Hepatic Peribiliary Cysts with Rapidly Progressive Refractory Obstructive Jaundice and Esophageal Varices

Michihiko Shibata¹, Masaaki Hiura¹, Michio Senju¹, Toru Matsuhashi¹, Shintaro Abe¹, Chie Morita², Kazuhiro Hayashida², Akinari Tabaru¹ and Masaru Harada¹

Abstract

A 54-year-old man with decompensated alcoholic liver cirrhosis presented with acute cholangitis. Although no localized lesions were detected in the liver on contrast-enhanced computed tomography and no risky varices were noted on endoscopy, hepatic peribiliary cysts (HPBCs) developed along the intrahepatic portal vein in the course of only 40 days. Moreover, esophageal varices with the red color sign grew rapidly during the same period, and the patient ultimately died due to rupture. HPBC formation is a rare complication of liver disease, including cirrhosis. Although HPBCs are generally harmless, on rare occasions they may induce the rapid progression of esophageal varices.

Key words: hepatic peribiliary cyst, liver cirrhosis, obstructive jaundice, esophageal varices, portal hypertension

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Introduction

Hepatic peribiliary cysts (HPBCs) were first reported among the pathological findings of eight autopsy cases by Nakanuma et al. in 1984 (1). These lesions consist of multiple small cysts in the Glisson sheath and constitute a rare complication of severe liver diseases with various etiologies. On imaging, such as computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP), they appear as a string of bead-like structures and/or foamy fringe along the hepatic, segmental and area ducts (2). HPBCs are often poorly recognized, as they are usually asymptomatic (3). However, serious cases have recently been reported in which HPBCs have induced acute cholangitis or obstructive jaundice (4-6). We herein report a case of alcoholic liver cirrhosis in which rapidly progressive HPBCs and esophageal varices developed within a very short period.

Case Report

A 54-year-old man with general fatigue and abdominal fullness was admitted to our hospital in 2008. He had consumed approximately 900 mL/day of Japanese rice wine (sake) (10-20% ethanol) for the past 35 years and had a history of endoscopic sclerotherapy for esophageal varices at 47 years of age. A blood test showed mild hypoalbuminemia, hyperbilirubinemia, hepatobiliary injury and coagulopathy, whereas viral hepatitis markers, antinuclear antibodies and anti-mitochondrial antibodies were all negative (Table). Contrast-enhanced CT (CE-CT) and ultrasonography (US) showed massive ascites, without localized lesions in the liver or other organs (Fig. 1). The patient was therefore diagnosed with decompensated alcoholic liver cirrhosis. The endoscopic findings obtained on the 30th hospital day revealed several small esophageal varices considered to have a low risk of rupture (Fig. 2A). Although the patient’s general condition improved with treatment with diuretics, he experi-

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aminotransferase (ALT) level of 121 IU/L, aspartate aminotransferase (AST) level of 209 IU/L, alanine transaminase (ALT) 29.5 mg/dL, direct bilirubin level of 21.3 mg/dL, aspartate aminotransferase (AST) 115 IU/L, alanine transaminase (ALT) 56 IU/L.

The 6th hospital day showed that the esophageal varices had grown rapidly with red wale marks and cherry red spots (Fig. 2C). The endoscopic findings on the 98th hospital day showed that the esophageal varices had grown rapidly with red wale marks and cherry red spots (Fig. 2C). The patient was given best supportive care; however, jaundice progressed rapidly, and he eventually died from ruptured esophageal varices on the 114th hospital day.

Although the inflammation associated with the cholangitis improved following treatment with antibiotics, jaundice gradually progressed, and a blood test performed on the 93rd hospital day showed a serum total bilirubin level of 29.5 mg/dL, direct bilirubin level of 21.3 mg/dL, aspartate aminotransferase (AST) level of 209 IU/L, alanine aminotransferase (ALT) level of 121 IU/L, alkaline phosphatase (ALP) level of 708 IU/L and gamma glutamyl transpeptidase (γ-GTP) level of 78 IU/L (Fig. 3). In addition, CE-CT revealed many small cysts on both sides of the hepatic lobes, primarily localized in the intrahepatic portal tracts (Fig. 4B); there was no portal vein thrombosis on CT or US. Meanwhile, Doppler US performed on hospital day 93 showed an antegrade blood flow in the portal vein, and MRCP disclosed multiple cystic lesions in the liver (Fig. 5A). We therefore diagnosed the patient with obstructive jaundice caused by HPBCs. We initially considered performing biliary drainage; however, percutaneous drainage was impossible due to the presence of ascites, and endoscopic retrograde cholangiography (ERCP) showed complete obstruction of the bilateral intrahepatic bile ducts as a result of extraductal cystic lesions (Fig. 5B). Hence, it was impossible to insert the guidewire into the intrahepatic bile ducts and perform drainage. The endoscopic findings on the 98th hospital day showed that the esophageal varices had grown rapidly with red wale marks and cherry red spots (Fig. 2C). The patient was given best supportive care; however, the jaundice progressed rapidly, and he eventually died from ruptured esophageal varices on the 114th hospital day.

