

A Case of Serous Cystadenoma Communicating with a Stenotic Santorini's Duct and a Dilated Main Pancreatic Duct

Hiroyuki Matsubayashi¹, Yurika Oka², Takaaki Ito², Katsuhiko Uesaka², Keiko Sasaki³, Hiroyuki Ono¹

Division of 1) Endoscopy,
2) Hepato-Biliary-Pancreatic
Surgery, and
3) Pathology,
Shizuoka Cancer Center,
Nagaizumi, Suntogun,
Shizuoka, 411-8777, Japan

Address for correspondence:
Hiroyuki Matsubayashi
Division of Endoscopy,
Shizuoka Cancer Center,
1007 Shimonagakubo,
Nagaizumi, Suntogun,
Shizuoka, 411-8777, Japan.
h.matsubayashi@scchr.jp

Received: 12.05.2016
Accepted: 06.06.2016

ABSTRACT

A 59-year-old woman was referred for investigation of a pancreatic cystic lesion. Computed tomography revealed a well-demarcated, multilocular cyst, approximately 4 cm in size, at the pancreas head. Endoscopic ultrasonography demonstrated honeycomb-like components at the cyst margin. The cyst was associated with a widely-dilated upstream main pancreatic duct (MPD). Endoscopic retrograde pancreatography demonstrated a communication between the stenotic Santorini's duct and the cyst. Aspiration cytology from the cyst demonstrated clusters of mucinous epithelial neoplasm cells. Branch-type intraductal papillary mucinous neoplasm, possibly invading to the MPD, was suspected and pancreatoduodenectomy was performed. Surprisingly, pathology of the resected pancreas showed mixed-type serous cystadenoma.

Key words: pancreas – serous cystadenoma – communication – pancreatic duct – diagnosis.

Abbreviations: CA19-9: cancer antigen 19-9; CEA: carcinoembryonic antigen; ERC: endoscopic retrograde cholangiography; ENPD: endoscopic naso-pancreatic drainage; ERP: endoscopic retrograde pancreatography; EUS: endoscopic ultrasonography; NET: neuroendocrine tumor; FNA: fine needle aspiration; IPMN: intraductal papillary mucinous neoplasm; MRCP: magnetic resonance cholangiopancreatography; MPD: main pancreatic duct; SCA: serous cystic neoplasms.

INTRODUCTION

Serous cystic neoplasms (SCAs) account for 8–17% of clinically encountered pancreatic cystic lesions [1, 2], 1-2% of all pancreatic exocrine neoplasms [3, 4] and typically appear evenly distributed throughout the pancreas. Serous cystic neoplasms are predominantly found in middle-aged women [2, 5-7]. Their communication to the pancreatic duct has been reported only occasionally (0-0.6%) [6, 8]. Most cases are benign, and surgical resection is recommended only when the lesions are symptomatic, difficult to definitively differentiate from other surgical lesions, or large in size [7]. Therefore, differential diagnosis is critical when a lesion mimics other cystic neoplasms, such as an intraductal papillary

mucinous neoplasm (IPMN) with high-risk stigmata [9]. This report documents a case of an SCA communicating with the stenotic Santorini's duct and dilated main pancreatic duct (MPD), mimicking branch-type IPMN that carries a surgical recommendation.

CASE REPORT

In April 2013, a 59-year-old woman was referred to our hospital for investigation of an asymptomatic pancreatic head cyst with a suspected diagnosis of branch-type IPMN. She was a habitual drinker and smoker (5 cans of beer per week and 5 cigarettes a day), and she had a medical history including hypertension, diabetes mellitus, gallstones, and bilateral arteriosclerosis obliterans of the lower extremities. Her blood tests showed elevated levels of the following: serum carcinoembryonic antigen (CEA) of 7.5 ng/mL (normal: ≤5.0 ng/mL), glucose of 125 mg/dL (normal: 70-109 mg/dL), and HbA1c of 8.3% (normal: 4.6-6.2%). Enhanced computed tomography (CT) revealed a multilocular cyst, approximately 4 cm in size, with partially thickened septum but without calcification (Fig. 1). Endoscopic ultrasonography (EUS) demonstrated a macroscopic multilocular cyst with honeycomb-like components at the marginal site of the cystic lesion (Fig. 2). No mural nodule was seen in the MPD. Ultrasonographic

