A Case of Pancreatic Serous Cystadenoma Penetrating Bile Duct Requiring Differentiation from Malignancy

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A 67-year-old man was admitted to our hospital with jaundice. A closer examination revealed that he had obstructive jaundice due to bile duct obstruction caused by a multifocal cystic tumor of the pancreas. Endoscopic retrograde cholangiopancreatography (ERCP) revealed stenosis of the distal bile duct and leakage of contrast medium into the pancreatic cyst. Pancreaticoduodenectomy was performed, and a pinhole fistula was found connecting the cyst and the bile duct. Histological examination led to the diagnosis of serous cystadenoma (SCA). Herein, we report a rare case of SCA with obstructive jaundice and penetration of the bile duct, which was treated by radical resection.

Key words: serous cystadenoma, obstructive jaundice, bile duct penetration

INTRODUCTION

Serous cystadenoma (SCA) is a relatively rare tumor that predominantly affects middle-aged women and accounts for 1–2% of all pancreatic tumors. Most cases have a benign course, but some are reportedly cancerous [1]. The details of its pathogenesis are poorly understood. There have been no reports of penetrating to the bile duct by SCA, a benign disease. Here we report a case in which malignancy could not be ruled out based on clinical features, such as penetration and jaundice, and the pathological diagnosis post-resection was SCA.

CASE REPORT

The patient was a 67-year-old man with abnormal liver (hepatic) dysfunction. He had a medical history of aortic regurgitation (post-prosthetic valve replacement), alcoholic liver dysfunction, hypertension, diabetes mellitus, and hyperuricemia. His current medications included aspirin, lansoprazole, ursodeoxycholic acid, trichloromethiazide, azilsartan, sitagliptin phosphate, glimepiride, and allopurinol. He was a heavy drinker (alcohol 200 g/day) and smoker (20 cigarettes/day). His family history included an older brother with hepatocellular carcinoma. He reported no history of allergies.

Physical findings: The patient had no fever, and his vital signs were normal. His abdominal wall was soft and flat, with no pain. His eyes and skin were markedly affected by jaundice.

Laboratory data: Results are shown in Table 1. His total bilirubin level was 20.6 mg/dL and direct bilirubin level was 15.9 mg/dL, indicating elevated levels of hepatobiliary enzymes with a predominance of the direct type. The tumor markers levels were within the normal range.

Abdominal ultrasonography (US): A 25 x 25 mm, well-defined, internally heterogeneous, hypoechoic mass with mild dilatation of the caudal pancreatic duct was observed in the pancreatic uncinate process (Fig. 1). The scattered hypoechoic areas inside the mass appeared to be microcysts, and cystic components of various sizes were mixed at the mass margin. Color Doppler showed no obvious increase in the blood flow signal in the mass. The common bile duct was obstructed by the mass and the intrahepatic bile duct was dilated.

Magnetic Resonance Cholangiopancreatography (MRCP): A 38 x 26 mm multifocal cystic lesion in the pancreatic hook area (Fig. 2). The distal bile duct was narrowed by the cystic lesions.

Endoscopic retrograde cholangiopancreatography (ERCP) was performed on the 2nd day of hospitalization. There was no obvious abnormality in the papillary findings. Pancreatography revealed no dilatation of the main pancreatic duct or evidence of cyst trafficking. Cholangiography revealed smooth stenosis of the distal bile duct, which was interpreted as tumor-induced compression, with mild dilatation of the common and intrahepatic bile ducts. The continuous injection of contrast medium into the cyst was observed from a part of the stenosis (Fig. 3). No obvious malignant findings were observed after carrying out bile cytology and brush-abrasion cytology. A direct biopsy of the stenosis was not performed because of the possibility of bile duct penetration, and

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Table 1 Laboratory test results of the patient

Hematology		Biochemistry	
White blood cells (/μL)	8200	AST (U/L)	44
Hemoglobin (g/dL)	13.2	ALT (U/L)	49
Hematocrit (%)	39.6	LDH (U/L)	151
Platelets (× 10^4/μL)	22.3	ALP (U/L)	200
		γ-GTP (U/L)	405
		BUN (mg/dL)	30
		Creatinine (mg/dL)	1.64
		Albumin (g/dL)	3.3
		Total bilirubin (mg/dL)	20.6
Tumor markers		Direct bilirubin (mg/dL)	15.9
CEA (ng/mL)	4.3	Sodium (mmol/L)	135
CA19-9 (U/mL)	1.0	Potassium (mmol/L)	3.6
		CRP (mg/dL)	2.35

