—Case Reports—

Surgical Resection of Cystic Intraductal Papillary Adenocarcinoma of the Bile Duct: Report of a Case

Tomohiro Shimoda[1,2], Hiroshi Yoshida[1,2], Atsushi Hirakata[1,2], Hiroshi Makino[1,2], Tadashi Yokoyama[1,2], Hiroshi Maruyama[1,2], Junji Ueda[1], Masataka Tanno[3], Zenya Naito[4] and Eiji Uchida[1]

[1]Surgery for Organ Function and Biological Regulation, Graduate School of Medicine, Nippon Medical School
[2]Department of Surgery, Nippon Medical School Tama Nagayama Hospital
[3]Department of Pathology, Nippon Medical School Tama Nagayama Hospital
[4]Department of Pathology, Nippon Medical School

Abstract

We describe a cystic intraductal papillary neoplasm of bile duct (IPNB) of adenocarcinoma treated with surgical resection. An 82-year-old man was admitted to our hospital because of distension of the right upper quadrant of the abdomen. On admission, a huge nontender mass was palpated in the right upper abdomen. Initial laboratory tests revealed the following serum values: aspartate aminotransferase, 123 IU/L; alanine aminotransferase, 113 IU/L; alkaline phosphatase, 376 IU/L; bilirubin, 1.6 mg/dL; alpha-fetoprotein, 7.4 ng/mL; CA19-9, 39.8 U/mL; carcinoembryonic antigen, 4.1 ng/mL; and Duke pancreatic monoclonal antigen type 2, 200 U/mL. Abdominal ultrasonography revealed an anechoic mass with an elevated papillary lesion in the right paramedian section. Computed tomography showed a low-density hepatic lesion, measuring 12 × 10 cm, with thick, irregular walls. A T2-weighted magnetic resonance scan showed mural nodules with signal intensity higher than that of the liver. The cystic lesion was suspected to be a cystic IPNB, but we could not determine whether it was a carcinoma. We performed extensive right paramedian sectionectomy and cholecystectomy. The resected multilocular tumor was filled with a yellow fluid, and the cut surface showed multiple, yellowish papillary nodules lining the cystic wall. On histologic examination, the neoplastic biliary epithelium showed papillary growth in the dilated lumen. Papillary and micropapillary lesions exhibited cellular atypia: nuclear enlargement and hyperchromasia, mutilayering, and mitosis. Ovarian-like stroma was not detected. The tumor was diagnosed as an IPNB (carcinoma in situ lesion). These lesions had expanded into several intrabiliary ducts. No recurrence has been detected 2 year after operation.
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Key words: intraductal papillary neoplasm, adenocarcinoma, bile duct, surgical resection

Correspondence to Hiroshi Yoshida, MD, Department of Surgery, Nippon Medical School Tama Nagayama Hospital, 1–7–1 Nagayama, Tama, Tokyo 206–8512, Japan
E-mail: hiroshiy@nms.ac.jp
Journal Website (http://www.nms.ac.jp/jnms/)

Introduction

Among the various kinds of cystic lesions that can involve the liver, simple hepatic cysts are the most common benign nonneoplastic lesions and are present in up to 2.5% of the general population. In contrast, biliary cystic neoplasms are rare and account for less than 5% of all intrahepatic cystic lesions arising from the bile duct[1–4].

Cystic tumors arising from the biliary epithelium were previously called biliary cystadenocarcinomas[5] or cystadenomas [6]. Recently, intrahepatic cholangiocarcinomas (ICCs) have been classified as conventional ICCs (bile duct ICCs), bile ductular ICCs, intraductal neoplasms, and rare variants[7]. Intraductal neoplasms of the bile duct are classified into 3 types: intraductal papillary neoplasm of bile duct (IPNB), intraductal tubular neoplasm of bile duct, and intraductal superficial spreading type[7].

We describe a cystic IPNB of adenocarcinoma treated with surgical resection.

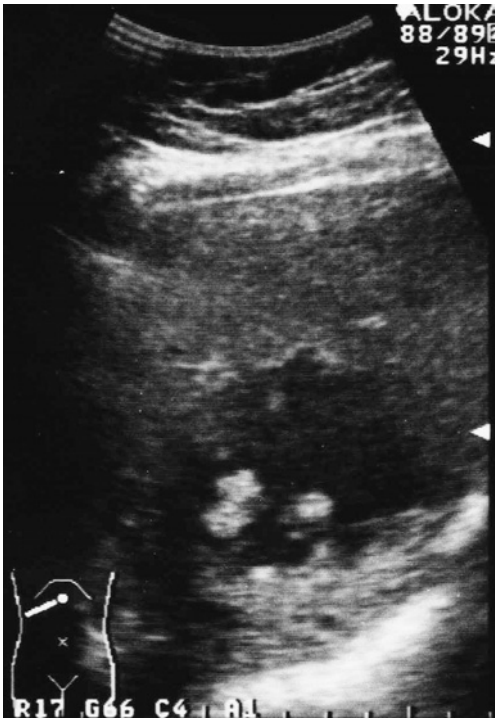

Fig. 1 Abdominal US reveals a unilocular oval mass with thick walls. The mass measured 12×10 cm and was located in the left hepatic lobe.