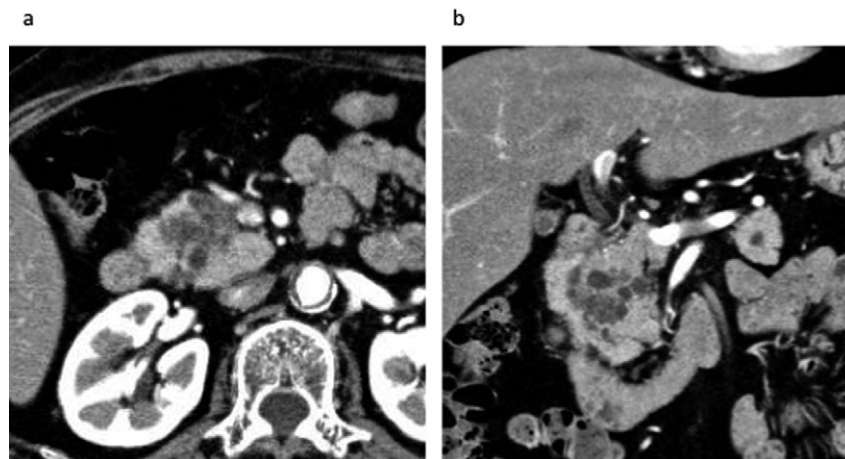


Fig. 1. Enhanced computed tomography (CT) showing a multilocular cyst at the pancreas head with thickened septum, horizontal (a) and coronal (b) views.

signs of early chronic pancreatitis were detected at the upstream pancreatic parenchyma, i.e. an irregularly dilated MPD with a high echoic margin, lobularity, high echoic foci, and strands. Magnetic resonance cholangiopancreatography (MRCP) demonstrated a 48 mm cystic lesion, with dilated upstream MPD (10 mm at the pancreatic body) (Fig. 3). The endoscopic retrograde cholangiography (ERC) was normal, except for the presence of gallstones, but pancreatography showed a compressed, atrophic Wirsung's duct (Fig. 4a), a stenotic Santorini's duct, connecting with the multilocular cyst at the pancreatic head (Fig. 4b) and a dilated upstream MPD (Fig. 4c). Intraductal ultrasonography from the Santorini's duct revealed similar findings as those of the EUS (Fig. 4d). A forceps biopsy (FB-44U, 1 mm, Olympus, Tokyo, Japan) was performed on the stenotic site, and cytology fluid was aspirated from the cyst (26 ml) and upstream MPD (8 ml). Finally, endoscopic naso-pancreatic drainage (ENPD) [10] was placed into the cyst for pancreatic juice cytology (Fig. 4e). The ENPD was withdrawn 40 hours later, after sampling the cystic fluid four times (total amount: 368 ml of autodrainage and 59 ml of lavage fluid). No adverse events occurred after ERCP. Cyst fluid analysis revealed a high level of pancreatic-type amylase (347,000 U/L, CA 19-9 (30,796 U/mL) but low level of CEA (4.5 ng/mL). The biopsy specimen did not show neoplastic tissue, and the initial cyst fluid cytology revealed a small cluster of benign mucous epithelial cells (class III); however all of the remaining ENPD fluid examinations showed non-neoplastic cells (class II). By the retrospective pathological review, epithelial cells obtained by the repeated ENPD fluid cytology were diagnosed as serous epithelia (Fig. 4f).

Findings of a multilocular cyst, over 4 cm in size, communicating with a stenotic pancreatic duct and a dilated upstream MPD (≥ 1 cm in width), along with mucinous neoplastic cells obtained from the cyst fluid, strongly suggested a branch-type IPMN with or without invasion to the pancreatic duct. A pancreatoduodenectomy was performed. A macroscopic view of the resected specimen showed a sponge-like lesion consisting of various sizes of cystic complex with a fibrous scar (Fig. 5a). Histology of the cyst was of serous cystadenoma without malignancy (Figs. 5b,c). The postsurgical course was uneventful, and the patient has been in good health for three years.

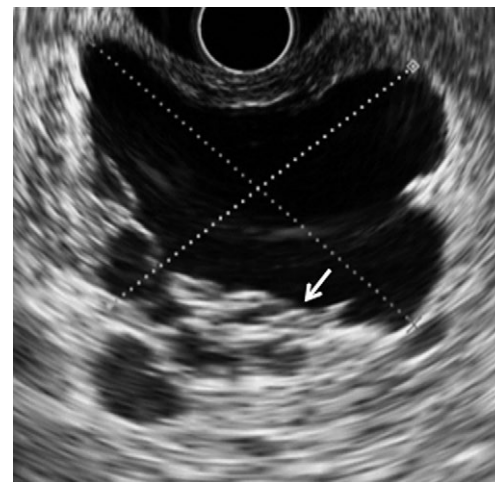


Fig. 2. Endoscopic ultrasonography showing a multilocular cyst, 49 mm in maximum diameter, with honeycomb-like component (arrow) at the peripheral site of the cyst.



Fig. 3. Magnetic resonance cholangiopancreatography (MRCP) showing a large cystic lesion accompanied with a dilated upstream main pancreatic duct.