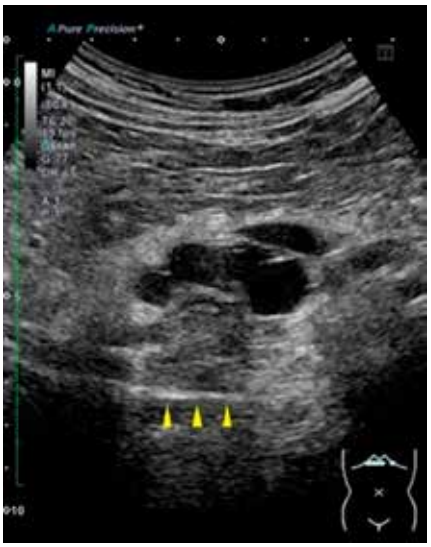

Fig. 1 A 25 x 25 mm hypoechoic mass was observed in the pancreatic hook area (arrowhead). There was a cluster of small cysts inside the mass, and cysts larger than 10 mm were scattered around the mass.

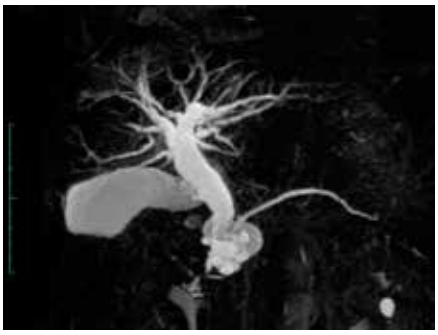

Fig. 2 Radiograph from Magnetic Resonance Cholangiopancreatography (MRCP) examination. A 38 x 26 mm large multilocular cystic lesion was observed in the pancreatic hook. The common bile duct was narrowed by the mass.

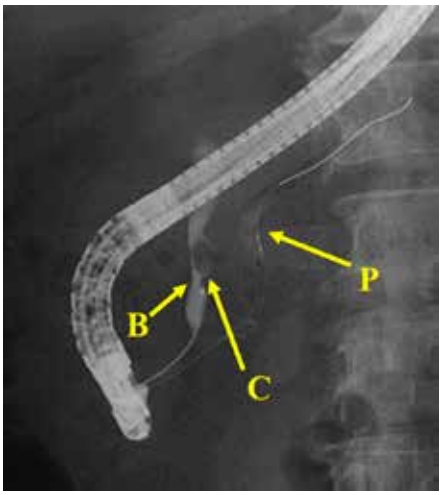

Fig. 3 Image acquired from an endoscopic retrograde cholangiopancreatography (ERCP) examination. Cholangiography showed a smooth stenosis of the distal bile duct. When the contrast agent was pressurized into the bile duct, a small amount of contrast flowing into the cyst. This suggested the formation of a fistula.
B; bile duct, C; cyst, P; pancreatic duct

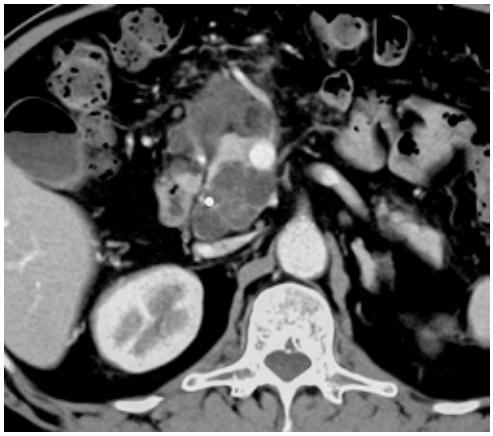

Fig. 4 Radiograph from an abdominal dynamic computed tomography (CT) scan. A > 40 mm multifocal cystic lesion was observed in the pancreatic head and a full area with a pale contrast effect was seen inside.