Case Report

The patient was an 82-year-old man with a 15-year history of hypertension. He was admitted to our hospital because of distension of the right upper quadrant of the abdomen. On admission, a huge nontender mass was palpated in the right upper quadrant. Initial laboratory tests revealed the following values: serum aspartate aminotransferase, 123 IU/L (normal, <38 IU/L); serum alanine aminotransferase, 113 IU/L (normal, <44 IU/L); serum serum alkaline phosphatase, 376 IU/L (normal 104 to 338 IU/L); serum lactic dehydrogenase, 217 IU/L (normal, 180 to 460 IU/L); serum gamma glutamic transpeptidase, 432 IU/L (normal, 16 to 73 IU/L); total serum bilirubin, 1.6 mg/dL (normal, 0.2 to 1.2 mg/dL); direct serum bilirubin, 0.7 mg/dL (normal, <0.4 mg/dL); serum hyaluronic acid, 71 ng/dL (normal, <50 ng/dL); prothrombin time, 68% (normal, 80% to 100%); and serum fibrinogen, 536 mg/dL (normal, 200 to 400 mg/dL). The serum concentration of PIVKA (proteins induced by vitamin k antagonism or absence) 2 was 20 mAU/mL (normal, <40 mAU/mL), that of alpha-fetoprotein was 7.4 ng/mL (normal, <6.92 ng/mL), that of CA19-9 was 39.8 U/mL (normal, <35.4 U/mL), that of carcinoembryonic antigen (CEA) was 4.1 ng/mL (normal, <4.75 ng/mL), and that of Duke pancreatic monoclonal antigen type 2 (DUPAN-2) was 200 U/mL (normal, <150 U/mL). The indocyanine green clearance rate at 15 minutes was 9.8% (normal, < 10%). Examinations for serum surface antigens of hepatitis B and antibodies against hepatitis C virus were negative.

Abdominal ultrasonography (US) revealed an anechoic mass with an elevated papillary lesion. The mass measured 12 × 10 cm and was located in the right paramedian section of the liver (**Fig. 1**). Computed tomography (CT) showed a low-density hepatic lesion, measuring 12 × 10 cm, with thick, irregular walls. Part of mass was slightly enhanced with contrast medium (**Fig. 2**).

A T2-weighted magnetic resonance scan showed mural nodules with signal intensity higher than that of the liver (**Fig. 3**). Drip infusion cholangiography showed no connection between the mass and the

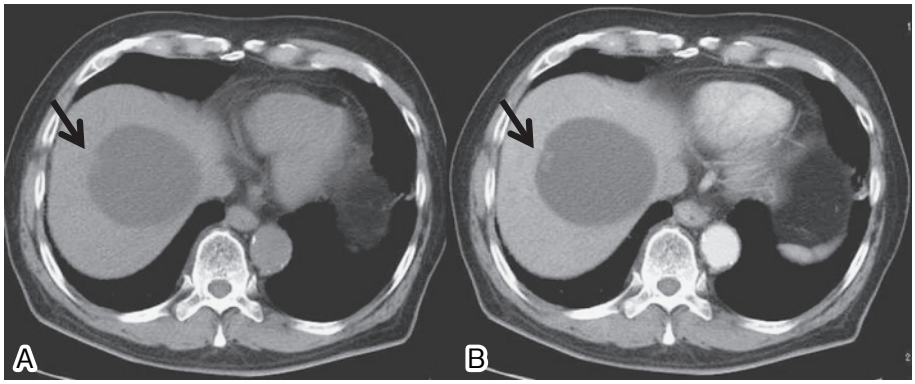

Fig. 2 Computed tomography shows a low-density hepatic lesion, measuring 12×10 cm, with thick, irregular walls and septa **(arrow)**. A part of mass was a slightly enhanced with contrast medium (A: plain, B: enhanced).

