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Editorial

Hepatic peribiliary cysts: clinically harmless disease with potential risk due to gradual increase in size and number

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Hepatic peribiliary cysts diagnosed by magnetic resonance cholangiography
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Peribiliary cysts, first described in 1984 by Nakanuma et al.,[1] were later confirmed by the same group to be cystic dilatations of the intrahepatic extramural peribiliary glands located on both sides of the intrahepatic bile ducts. The cysts are round or ovoid with thin walls, and are detected exclusively in the hepatic hilum and along the larger portal tract, where the periductal glands exist. Most peribiliary cysts are small, their diameters ranging from 0.2 to 2.5 cm.[2]

Both the extramural glands and their conduits show luminal dilatation of varying degrees. This finding itself is not uncommon; about 20% of consecutive autopsy livers showed cystic dilatation of the peribiliary glands, although a majority of cases are identifiable only under a microscope.[3] Some glands dilate to a grossly recognizable size, and are preferentially found along marginal portal tracts facing the hepatic parenchyma. The cysts are usually multiple and assume unilocular, expanded, round, and thin-walled structures containing serous fluid.[1] Histologically, dilated cysts are lined by a cuboidal-to-columnar epithelia (some are mucin-positive) surrounded by thin fibrous tissues, and they are admixed with nondilated or mildly dilated extramural glands with conduits.[1,3,4] Disturbed portal venous blood flow is thought to be essential for the formation of cysts.[1] Approximately 10% of these histologically identifiable peribiliary cysts are detectable by imaging.[5] Hepatic peribiliary cysts are generally diagnosed easily with a combination of several imaging modalities. Among the various kinds of hepatic cysts, hepatic peribiliary cysts are characterized by their peculiar distribution and small size.[5]

On ultrasound (US) scans, the cysts are detected within the echogenic larger portal tract, or they may appear as an echoic area adjacent to or connecting with the portal vein (hilar multicystic echo complex around the portal venous branches near the hepatic hilum).[6]

On computed tomography (CT) scans, hepatic peribiliary cysts assume a discrete appearance; that of a tubular structure running parallel to the portal structure, or a string of cysts that simulate abnormal bile ducts.[6–9] These cysts, observed exclusively in the hepatic hilum, are distributed along the larger portal vein, or they may occasionally be found in both the hilum and portal vein.[5] Drip infusion cholangiography-CT (DIC-CT) is reportedly the most favorable technique for differentiating these cysts from dilated bile ducts, such as those seen in Calori's disease, or obstructive bile ducts.

Recently, magnetic resonance cholangiopancreatography (MRCP) has been reported to be useful in the diagnosis of hepatic peribiliary cysts.[10–12] MRCP clearly portrays multiple cysts as a string of bead-like structures or a foamy fringe along the hepatic hilum or larger bile ducts. Although a connection with the biliary tract cannot be diagnosed by MRCP, this modality, when the most advanced MR device is employed, shows high sensitivity in depicting cystic lesions around the hepatic hilum, with three-dimensional perspectives in association with the bile duct, the sensitivity being superior to that of CT.

Previous reports show the incidence of peribiliary cysts to be higher in patients with chronic liver diseases such as liver cirrhosis, hepatocellular carcinoma, idiopathic portal hypertension, portal venous thrombotic obstruction, intrahepatic cholangitis, obstructive jaundice, systemic infection or septicemia; and autosomal-dominant polycystic kidney disease.[8,9,13] Therefore, two etiologic mechanisms have been considered to be involved in the formation of peribiliary cysts: one associated with inflammation or circulatory disturbance, leading to glandular obstruction, and the other associated with hereditary factors.[1,3,13]

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Peribiliary cysts have usually been considered to be clinically harmless. However, in recent years, several authors have noted that hepatic peribiliary cysts gradually increase in size and number. Terayama et al.[14] found a gradual enlargement in size and an increase in the number of cysts in three of six patients with cirrhotic liver. Hoshiba et al.[15] have noted increases in the size and number of cysts in one patient with cirrhotic liver, and suggest that peribiliary cysts in liver cirrhosis increase in size and number as the cirrhosis progresses. Ahmadi et al.[16] have, further, demonstrated that peribiliary cysts increase in size (from less than 10 mm to more than 38 mm) and number in a patient with cirrhosis and hepatocellular carcinoma. In this issue of the *Journal of Gastroenterology*, Motoo et al.,[10] using endoscopic retrograde cholangiopancreatography (ERCP), showed bile duct stenosis caused by the extraluminal compression of enlarged peribiliary cysts, although, clinically, obstructive jaundice was not observed. Similarly, Fujioka et al.[4] reported three patients with peribiliary cysts, and observed, that, pathologically, in two patients, the biliary cysts compressed the original bile passage. They speculated that, had these patients lived longer, obstructive jaundice would have developed.

Actually, in the patients reported earlier, the peribiliary cysts eventually presented as obstructive jaundice,[1,17,18] causing death in two patients, although this is an extremely rare outcome. Similar to the findings in the patient reported by Fujioka et al.,[4] clinical findings in the patient reported by Motoo et al.,[10] such as jaundice and the laboratory data, were not as prominent when compared with the severity of stenosis of the bile duct demonstrated on the imaging study. Based on these reports, it is speculated that only a few patients present with complete obstruction because of extraluminal compression by the peribiliary cysts. However, as this is a progressive disease, the risk of obstructive jaundice should be kept in mind in the clinical follow-up of such patients.

Clinically, hepatic peribiliary cysts could present with stenosis of the large hepatic duct or common bile duct on ERCP or MRCP, leading rarely, to obstructive jaundice. In addition, as noted earlier, peribiliary cysts often increase in size and number, suggesting this disease state is progressive in nature. Hepatic peribiliary cysts can be misdiagnosed as cholangiocellular carcinoma[18] or as localized primary sclerosing cholangitis.[19] Usually, hepatic peribiliary cysts have been thought to be a clinically harmless disease entity; however, they may gradually grow in size and number, resulting in obstructive jaundice. Clinicians should be aware of the possible harmful outcome, which eventually requires medical or surgical intervention. Furthermore, of the 1000 consecutive autopsy cases studied, 5 well differentiated adenocarcinomas and 8 atypical hyperplasias of intramural and/or extramural peribiliary gland origin were incidentally diagnosed.[2] The incidence of biliary cystadenoma or cystadenocarcinoma that arises from the peribiliary glands has not been determined as yet. In other words, it remains unclear what percentage of cholangiocarcinomas arise from the peribiliary glands, and which carcinogenic processes are operating in these cholangiocarcinomas.[20] Although an association between cystic dilatation and malignant change in the intrahepatic peribiliary glands has not yet been reported, an association of these two disease conditions should also be borne in mind during the clinical follow-up of these patients.

In summary, clinicians should pay close attention to hepatic biliary cysts, and they should know that this disease can be differentiated from other similar abnormal conditions, such as biliary dilatation, solitary simple cysts, and periportal lymphomas, by the use of US, CT, DIC-CT, or MRCP. In addition, clinicians should take note that a gradual increase in the size and number of the cysts over time is a fairly common developmental process in this disease. Furthermore, it should also be borne in mind that this disease entity is, although only rarely, harmful, when compression of the biliary tract becomes complete, resulting in obstructive jaundice. Therefore, careful follow-up studies by imaging are warranted. However, the making of an accurate preoperative diagnosis is extremely difficult when obstructive jaundice is the first manifestation in patients with peribiliary cysts without follow-up studies.

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