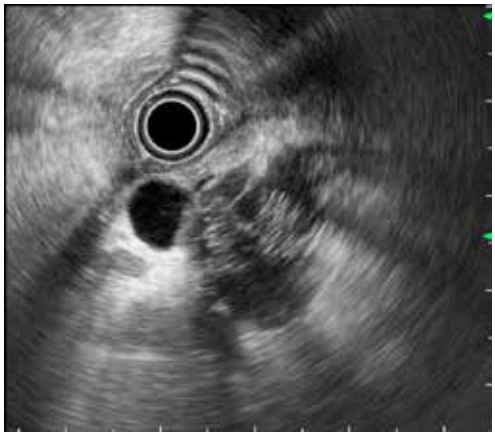

Fig. 5 Image acquired from ultrasonography endoscopy. A large multifocal cystic lesion was observed in the pancreatic head and a cluster of small cysts was seen in the center of the tumor.

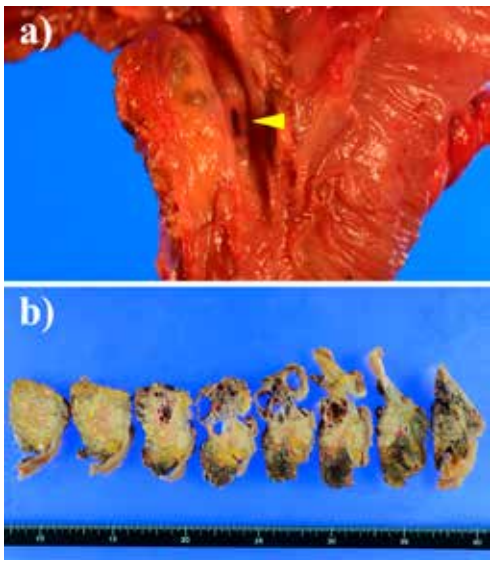

Fig. 6 Gross findings of the resected specimen. a) Pinhole fistula formation in the distal bile duct (arrowhead). b) Split view after formalin fixation. Small cysts and large cysts are mixed and clustered.

the procedure was terminated after biliary stent placement. Since the renal dysfunction was ameliorated by supplemental fluid administration, a dynamic CT scan of the abdomen was performed on the 5th day of hospitalization. A multifocal cystic lesion measuring more than 40 mm was observed in the pancreatic head, and a well-developed area with a pale contrast effect was observed at the center of the tumor (Fig. 4). A small calcified lesion was also observed in the enhancement area. Endoscopic ultrasound (EUS) was performed on the 11th day of hospitalization. The tumor in the pancreatic head was visible as a large multifocal cystic lesion, in the center of which a cluster of small cysts was observed (Fig. 5). EUS revealed no obvious increase in blood flow signals inside the tumor. The patient was treated conservatively and discharged from the hospital on the 19th day after showing improvement in hepatobiliary enzymes and relief from the pancreatitis after ERCP.

However, since the patient had bile duct obstruction and possible bile duct penetration due to bile duct invasion could not be ruled out, serous cystadenocarcinoma (SCAC) or intraductal papillary mucinous carcinoma (IPMC) were also considered. Therefore, a pancreaticoduodenectomy was performed about one month later.

Surgical findings: A laparotomy was performed through a median upper abdominal incision. A cystic lesion was observed in the pancreatic head, and a subtotal stomach preserving pancreaticoduodenectomy was performed. During surgery, there was no cancer cells (tissues) seen at the stump of the pancreas in the frozen section. The reconstruction was performed using the modified Child method. A choledocho-jejunostomy was performed intermittently on the posterior wall and continuously on the anterior wall. The pancreatic duct was anastomosed to the jejunal mucous membrane using the modified Blumgart method. A 5-Fr lost stent was indwelled in the pancreatic duct, and a closed suction drain was inserted at the back of the anastomosis between the pancreatic duct and the jejunum. A gastrojejunostomy was performed end-to side using Albert–Lembert anastomosis. Moderate inflammation and adhesions made the dissection difficult; however,

