, but a mass was detected in the liver. The same antibiotic was continued and the crystalloid fluid was instilled, and the pain improved. The patient was then referred because of concern about exacerbation of UC and the malignant potential of the liver mass. Laparoscopic partial hepatectomy was performed. Histopathological findings revealed a conglomerate hyperplasia of lymphoid follicles with germinal centers. Infiltrating lymphocytes were non-neoplastic. Final diagnosis was RLH of the liver. UC is chronic inflammatory bowel disease and may be related to RLH, but there is no clear explanation at this point. This is the first known reported case of RLH of the liver in a patient with UC. But the relationship between the RLH and UC remains uncertain. Further investigation and case accumulation are necessary.

2. Case Presentation

A 55-year-old woman with a seventeen-year history of UC presented with sudden but manageable localized right lower abdominal pain and went to an outpatient clinic. Oral sitafloxacin hydrate was prescribed with a presumed diagnosis of acute appendicitis. The pain did not improve, and the patient presented again to the emergency. Ultrasonography (US) and abdominal computed tomography (CT) ruled out appendicitis, but a mass was detected in the liver. The same antibiotic was continued and the crystalloid fluid was instilled, and the pain improved. The patient was then referred because of concern about exacerbation of UC and the malignant potential of the liver mass. No abdominal pain was noted.

She had been diagnosed with UC at 38 years old and prescribed 5-aminosalicylic acid until 49 years old. She had no
drinking habit, but her mother had history of kidney cancer. Vital signs were within normal range. The abdominal pain remained resolved, and other abdominal findings were also normal. Laboratory tests, including aspartate aminotransferase, alanine transaminase, total bilirubin, albumin, alkaline phosphatase, γ-glutamyltransferase, platelet count, and prothrombin time, were within normal range. Tumor markers, such as α-fetoprotein, protein-induced vitamin K absence-II, carcinoembryonic antigen, and carbohydrate antigen 19-9, were also within normal range. Hepatitis B virus (HBV) surface antigen and hepatitis C virus (HCV) antibody were both negative. A low echoic mass (12.8 × 12.0 mm) with blood flow signal was detected in segment 3 of the liver on abdominal US (Figure 1). On plain CT, the mass was detected as a low-density lesion. The mass was not enhanced on contrast-enhanced CT in the arterial phase, was slightly enhanced in the portal phase, and was detected as low-density lesion in the delayed phase (Figures 2(a)–2(d)). On magnetic resonance imaging (MRI), the mass was recognized as low signal in T1-weighted image (T1WI) and high signal in T2-weighted image (T2WI). On diffusion-weighted image, the mass was shown as an area of high signal intensity. It was shown as an area of low signal intensity in the hepatobiliary phase on gadolinium ethoxybenzyl diethylene-triamine pentaacetic acid-enhanced MRI (Figures 3(a)–3(d)). Colonoscopy revealed the remission of UC, and there were no malignant findings on esophagogastroduodenoscopy. Definitive diagnosis was very difficult because there were no typical findings of malignant tumor, such as hepatocellular carcinoma or metastatic carcinoma. Furthermore, there was no elevation of tumor marker levels or hepatitis virus marker levels. As a differential diagnosis, highly differentiated hepatocellular carcinoma and slow-staining hemangioma were considered, but clear evidence was lacking. Regular image follow-up was recommended as watchful waiting, but the patient strongly requested surgery for diagnosis because of family history of malignant disease. Surgery was planned, and laparoscopic partial hepatectomy was performed. In the operative findings, a discolored area was observed in both lobes of the liver, suggesting chronic inflammation. The mass was recognized at segment 3 in the discolored area (Figures 4(a)–4(c)). The resected specimen was an elastic, hard, well-demarcated whitish mass measuring 12 × 10 mm (Figure 5). Histopathological findings revealed a number of lymphoid follicles with a germinal center. Infiltrating lymphocytes were non-neoplastic and lymphoepithelial lesions were not recognized. On immunohistochemical staining, lymphoid follicles were CD20- and CD3-positive and Bcl-2-negative. There was no mononclality on immunoglobulin (Ig) kappa and lambda. Mild IgG-positive histiocytes and plasma cells were observed between the follicles, but there was no significant increase in IgG4-positive cells (Figures 6(a)–6(f)). Inflammatory findings in the background liver tissue were mild. Pathological diagnosis was RLH of the liver. Postoperative course was uneventful, and the patient was discharged on postoperative day 6. Blood tests including anti-nuclear antibody (ANA), IgG, anti-Sm antibody, and anti-mitochondrial antibody were examined after the operation, but all were within normal range. The patient is currently under outpatient follow-up, but there have been no signs of recurrence after approximately two years. The patient also never developed recurrence of abdominal pain.