DISCUSSION

The gross appearances of pancreatic SCAs are divided into four categories: microscopic-type, macroscopic-type, mixed-type, and solid-type [7]. Branch-duct type IPMNs need to be differentiated from cases of SCAs with macrocystic lesions, and from vascular-rich tumors, such as a neuroendocrine tumor (NET), in cases of solid-type SCAs [7, 11]. Accurate

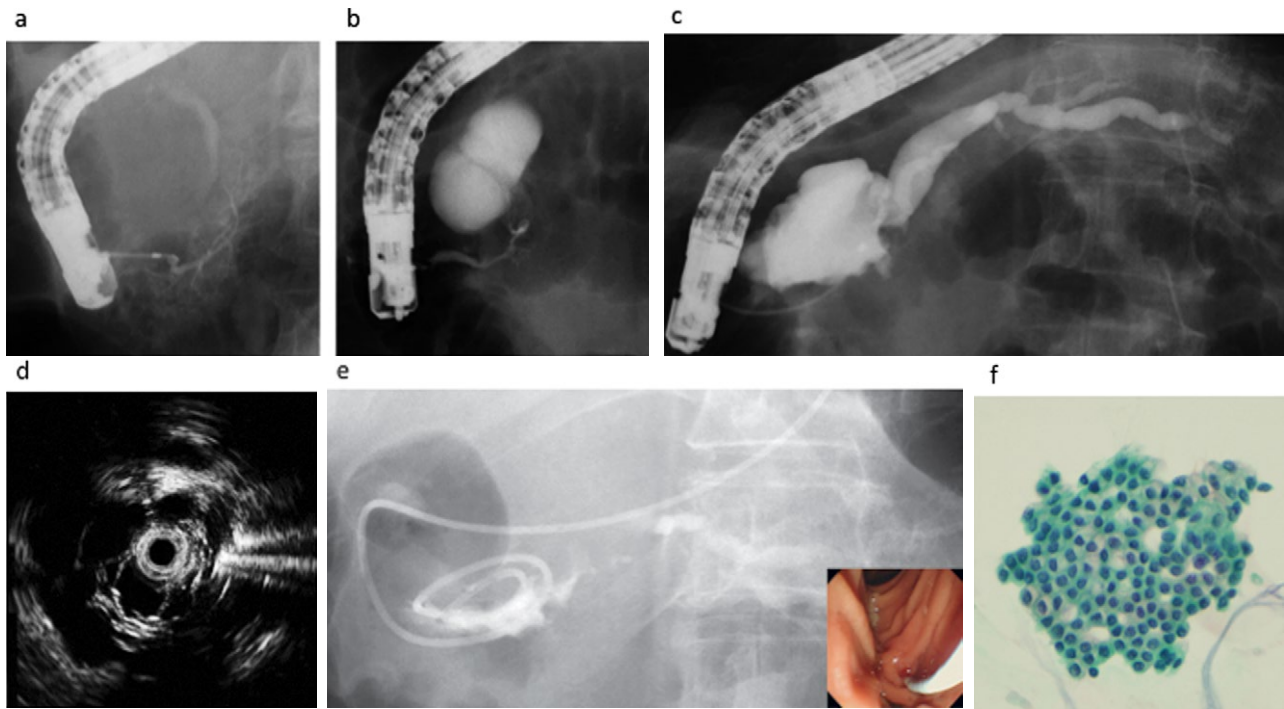


Fig. 4. Endoscopic retrograde pancreatography (ERP) (a–c): contrast injection from the duodenal major papilla showing an atrophic and compressed Wirsung's duct (a); ERP from the minor papilla showing the connection of the narrowed Santorini's duct with the cystic lesion (b); further contrast injection revealing the communication with the upstream main pancreatic duct (c). Intraductal ultrasound inserted into Santorini's duct showing multilocular cystic lesions around the probe, with partially thickened septum (d). Naso-pancreatic duct drainage (ENPD) tube placed into the cystic lesion at the pancreas head (e). A sheet of serous epithelial cells obtained by the endoscopic aspiration directly from the cyst (Papanicolaou, x200)(f).

preoperative diagnosis of SCAs is reported to be fairly low and differs by their gross type [7, 11]: for example, 57–85% in the microscopic-type; 50% in the mixed-type; 32–38% in the macroscopic-type; and 0–17% in the solid-type. A so-called honeycomb appearance is a trademark of microscopic cysts, and a central scar (star-like fibrosis) or central calcification can also indicate a diagnosis of SCA [3, 4, 6, 7, 11]. Our case showed large macrocysts and honeycomb-like components at the peripheral area of the cyst, and SCA was included in the differential diagnosis by the earlier image examinations (CT and EUS). However, other findings suggested branch-type IPMN with high-risk stigmata [9].

