CASE REPORT

Differentiation of mucinous cystic neoplasm and cystic changes associated with pancreatic adenocarcinoma

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SUMMARY

A 63-year-old woman presented to the hospital with persistent nausea, dyspepsia and weight loss for 6 months. Abdomen CT showed a low-attenuation mass, approximately 7.6 cm diameter, in the region of the body and tail of the pancreas. Cystic lesions, 5.5×4.9 cm and 4.6×3.7 cm in size, were observed in the body and tail of the pancreas, respectively, associated with the low-attenuation mass. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) revealed fetal carcinoembryonic antigen levels of >1000 ng/mL and necrotic cells with no malignant cells. On the basis of the imaging and EUS-FNA results, a putative diagnosis of mucinous cystadenoma accompanying pancreatic adenocarcinoma was made, and distal pancreatectomy and splenectomy were performed. Final biopsy using the surgical specimen confirmed pancreatic adenocarcinoma with moderate differentiation accompanied by degenerative cystic changes.

BACKGROUND

Pancreatic adenocarcinoma mainly occurs as a solid tumuor, with a poor prognosis, and therefore is often inoperable at the time of diagnosis.[1] Necrosis of the central part of pancreatic adenocarcinoma can rarely cause cystic change, and this can be mistaken for benign cystic lesions of the pancreas on radiological tests. Therefore, appropriate care should be taken during diagnosis.[2] Approximately 10% of pancreatic cystic lesions are cystic neoplasm, which account for 1% of all pancreatic tumours.[3] Pancreatic cystic neoplasms occur with diverse presentations ranging from benign cystic neoplasms to malignant cystic neoplasms, thus making its diagnosis particularly challenging. These neoplasms are also associated with varying degrees of prognosis, and therefore, an accurate diagnosis and early intervention is essential.[4] The frequency of precancerous and malignant lesions was reported to be 30–47% in earlier studies on patients undergoing surgery for cystic neoplasms.[5] Since it is difficult to accurately distinguish between benign and malignant lesions in cases of pancreatic cystic neoplasm by preoperative imaging studies, various methods such as other radiological tests and fine needle aspiration are being developed to help in the diagnosis.[6]

We present a case of a pancreatic cystic lesion accompanying pancreatic adenocarcinoma as mucinous cystadenoma diagnosed by imaging and endoscopic ultrasound (EUS). Surgery was performed accordingly, and a final histological diagnosis of pancreatic adenocarcinoma accompanied by pancreatic cystic lesions was made.

CASE PRESENTATION

A 63-year-old woman visited the hospital with persistent nausea, dyspepsia and weight loss for 6 months. Five years earlier, she had been diagnosed with hypertension and she has been taking amlodipine 5 mg daily. Her family history was unremarkable.

Physical vital signs recorded included blood pressure (120/80 mm Hg), heart rate (68 bpm), respiratory rate (20 breaths/min) and temperature (36.8 °C). On physical examination, no tenderness or rebound tenderness was noted in the abdomen and no mass was palpable. There was no abdominal distension, and bowel sounds were normal. Blood test results were within the normal range: haemoglobin 12.3 g/dL; white blood cell count 4540/mm^3 (neutrophils, 50.9%; lymphocytes, 39.0%; eosinophils, 1.8%); platelet count, 175 000/mm^3; aspartate transaminase level 24 U/L; alanine transaminase level 9 U/L; alkaline phosphatise 77 U/L and total bilirubin 0.6 mg/dL. The plasma carcinoembryonic antigen (CEA) level was elevated (4.02 ng/mL) and the CA19–9 level was within the normal range (2.42 U/mL). There were no remarkable findings on chest radiography and simple abdomen examination. Abdominal CT showed a low-attenuation region, approximately 7.6 cm in diameter around the body and tail of the pancreas. Cystic lesions, 5.5×4.9 cm and 4.6×3.7 cm in size, were observed in the body and tail of the pancreas, respectively, associated with the low-attenuation region (figure 1). On MRI, the low-attenuation region seen on CT showed low-signal intensity on a T1-weighted image and high-signal intensity on T2-weighted image and thus, pancreatic cancer was suspected. Narrowing of superior mesenteric vein was observed, which led us to suspect blood vessel invasion. No connection was observed between the pancreatic cystic lesion around the mass and the pancreatic duct (figure 2).