3. Discussion

RLH, also known as pseudolymphoma or nodular lymphoid lesion, is a benign disease characterized by the proliferation of non-neoplastic polyclonal lymphocytes that form follicles with reactive germinal centers; it rarely occurs in the liver [1, 2]. RLH predominately occurs in middle-aged women, with some type of autoimmune disease in about 40% of the cases [2]. Many patients have no symptoms, and they are often found incidentally on imaging study [2]. In our case, CT was performed to investigate the cause of abdominal pain happened to reveal a mass in the liver. However, we considered that there is no relationship between abdominal pain and liver mass because of its small size. Moreover, we have no explanation for the abdominal pain which was surely nonspecific.

There were no specific tumor markers for the RLH, but since the tumor was very small, so it is unlikely to be useful.

Figure 1: US findings. (a) On US, a low echoic mass was pointed out in segment 3 of the liver (red dotted area). (b) Blood flow signal was observed around the mass (white arrow).
for diagnosis. The imaging study showed a small hypoechoic lesion on US, and hyper- to hypovascular on contrast CT or MRI was also nonspecific, so it was difficult to rule out hepatocellular carcinoma or metastatic carcinoma or even differentiate between each other [4–6]. In our case, the patient had no background of chronic hepatic inflammation such as HBV and HCV or notable use of alcohol. Additionally, the tumor markers were within all normal range. Therefore,
she was firstly recommended watchful waiting follow-up because there were no typical findings of malignant disease. Surgery was performed owing to the strong demand of the patient, and as a result, it was considered appropriate because definitive diagnosis could be done and because of a previous report of a case in which lymphoma progressed after being diagnosed with RLH of the liver [7]. Preoperative diagnosis of RLH is thought to be difficult, and many cases have been diagnosed after surgical resection [2]. Preoperative liver biopsy may be useful for diagnosis, but several reports have pointed out the risk of dissemination if the lesion has the malignant potential [8, 9], so careful judgment.

Figure 4: Intraoperative findings. (a) A discolored area was observed in the right lobe of the liver (yellow-dotted area), and it suggested chronic inflammation. (b) An area of the tone was also observed in left lobe, and a mass was observed in the area (yellow-dotted area). (c) Laparoscopic partial hepatectomy was performed.

Figure 5: The resected specimen was a hard, elastic, well-demarcated whitish mass.
is required. On pathological findings, RLH is also characterized by a localized, well-demarcated lesion, with the presence of hyperplastic lymphoid follicles with polyclonal and polymorphic small mature lymphocytes, macrophages, and plasma cells [10]. Diseases such as inflammatory myofibroblastic tumor, low-grade lymphomas with a nodular growth pattern, primary marginal zone lymphoma, and follicular lymphoma must be differentiated from RLH of the liver [2, 6]. Differentiation from lymphoma is especially very important. Reactive lymphoid follicles are also contained in marginal zone lymphoma, but lymphoepithelial lesions and cellular atypia were reported to be observed in mucosa-associated lymphoid tissue lymphoma, not in relation with RLH of the liver [6]. Additionally, follicular lymphoma often exhibits more densely packed follicles of uniform size and shape [6]. In our case, no atypical change was observed in the infiltrating lymphocyte, and there was no detection of monoclonality in Ig kappa or lambda. It suggested the non-neoplastic lesion. Lymphoepithelial lesions were not also observed, so mucosa-associated lymphoid tissue lymphoma was ruled out. Lymphoid follicles with germinal center were positive for CD-20 and negative for Bcl-2. Lymphoma, especially follicular lymphoma, therefore could be ruled out. Additionally, mild IgG-positive histiocytes and plasma cells were observed between the follicles, but there was no significant increase in IgG4-positive cells, so the IgG4 related diseases could also be ruled out. The pathogenesis of RLH of the liver is still unclear [1, 2, 4–6, 9]. Reactive immune phenomena to various immune stimulants are presumed to be the trigger, such as various autoimmune diseases, viral hepatitis, or cancer [1, 2]. Kanno et al. summarized 76 cases of RLH of the liver, 35.5% had liver disease, 17.1% had autoimmune disease, and 27.6% had malignant tumor [9]. Common diseases were reported to be viral such as hepatitis B, primary biliary cirrhosis (now called primary biliary cholangitis), autoimmune hepatitis, chronic thyroiditis,
colitis that is reported. The association between both conditions however remains probably coincidental and speculative. Therefore, further investigation is necessary to accumulate reports.

**Data Availability**

All data generated during this study are included in this published article.

**Consent**

The patients provided informed consent for the publication of this case report.

**Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this article.

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**References**