Our first mistake was the misinterpretation of communication with the stenotic pancreatic duct as invasion or inflammatory stenosis associated with IPMNs. In cases of SCAs, communication with the pancreatic duct has been reported to be very rare in the previous literature (0–0.6%) [6, 8]. However, a 2012 Japanese nationwide survey publicized that this pancreatic duct communication existed with SCAs, although at a low rate: 8% in the microscopic-type, 0% in mixed-type and solid-type, and 15% in the macroscopic-type [7]. According to our PubMed keyword survey, within four previous cases of SCAs with communication to the pancreatic ducts [12–15], Furukawa et al. reported a similar case with narrowing of the MPD, compressed by an SCA, 4 cm in size, at the pancreatic head [14]. In performing the critical differential diagnosis, we must bear in mind the possible communication of SCA and the pancreatic duct system.

The second pitfall occurred in the cyst fluid analyses including tumor markers and cytology. Pooled analysis of

12 studies, which collected cyst fluid from 450 patients [16], demonstrated that CEA <5 ng/mL suggested an SCA or a pseudocyst with 50% sensitivity and 95% specificity. However, the CA19-9 level of the cyst fluid >30,000 is too high for SCAs and suggests mucinous neoplasms [17]. In addition, an amylase level >30,000 is extremely high, which suggests a pseudocyst [16]. This discrepancy may be due to the pancreatic juice inflow through the communication with the pancreatic duct, which is stenotic and may be inflamed by the cyst compression. For cyst fluid cytology, mucous epithelial cells were only positive in the initial aspiration but negative in the following cyst fluid samples using ENPD, which is very unusual in our experienced cases of IPMN. The small number of mucous epithelial cells may be a contamination of exfoliates from the upstream pancreas. Additionally, the Japanese pathologist is not familiar with the cytological appearances of SCA, as EUS-guided fine needle aspiration (FNA) for the diagnostic purpose of a pancreatic cystic lesion is prohibited in Japan, because of the concern for complications or cyst fluid leakage [9]. Even with FNA samples, cytological diagnosis of SCA is quite difficult due to the lack of cellularity. In such cases, cytological features combined with α -Inhibin immunostaining is helpful in the differential diagnosis of SCA among various pancreatic cystic lesions [18]. To exclude IPMNs, mucus immunohistochemistry and molecular analysis, such as GNAS19 and K-ras [20] are considered helpful.

CONCLUSION

This case report documented a rare case of a mixed-type pancreatic SCA communicating with a stenotic Santorini's

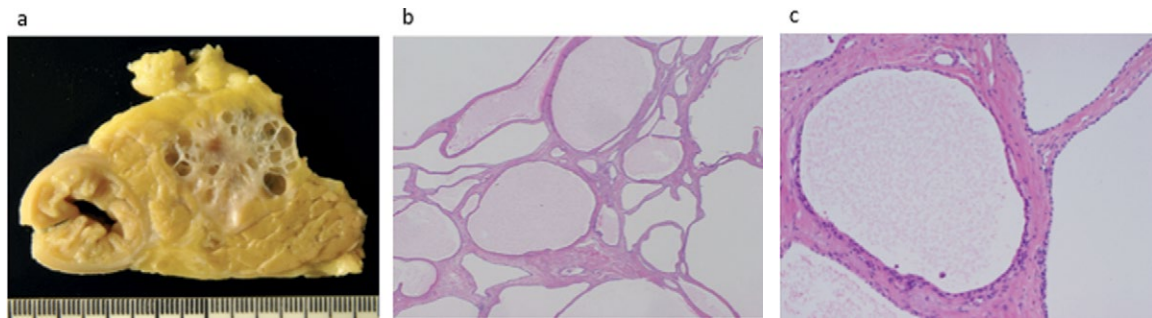


Fig. 5. Pathological findings (a–c): cut surface of the lower portion of the pancreatic head showing a multilocular cyst with a sponge-like appearance (a); low-power view of the cystic lesion showing various size of the cysts connected by the fibrous septum (H&E $\times 20$) (b); high-power view showing flattened cuboidal serous epithelia covering the cystic lesions (H&E, $\times 100$) (c).

duct. Communication to the pancreatic duct is not a definitive item that excludes an SCA. Today, cases with pancreatic cystic lesions, suspected for IPMN, are followed in our daily clinic [9]. Among them, probably in a minor proportion, there are macrocystic-type or macrocyst-predominant SCAs. We must be careful in the interpretation of SCA clinicopathological findings, particularly in the timing of surgical intervention.

Conflict of interest and sources of funding: None to declare.

Authors' contributions: H.M. performed the endoscopic and radiological examinations; Y.O., T.I. and K.U. performed surgery and managed the patient; K.S. made pathological diagnosis; H.M. wrote and H.O. reviewed the manuscript. All authors read and approved the final version of the manuscript.

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