Hepatic Inflammatory Pseudotumor Associated with Xanthogranulomatous Cholangitis Mimicking Cholangiocarcinoma

Sung Kwan Bae, Seigo Abiru, Yukio Kamohara, Satoru Hashimoto, Masashi Otani, Akira Saeki, Shinya Nagaoka, Kazumi Yamasaki, Atsumasa Komori, Masahiro Ito, Hikaru Fujioka and Hiroshi Yatsuhashi

Abstract

Inflammatory pseudotumor (IPT) is a rare benign condition often misdiagnosed as malignancy. An 80-year-old man was referred to our clinic for an asymptomatic hepatic mass detected on plain abdominal CT. Abdominal ultrasonography identified the lesion as a poorly defined hypoechoic mass. Although a liver biopsy did not provide any evidence of malignancy, imaging modalities suggested a diagnosis of cholangiocarcinoma. The patient underwent left lobectomy, and the pathological findings were consistent with the features of xanthogranulomatous cholangitis. This case is the first report of hepatic IPT originating from xanthogranulomatous cholangitis without symptoms and illustrates the importance of obtaining a preoperative diagnosis in order to avoid a misdiagnosis of malignant tumor.

Key words: inflammatory pseudotumor, xanthogranulomatous cholangitis, cholangiocarcinoma

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Introduction

Inflammatory pseudotumor (IPT) is a rare benign lesion reported in almost all organs and occasionally in the liver. Hepatic IPT was first described in 1953 by Pack and Baker as a rare hepatic lesion (1). In a study of resected focal lesions in 403 patients, the incidence of hepatic IPT was reported to be 0.7% (2). This lesion commonly presents in men in their 30’s and 40’s and is often associated with symptoms such as abdominal pain, fever, weight loss and jaundice (3). Unfortunately, due to a lack of characteristic clinical and radiological features, IPT is easily mistaken for malignant tumors, such as cholangiocarcinoma, leading to unnecessary surgery. Accordingly, most cases are diagnosed after surgical resection. We herein report a pathologically confirmed rare case of liver IPT with xanthogranulomatous cholangitis in a patient who underwent left lobectomy for clinical findings suggestive of cholangiocarcinoma.

Case Report

An 80-year-old man was referred to our clinic after an asymptomatic hepatic mass was detected on plain abdominal CT. The patient was afebrile, and there were no abnormalities in the abdomen or pitting edema in the legs. Furthermore, blood tests indicated no serious abnormalities, and the levels of tumor markers were within the normal limits. On plain CT, the lesion appeared as a relatively low-density area. Contrast-enhanced abdominal CT revealed a 20-mm mass with poorly delineated margins adjacent to the umbilical portion of the left portal vein. During dynamic contrast-enhanced CT, the lesion was enhanced in the early phase and remained enhanced during the late phase (Fig. 1). Contrast-enhanced abdominal magnetic resonance imaging (MRI) also detected the lesion as a low-intensity area on T1-weighted images and a heterogeneous high-intensity area on T2-weighted images. There was signal enhancement dur-
Figure 1. On plain CT (A), the lesion appeared as a relatively low-density area adjacent to the umbilical portion of the left portal vein (black arrow). On contrast-enhanced abdominal CT, the lesion was enhanced in the early phase (B) and remained enhanced during the late phase (C).

Figure 2. On contrast-enhanced abdominal MRI, there was signal enhancement (black arrow) during the early (A) and late (B) phases of the dynamic scan, with a reduced uptake of contrast media in the hepatocyte phase (C).

Figure 3. Abdominal ultrasonography. The lesion was identified as a poorly defined hypoechoic mass.

Abdominal ultrasonography identified the lesion as a poorly defined hypoechoic mass (Fig. 3). Although an ultrasound-guided percutaneous liver biopsy did not show any evidence of malignancy, imaging of the liver was suggestive of cholangiocarcinoma. The patient subsequently underwent left lobectomy, which showed fibrosis on the surface of the left lobe, indicative of chronic cholangitis. Pathology confirmed the presence of a white-yellowish nodular lesion on the left margin of the left intrahepatic bile duct, and the intrahepatic bile ducts were destroyed by dense inflammatory cell infiltration (xanthogranulomatous inflammation), resulting in narrowing of the luminal space. The peribiliary regions contained a wide variety of inflammatory cells, including eosinophils, lymphocytes, plasmacytes, histiocytes and foam cells. Immunohistochemistry for CD68 confirmed that the majority of lipid-laden macrophages were histiocytes (Fig. 4). However, there was no evidence of primary sclerosing cholangitis (e.g., onion skin-like lesions) or immunoglobulin G4 (IgG4)-related diseases (e.g., massive
infiltration of plasmacytes). These findings were consistent with a diagnosis of IPT with xanthogranulomatous cholangitis. The patient had an uneventful postoperative course and was found to be doing well at the time of this report.

**Discussion**

The etiology of hepatic IPT remains unclear, although infection, biliary obstruction, chronic cholangitis (4) and primary sclerosing cholangitis (5) have all been suggested as possible causes. For instance, cases of IPT have been reported in patients with viral infections (6), including the hepatitis B or C virus (7-9). Still, there is no clear evidence of an association between hepatic IPT and the detection of infectious organisms. In the present case, the findings of a physical examination, laboratory tests and imaging modalities did not support the presence of biliary obstruction, cholangitis or chronic inflammation as possible causes of IPT. Therefore, it is difficult to speculate regarding the etiology of IPT in this case. However, the intraoperative findings of fibrosis on the surface of the left lobe and the postoperative histological findings indicated the existence of asymptomatic chronic cholangitis.