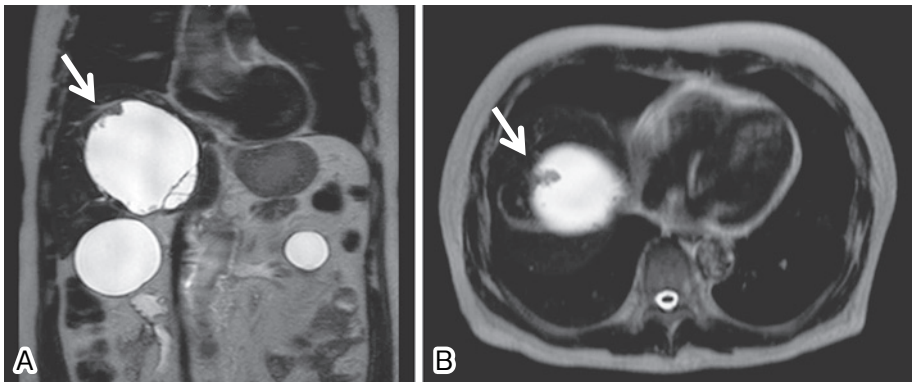

Fig. 3 A T2-weighted magnetic resonance image shows mural nodules **(white arrow)** with signal intensity higher than that of the liver (A: coronal plane, B: horizontal plane).

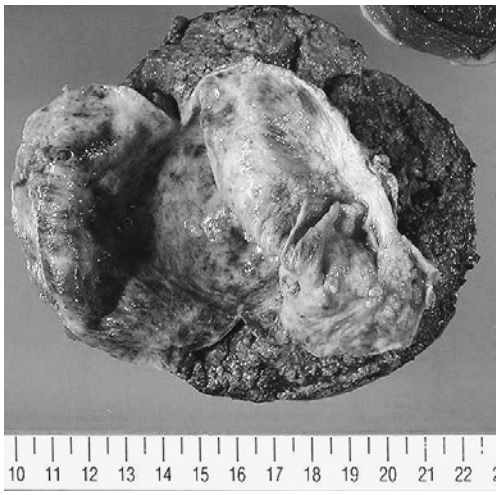

Fig. 4 The resected multilocular tumor was filled with a yellow fluid, and the cut surface showed multiple, yellowish papillary nodules lining the cystic wall.

intrahepatic bile ducts. The cystic lesion was suspected of being a cystic IPNB, but we could not determine whether it was a carcinoma. Fine-needle aspiration could not be performed, because peritoneal carcinomatosis can develop after aspiration of a cystic IPNB carcinoma. After informed consent was obtained we performed liver resection, rather than enucleation, to treat the cystic IPNB.

A large tumor with a smooth surface was present in the right paramedian section. The patient underwent extensive right paramedian sectionectomy and cholecystectomy. On macroscopic examination, the resected multilocular tumor was filled with a yellow fluid, and the cut surface showed multiple, yellowish papillary nodules lining the cystic wall **(Fig. 4)**. On histologic examination, the neoplastic biliary epithelium showed papillary

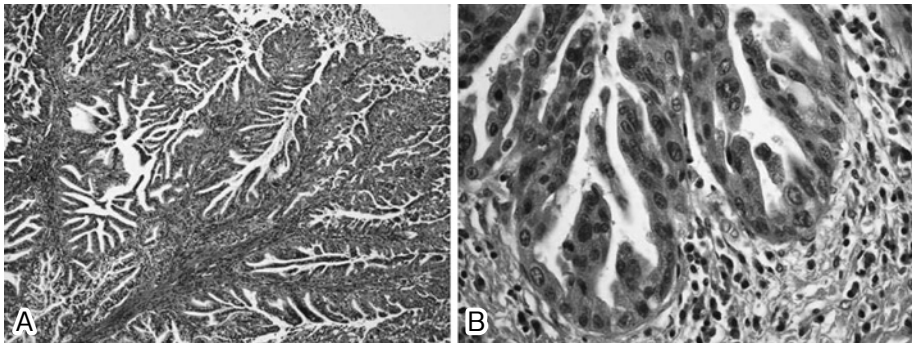

Fig. 5 The neoplastic biliary epithelium shows papillary growth in the dilated lumen (A: hematoxylin and eosin, ×100). Papillary and micropapillary lesions exhibit cellular atypia as nuclear enlargement and hyperchromasia, mutilayering, and mitosis. Ovarian-like stroma is not detected (B: hematoxylin and eosin, ×600). The tumor was diagnosed as an intraductal papillary neoplasm (carcinoma in situ lesion) of bile duct. These lesions expanded into several intrabiliary ducts.

growth in the dilated lumen. The communication between the tumor and the bile duct was unclear. Papillary and micropapillary lesions exhibited cellular atypia : nuclear enlargement and hyperchromasia, mutilayering, and mitosis. These features are not present in metastatic adenocarcinoma. Immunostaining of the tumor for CEA and CA19-9 was negative. Ovarian-like stroma was not detected, so this tumor differed from biliary mucinous cystic neoplasm. The tumor was diagnosed as an IPNB (carcinoma in situ lesion). These lesions expanded into several intrabiliary ducts (**Fig. 5**). The concentrations of CEA and CA19-9 in the cyst contents were 4,744 IU/L and 6,400,000 IU/L, respectively. No recurrence has been detected 2 year after operation.