**Table.** Laboratory Findings on Admission

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Biochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 5,700 /µL</td>
<td>TP 6.7 g/dL</td>
</tr>
<tr>
<td>RBC 4.47×10^12 /µL</td>
<td>Alb 3.6 g/dL</td>
</tr>
<tr>
<td>Hb 15.4 g/dL</td>
<td>T-bil 2.4 mg/dL</td>
</tr>
<tr>
<td>Ht 47.8 %</td>
<td>D-bil 1.1 mg/dL</td>
</tr>
<tr>
<td>Pt 19.6×10^4 /µL</td>
<td>AST 115 IU/L</td>
</tr>
<tr>
<td>ALT 56 IU/L</td>
<td>ALP 880 IU/L</td>
</tr>
<tr>
<td>CRP 1.86 mg/dL</td>
<td>γ-GTP 609 IU/L</td>
</tr>
<tr>
<td>IgG 1,736 mg/dL</td>
<td>ChE 74 IU/L</td>
</tr>
<tr>
<td>ANA (-)</td>
<td>T-cho 127 mg/dL</td>
</tr>
<tr>
<td>AMA (-)</td>
<td>TG 91 mg/dL</td>
</tr>
<tr>
<td>HBsAg (-)</td>
<td>BUN 4.7 mg/dL</td>
</tr>
<tr>
<td>HCV-Ab (-)</td>
<td>Cre 0.6 mg/dL</td>
</tr>
<tr>
<td>IgA 156 mg/dL</td>
<td>γ-GTP 156 IU/L</td>
</tr>
<tr>
<td>FDP 3.8 µg/mL</td>
<td>L DH 314 IU/L</td>
</tr>
<tr>
<td>PT% 65.5 %</td>
<td>ALP 280 IU/L</td>
</tr>
<tr>
<td>APTT 41.3 sec.</td>
<td>ChE 74 IU/L</td>
</tr>
<tr>
<td>Fibrinogen 308 mg/dL</td>
<td>γ-GTP 156 IU/L</td>
</tr>
</tbody>
</table>

**Discussion**

HPBCs originate from cystic dilatation of the extramural peribiliary glands of the bile duct located in the connective tissue of the hepatic hilum and within the larger portal tracts (7, 8). HPBCs are lined by one layer of cuboidal or columnar biliary epithelial cells and do not communicate with the lumen of the intrahepatic bile ducts (1, 9). Terada et al. reported cystic changes in the peribiliary glands in approximately 20% of autopsied livers, including systemic diseases, such as infectious and liver diseases, although the majority of conditions were identifiable only under a microscope (10). The pathogenesis of HPBC remains unclear. However, a microcirculatory disturbance in the liver is thought to be a possible pathogenic factor, as almost all HPBC patients have portal hypertension associated with cirrhosis, especially those with alcoholic liver disease (7). Matsubara et al. reported that 11 of 31 patients with HPBC ex-
On all imaging modalities, an important feature is the pres-
\[\textit{ally easy using a combination of several imaging modalities.}\]

Diagnosing HPBC is gener-
\[\textit{ory jaundice.}\]

However, we did not perform pathological examinations,
\[\textit{alcoholic liver disease or alcoholic pancreatitis, while 29 of 202 autopsy cases involving a history of heavy drink-
\[\textit{CHD}]; however, they subsequently grew in size with red wale marks and cherry red spots, as observed on hospital day 98 (C).

The pathological features of HPBCs include the develop-
\[\textit{the connection between the biliary tract and cyst cannot be distinguished. On the other hand, drip infusion cholangiography-CT (DIC-CT) is reported to be useful for differentiating these cysts from obstructive bile ducts or dilated bile ducts, such as those seen in Caroli’s disease (6, 9, 17, 18).}\]

Most cases of HPBC are clinically harmless and diag-
\[\textit{ated alcoholic liver disease or alcoholic pancreatitis, while 29 of 202 autopsy cases involving a history of heavy drinking had HPBCs (11). Moreover, portal vein thrombosis, orthotopic hepatic transplantation, cholangitis and sepsis are associated with HPBC formation (3). The present patient also suffered from decompensated alcoholic liver cirrhosis, and the HPBCs became apparent on imaging modalities soon after the onset of acute cholangitis, leading to refractory jaundice.}\]

