INTRODUCTION

Reactive lymphoid hyperplasia (RLH) is a rare benign condition that forms a mass-like lesion characterized by proliferation of non-neoplastic lymphocytes forming follicles and germinal centers. RLH is thought to represent a reactive immunological response, and some cases may arise in association with malignancy and hepatitis.\(^1\) Radiologically, RLH of the liver may mimic a primary or metastatic hepatic malignancy. Therefore, it is very difficult to diagnose correctly without pathological examination. In this issue, we present a case of hepatic RLH and discuss the histopathologic findings with a review of the literatures.

CASE SUMMARY

A 74-year-old woman was referred to our hospital for further evaluation of an intrahepatic bile duct dilatation detected by abdominal ultrasonography (US). She had a history of common bile duct cancer (adenosquamous carcinoma, pT1N0M0), which was resected 4 years ago in our hospital. Physical examination showed intermittent abdominal pain. Blood cell counts and chemical findings, including liver enzymes, were within normal limits. Hepatitis B virus surface antigen was positive and the levels of tumor markers, including carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and alpha-fetoprotein (AFP) were all within normal ranges. Abdominal US showed intrahepatic bile duct dilatation of the left lobe. Computed tomography (CT) showed bile duct dilatation with mild ductal wall thickening and enhancement of the left intrahepatic bile ducts (IHBD) (Fig. 1A) and about 1.5 cm sized ill-defined mass like lesion at hepatic segment 2, proximal to the dilated left intrahepatic bile ducts (Fig. 1B). Also, an enlarged sub-hepatic lymph node was detected. Magnetic resonance imaging (MRI) demonstrated multiple IHBD stones that showed a heterogeneous high-intensity on T1-weighted images and low-intensity on T2-weighted images in segment 2. Since these findings suggested cholangitis combined with IHBD stones, the patient underwent left lateral sectionectomy of the liver.

PATHOLOGIC FINDINGS

Macroscopically, the resected lateral segment of the liver had a smooth surface and appeared normal. On the cut section, there were some dilated IHBD without obvious mass-like lesion (Fig. 2A). Microscopically, the lesion exhibited an infiltration of the lymphoid cells with follicles formation and hyalinized interfollicular spaces (Fig. 2B). The lymphoid follicles varied in size and shape...
with germinal centers composed of small or large lymphoid cells and tingible body macrophages (Fig. 2C). Interfollicular areas were composed of small mature lymphocytes without cytologic atypia. No evidence of recurrent cholagiocarcinoma was observed. Lymphoid cells positive for B cell marker were distributed mainly in the germinal centers, while those positive for T cell marker were observed around the germinal centers (Fig. 2D). Germinal centers were negative for bcl-2. On the basis of the histological and immunohistochemical findings, a final diagnosis of RLH of the liver was made. Post-operatively, no obvious recurrence of the liver nodule was detected during the 3 months medical follow-up.

**DISCUSSION**

RLH of the liver is an unusual benign lymphoproliferative lesion, first reported by Snover et al in 1981. Since then, 41 cases of RLH in the liver have been reported in the English literature, including 2 cases of Korea. It is characterized by formation of follicles with polymorphic and polyclonal cell population and active germinal centers. RLH can occur in various organs such as skin, orbit, thyroid, breast, lung and gastrointestinal tract, but it is rare in the liver. Diagnoses of RLH have become frequent during the past two decades due to the use of advanced various imaging modalities and increased population of health screening. Among 42 reported RLH cases, 37 cases are female, while the other 5 cases are male (male-female ratio, 1:7.4), with the mean age of 57 years (range: 15-85 years). The size of the lesion is less than 40 mm in 38 cases and the other 4 cases are more than 40 mm in the greatest dimension (44.4 mm in average; range: 15-105 mm). Most hepatic RLH are single (n=36), but may also be multiple (n=6).

The etiology of RLH is still unclear. In previous reviews, RLH is thought to be associated with an immune-mediated reactive phenomenon. Because one-third of the reported cases had various autoimmune disorders, such as Sjögren’s syndrome, CREST syndrome (the limited cutaneous form of systemic scleroderma), autoimmune thyroiditis, primary biliary cirrhosis and primary immunodeficiency. Another one-third of the cases had a history of malignancies in various organs, as in our case (Table 1). Therefore, it can be considered that the pathogenesis of RLH of the liver in patients with malignant tumor may be related to an immunologic abnormality that is caused by the malignant tumor itself or previous surgery for the tumors.

Pre-operative diagnosis of hepatic RLH is extremely difficult by using imaging studies alone. RLH of the liver may mimic a primary or metastatic hepatic malignancy radiologically, especially in patients with chronic hepatitis or internal malignancies. Fifteen cases out of 41 reported cases before the operation of hepatic RLH had most frequently been misdiagnosed as hepatocellular carcinoma (HCC). Some authors described subtle differences in radiological...