The radiological features of IPT are nonspecific and mimic those of malignant neoplasms, such as cholangiocarcinoma, hepatocellular carcinoma, metastatic adenocarcinoma and hepatic abscesses. In previous studies, Fukuya et al. reported that IPT should be included in the differential diagnosis when the mass shows contrast enhancement on delayed-phase CT scans (10). This finding is explained by the accumulation of extravascular contrast media in fibrotic components within the mass (11, 12). In the current case, the enhancement of the lesion remained until the delayed phase on CT scans, which may be explained by the pathologic findings, including the presence of fibrous tissue and dense cellular infiltrates (10). However, the exact correlation with the pathological findings of the resected specimen cannot be confirmed.

In the majority of cases, obtaining a preoperative diagnosis of IPT is difficult, and the diagnosis is established postoperatively. Hence, attempting to make the preoperative diagnosis based on the findings of a percutaneous needle biopsy is important, although needle biopsies lead to the diagnosis of IPT in only a few cases (8, 13). Kim et al. reported a case of IPT diagnosed according to a needle biopsy in a patient with hepatitis C and concluded that supplemental biopsies should be obtained in order to differentiate between IPT of the liver and hepatocellular carcinoma (HCC) (8). Yamaguchi et al. also reported a case of IPT confirmed via percutaneous biopsy without surgical resection (13). In the present case, the liver biopsy specimen showed almost normal liver tissue, although the possibility of sampling error...
cannot be entirely excluded. Liver biopsies have several disadvantages, including sampling error and a risk of complications; however, serial liver biopsies should have been performed in order to obtain an accurate diagnosis in this case.

In 1978, Someren classified hepatic IPT into three distinct types: (1) hyalinized sclerosing, (2) plasma cell granuloma, and (3) xanthogranuloma (14). However, there is still no consensus regarding IPT classification. Zen et al. proposed a new pathological classification of IPT with respect to IgG4-related disease: fibrohistiocytic and lymphoplasmacytic types (15). The features of fibrohistiocytic IPT include xanthogranulomatous inflammation, neutrophilic infiltration and multinucleated giant cells forming lesions primarily in the peripheral hepatic parenchyma. This type of IPT also involves venous occlusion without periductial fibrosis, but with little inflammation or cholangitis. In contrast, lymphoplasmacytic IPT is characterized by the presence of eosinophilic-dominant infiltration and diffuse lymphoplasmacytic infiltration surrounding the hepatic hilum, as well as obliteratorive phlebitis and cholangitis with periductal fibrosis. The current case involved infiltration of a wide variety of inflammatory cells and displayed features histologically consistent with those of fibrohistiocytic IPT. Patients with unicentric Castleman’s disease (UCD) also present as asymptomatic and are often diagnosed incidentally. However, the present patient did not exhibit the typical pathological findings of UCD, such as hyalinized follicles surrounded by small lymphocytes or germinal centers with plasma cells.

Xanthogranulomatous cholangitis is rare, although there are some reports of bile duct stenosis due to extension of gallbladder xanthogranulomatous cholecystitis (XGC) into the liver, which is a chronic benign inflammatory condition. In one series, only four cases of inflammatory stricture of the extrahepatic biliary tract were diagnosed among 620 cases of XGC (16). The pathogenesis of xanthogranulomatous cholangitis has been suggested to involve an inflammatory response to extravasated bile, as proposed for XGC (17, 18), in which macrophages are recruited to phagocytose the released bile pigments, resulting in the formation of xanthoma cells. The histological differential diagnosis in this anatomic region includes cholangiocarcinoma, inflammatory myofibroblastic tumors, atypical lymphoid lesion, and (3) xanthogranuloma (14). However, there is still no consensus regarding IPT classification. Zen et al. proposed a new pathological classification of IPT with respect to IgG4-related disease: fibrohistiocytic and lymphoplasmacytic types (15). The features of fibrohistiocytic IPT include xanthogranulomatous inflammation, neutrophilic infiltration and multinucleated giant cells forming lesions primarily in the peripheral hepatic parenchyma. This type of IPT also involves venous occlusion without periductal fibrosis, but with little inflammation or cholangitis. In contrast, lymphoplasmacytic IPT is characterized by the presence of eosinophilic-dominant infiltration and diffuse lymphoplasmacytic infiltration surrounding the hepatic hilum, as well as obliteratorive phlebitis and cholangitis with periductal fibrosis. The current case involved infiltration of a wide variety of inflammatory cells and displayed features histologically consistent with those of fibrohistiocytic IPT. Patients with unicentric Castleman’s disease (UCD) also present as asymptomatic and are often diagnosed incidentally. However, the present patient did not exhibit the typical pathological findings of UCD, such as hyalinized follicles surrounded by small lymphocytes or germinal centers with plasma cells.

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In conclusion, hepatic IPT associated with xanthogranulomatous cholangitis is a rare condition. Nonetheless, this disorder should be considered in the differential diagnosis of mass lesions located around the biliary tree in patients with or without a history of cholangitis. In particular, preoperative serial liver biopsies are essential for making an accurate diagnosis and preventing a misdiagnosis of malignant tumor.

The authors state that they have no Conflict of Interest (COI).

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References


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