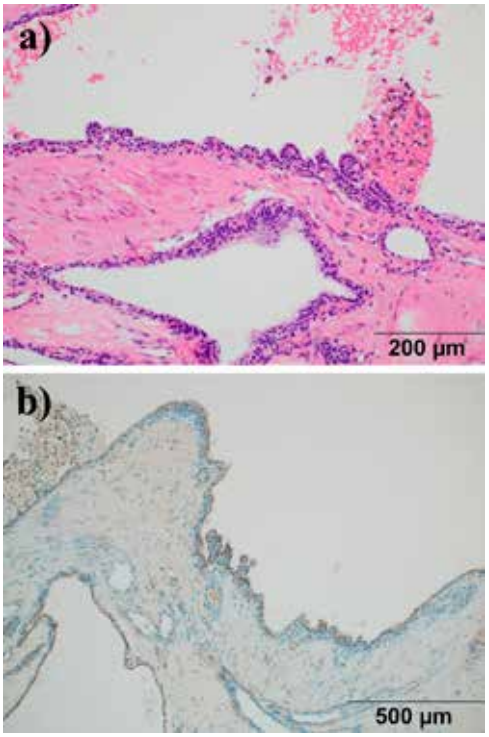

Fig. 7 Histopathological findings. a) In hematoxylin-eosin stain, nuclei were small, uniform and poorly atypical. b) Immunostaining of MUC-6 were diffusely positive.

the surgery was completed without complications. The surgical duration was 276 min, and the blood loss was 1220 mL. No blood transfusions were required. No major postoperative complications were reported, and the patient was discharged within 11 days.

Gross findings of the resected specimen: Pinhole-like fistula formation with cystic traffic was observed in the distal bile duct (Fig. 6).

Histopathological findings: The tumor was lined by small round nuclei and pale, glycogen-rich cytoplasm, and was in close contact with the bile ducts. The tumor cells were strongly positive for periodic acid–Schiff (PAS) staining and negative for PAS staining after diastase treatment. Immunostaining was positive for Neuron specific enolase (NSE), MUC1 was focally positive, and MUC-6 and CAM5.2 were diffusely positive, suggesting a histologically mixed type of SCA (Fig. 7). There was no direct invasion of tumor cells into the bile ducts. There was no direct invasion of tumor cells into the bile ducts.

DISCUSSION

SCA was first described by Compagno and Hodgkinson in 1978 [2, 3]. Although SCA is relatively rare, the possibility of its accidental detection has increased with the development of diagnostic imaging and widespread use of medical screening. Until recently, SCA was considered to be a slow-growing tumor with few symptoms, and therefore, it was usually considered to be amenable to observation. However, SCA can reportedly become malignant. The malignant transformation rate of asymptomatic lesions is estimated to be 1–3% [4, 5]. Most cases of malignant transformation could not be diagnosed based on preoperative histological examination alone. SCAC is diagnosed by the postoperative evaluation of resected specimens and by the clinical picture indicating malignancy, such as metastasis and invasion [6]. In the analysis of more than 100 patients with SCA, resection was recommended for those with symptoms attributable to the tumor, those in whom the possibility of a mucinous or other malignancy could not be readily excluded, and those with SCAs of a maximum diameter ≥ 4 cm [7]. In another previous report, locally aggressive behavior was indicative of increased proliferative ability and malignant potential [8]. In examining 35 patients with SCAC, 10 patients had distant metastases and 20 patients had locally advanced findings [6]. In the case of our patient, the size was less than 4 cm, but the clinical findings of perforation and jaundice, which were suggestive of local invasion, led to surgery.

A search in PubMed using the keywords “pancreatic serous cystadenoma” and “penetration” or “perforation” revealed no previous reports of SCA forming a fistula. Hence, the present case represents an extremely valuable description of this rare condition.

Intraductal papillary mucinous neoplasm (IPMN), a cystic tumor of the pancreas, is known to cause penetration into the surrounding organs. The probability of having a penetration is reported to be 1.9% to 6.6% in patients with IPMN [9, 10]. The mechanism of fistula formation caused by IPMN remains controversial. Several theories have been proposed regarding the pathogenesis of fistula formation, such as direct invasion of tumor cells, mechanical penetration, autodigestion by pancreatic enzymes, increased intraductal pressure due to elevated mucus production, and inflammatory changes [9, 11, 12]. In the case of our patient, the pathological findings showed no strong atypia or invasion into surrounding organs suggestive of malignancy. We speculated that the bile duct wall became fragile and perforated due to the increase in

intracystic pressure caused by the increase in SCA mass and the increased inflammation caused by the cholangitis.

SCA is a rare pancreatic tumor, and the details of its pathogenesis are poorly understood. Here, we described a case of pancreatic SCA penetrating to the bile duct that required differentiation from malignancy.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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