On EUS, two cystic lesions, 6.3 and 4.6 cm in diameter, were observed around the body and tail of the pancreas, respectively. These lesions were well-defined, anechoic, large, multilobulated cysts with an irregular solid component and a septum on the inside (figure 3). EUS-guided fine needle aspiration (FNA) and pathological examination were performed. Blood tests results were as follows:

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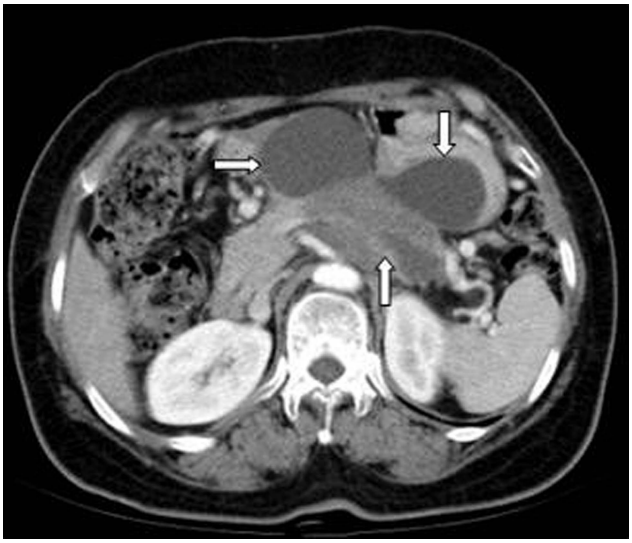

Figure 1 Abdominal CT showing 5.2×4.8 cm, 3.4×3.6 cm cysts adjacent to a tumour with low attenuation in the body and tail of the pancreas.

amylase level 55 U/L; CEA level >1000 ng/mL; CA19–9 level 10.85 ng/mL. Cytology of the FNA specimen showed the presence of mainly macrophages and neutrophils; no tumour cells were observed.

DIFFERENTIAL DIAGNOSIS

On CT and MRI, the pancreatic cystic lesions were associated with the mass, but with a distinct boundary, and on EUS, these appeared as well-defined, multilobulated, macrocystic, anechoic lesions, which included a solid component and so, differentiation between mucinous cystadenoma of the pancreas and mucinous cystadenocarcinoma was considered possible. In addition, because the cysts were present in the body and tail of the pancreas of a middle-aged woman, the level of CEA in the cystic fluid was high, and no cancer cells were observed on histological examination, the possibility of mucinous cystadenoma was considered.

TREATMENT

On the basis of the aforementioned findings, a putative diagnosis of mucinous cystadenoma accompanying pancreatic adenocarcinoma was made, and a pancreatectomy involving the tail and splenectomy were performed. During the surgical procedure, the masses in the body and tail of the pancreas were hard on palpation, and around it, ruptured cysts were seen adhering to adjacent tissues. The cyst was filled with mucus. A pancreatic mass, 6×3×3.2 cm in size was resected during the procedure; the resected mass was greyish-white and granular with focal necrotic regions and peripheral cystic spaces (figure 4). On histopathological examination, the mass was confirmed to be pancreatic adenocarcinoma with moderate differentiation (figure 5). The cystic component of the tumour was lined by malignant columnar epithelium and was similar in histology to the tumour in the distal pancreas (figure 6). Ovarian stroma was not observed in the wall of the cystic mass. Further, no dysplastic or malignant cells were observed in the pancreatic resection margin and no peripheral lymph node metastasis was noted. However, the adjacent duodenal serosa showed the presence of malignant cells.

OUTCOME AND FOLLOW-UP

After pancreatectomy involving the tail and splenectomy, the patient was finally diagnosed as having pancreatic adenocarcinoma (T4N0M0, stage III) and in the third postoperative week, chemotherapy with gemcitabine and cisplatin was initiated. The patient is currently on this treatment.