The pathological features of HPBCs include the develop-
\[\textit{opportunistic infections due to dilatation of the peribiliary glands along larger bile ducts. This pathological feature is important for making the diagnosis of HPBC. However, we did not perform pathological examinations, such as a liver biopsy or autopsy, in the present case. Therefore, the patient was diagnosed with HPBC based on the findings of CE-CT and MRCP. Diagnosing HPBC is generally easy using a combination of several imaging modalities. On all imaging modalities, an important feature is the presence of multiple relatively small-sized cystic lesions along larger portal tracts, being more common on the left than the right intrahepatic duct (8). As for conventional methods, HPBCs consist of a tubular structure running parallel to the portal structure and/or a string of cysts simulating abnormal bile ducts on ultrasonography and CT scans (12-16). MRCP is also useful for obtaining a diagnosis of HPBC (2, 17, 18); however, the connection between the biliary tract and cyst cannot be distinguished. On the other hand, drip infusion cholangiography-CT (DIC-CT) is reported to be useful for differentiating these cysts from obstructive bile ducts or dilated bile ducts, such as those seen in Caroli’s disease (6, 9, 17, 18).}\]

Most cases of HPBC are clinically harmless and diag-
\[\textit{most cases of HPBC are clinically harmless and diagnosed incidentally on medical examinations (5, 9). Therefore, the prognosis of HPBC itself is usually good, and management is generally based on treating the underlying disease, such as cirrhosis. However, it has recently been recognized that HPBC can be harmful in some cases. For ex-
doscopic drainage. The prognosis of HPBC patients with HPBCs was so severe that it was impossible to perform en-
case, the compression of the bilateral hepatic ducts by the
16% had biliary infections, such as ascending cholangi-
an average observation period of approximately four years and
an increase in the size and/or number of lesions during an
38 Japanese HPBC patients and found that 41% exhibited
to ours involving obstructive jaundice (6, 14, 19, 20).
HPBCs usually present as multiple cystic lesions along the
bile ducts, with consecutive cysts tending to form relatively
long segments. Therefore, it is difficult to treat HPBCs com-
pressing the original bile passage, thus inducing ascending cholangitis and/or obstructive jaundice, effectively with
either endoscopic or percutaneous drainage. In the present
case, the compression of the bilateral hepatic ducts by the
HPBCs was so severe that it was impossible to perform en-
doscopic drainage. The prognosis of HPBC patients with
these hepatobiliary diseases is very poor.
Portal hypertension is defined as an increase in the porto-
systemic pressure gradient in any portion of the portal ve-
nous system. Portal hypertension results from pre-hepatic
(e.g., portal or splenic vein thrombosis), hepatic (e.g., cir-
rhosis) and post-hepatic abnormalities (e.g., Budd-Chiari
syndrome), with cirrhosis being the most common cause.
Esophageal varices are one pathological factor related to the
development of portal hypertension and their formation is
closely associated with a hepatic venous pressure gradient
above 12 mmHg (21). The red color sign and variceal size
(medium to large grade) on endoscopy, severity of liver dys-
function and ascites are important risk factors for variceal
bleeding (22, 23). Although the esophageal varices observed
in this case had been treated with endoscopic sclerotherapy
seven years earlier and remained small and without signs of
rupture until the 55th hospital day, they subsequently grew
to a risky size within a very short period of time (approximately six weeks). There are no reports regarding the rela-
tionship between the presence of esophageal varices and
HPBCs. However, HPBCs are closely aligned with and can
easily compress the portal veins, thereby inducing portal hy-
pertension. In other words, HPBCs may be a causative fac-
tor for pre-hepatic portal hypertension. In addition, the pres-
ence of HPBCs and portal hypertension may have a poten-
tial synergistic effect, thus resulting in mutually accelerated
progression.
In conclusion, we herein reported a case of HPBCs that
grew rapidly and induced progressive refractory obstructive
jaundice and esophageal varices. Early treatment for ob-
structive jaundice and portal hypertension should be consid-
ered in patients with rapidly progressive HPBCs.

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

References
1. Nakamura Y, Karumaya H, Ohta G. Multiple cysts in the hepatic
hilum and their pathogenesis: a suggestion of periductal gland ori-

Figure 4. On the 55th hospital day, the ascites had decreased, and there were no lesions in the liver (A). On the 93rd hospital day, many tiny cysts closely localized along the intrahepatic portal tracts were noted around both sides of the hepatic lobes (B, arrows).

Figure 5. MRCP performed on the 93rd hospital day showed multiple cystic lesions presenting as a string of bead-like structures along the bilateral hepatic ducts and first branches of the bile ducts (A, arrows), although the image was blurred due to a large amount of ascites. The peripheral branches of the bile ducts were slightly dilated, and the common bile ducts were not visible (A, arrowheads). ERCP performed on the 95th hospital day. (B) The bilateral hepatic ducts were completely occluded by compression from the HPBCs, and the intrahepatic bile ducts were not contrasted (B, arrows). It was impossible to insert a guidewire.