Discussion

The prevalence of congenital hepatic cysts in the general population is estimated to be 2% to 4%[8]. Most benign, nonparasitic hepatic cysts are asymptomatic, but complications can occur. Documented complications include obstructive jaundice[9,10], rupture[11–13], intracystic hemorrhage[13–16], and infection[17–19].

Cystic tumors arising from the biliary epithelium were previously called biliary cystadenocarcinomas[5] or cystadenomas[6]. In 1943, Willis[20] was the first to report a case of hepatic cystadenocarcinoma. The wider use of imaging techniques, such as US and CT, has increased the number of cases reported. However, these neoplasms still represent less than 5% of all solitary nonparasitic cysts of biliary origin[21].

A new category, IPNB, is now being accepted as a counterpart of intraductal papillary mucinous neoplasm of the pancreas[22]. IPNB is classified into a papillomatosis or papilloma type, an intraductal growing type, a mucin-producing type, and a cystic type[23,24]. This case was diagnosed as a cystic IPNB, intraductal growing type, of adenocarcinoma. Biliary mucinous cystic neoplasm is characterized by an ovarian-like stroma in the wall of the cystic neoplasm[23,24]. This type of neoplasm usually does not communicate with the bile duct lumen.

Symptoms vary and include epigastric pain or discomfort, a palpable abdominal mass, jaundice, and vomiting. Some patients are asymptomatic, with lesions being found incidentally during diagnostic radiologic procedures or surgical exploration for unrelated conditions. In our patient, the tumor was detected owing to distention of the right upper quadrant.

Diagnostic-imaging techniques, such as CT and US, are useful for distinguishing simple cysts from cystic IPNB, which has characteristic features. The presence of a solid, nodular, multilocular cystic mass with coarse calcifications along the walls or septa strongly suggests a cystic IPNB[25]. Despite improvements in imaging techniques, differentiating a carcinoma from other lesions is often difficult with preoperative and intraoperative radiologic

examinations. Although fine-needle aspiration and needle biopsy are useful diagnostic procedures, they should not be performed for differential diagnosis, because peritoneal carcinomatosis can develop after the biopsy of a carcinoma[26].

Woods[27] has proposed that the cystic IPNB of adenocarcinoma develops by malignant transformation of the epithelium of a benign adenoma. Further indirect support for malignant transformation is provided by a histochemical study showing that the expression of tumor-associated antigens, such as CA19-9, CEA, early membrane antigen, and DUPAN-2, differs between adenoma and adenocarcinoma[28]. In our patient, serum concentrations of CA19-9 and DUPAN-2 were slightly elevated, but the serum concentration of CEA was not elevated.

There is a general consensus that the cystic IPNB of adenocarcinoma should be completely removed through either enucleation or liver resection because incomplete resection is associated with recurrence rates as high as 90%[29–31]. Chemotherapy might be performed for patients who are not candidates for radical excision because of tumor recurrence or metastasis[32]. Satisfactory results have been reported with enucleation along the dissection plane between the tumor and liver tissue[29,33,34]. Enucleation, which allows maximum preservation of hepatic parenchyma, is an appropriate procedure for benign lesions. One concern is that a cystic IPNB of adenocarcinoma can harbor a malignancy that might be missed on preoperative imaging studies. In such cases, enucleation would be inappropriate, even for patients with noninvasive carcinoma[35]; therefore, the preferred procedure is hepatectomy with negative surgical margins.

In conclusion, the cystic IPNB of adenocarcinoma lacks typical symptoms and specific characteristics on imaging and laboratory examinations. A definitive diagnosis often depends on biopsy or postoperative pathologic examination. Preoperative definitive diagnosis with US and CT remains difficult. When the diagnosis is unclear, surgical exploration of the lesion is indicated, and biopsy should be performed. The procedure of choice for cystic IPNB of adenocarcinoma is radical resection, whereas palliative procedures are justified only in patients with poor general condition or poor liver function.

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