DISCUSSION

Pancreatic adenocarcinoma occurs mainly in the form of a solid tumour, but when it is accompanied by cystic changes, several other conditions will have to be considered in the differential diagnosis, thus making an accurate diagnosis challenging. Kosmahl *et al*[7] reported that 38 of 483 pancreatic ductal adenocarcinoma (PDAC) patients showed cystic features, accounting for 8% of all such cases. Kosmahl *et al*[8] reported that 30 of 416 (7%) patients with pancreatic cystic lesion in their study showed ductal adenocarcinoma with cystic changes. This implies that ductal adenocarcinoma with cystic changes is not very uncommon and that an active evaluation for carcinogenic changes of all pancreatic cystic lesions is needed.

Cystic changes associated with PDAC vary in nature and etiopathogenesis.[7] The most common form involves the presence of larger infiltrative ducts than ordinary ductal adenocarcinomas.[9] The next most common type is degenerative changes caused by extensive central tumour necrosis. These lesions are large, with haemorrhagic debris on the inside, and have irregular borders. Most of these tumours show a high proliferation rate and are classified as undifferentiated pleomorphic tumours or moderately differentiated pancreatic adenocarcinoma, and are more commonly large tumours.[7] The third type of cystic changes involve non-neoplastic retention cysts that occur when the main pancreatic duct or secondary pancreatic ducts are restricted by pancreatic adenocarcinoma.[10] These cysts are located mainly at the edge of the tumour and can be differentiated from large-gland type PDAC on the basis of CEA, human tumour antigen and MUC1 levels and the absence of p53 expression.[7] The fourth type involves pseudocysts attached to the tumour, caused by tumour-associated pancreatitis.[11] These cysts have unknown aetiology but occur in 5% of all cases of pancreatitis,

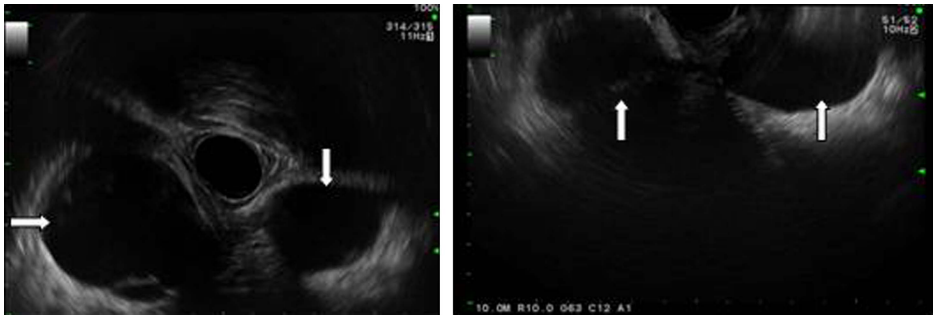

Figure 2 Endosonographic image showing macrocystic, multilobulated, septated cysts, 6.3 cm, 4.6 cm in size.

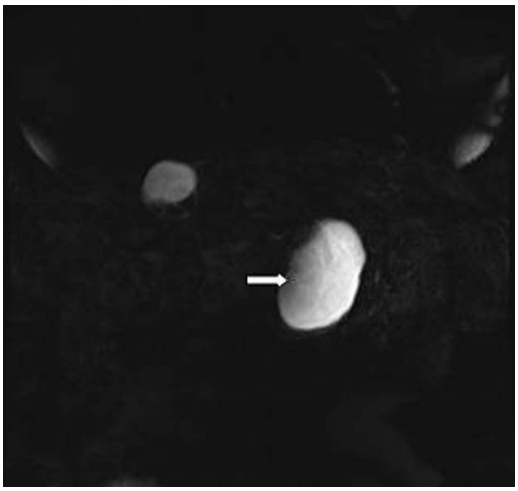

Figure 3 MR cholangiopancreatography image showing no communication between the cystic lesion and the pancreatic duct.

and ductal obstruction by the tumour is believed to induce such change.[7] In our case, two cystic lesions, 6.3 and 4.6 cm in diameter, were observed in the body and tail of the pancreas, respectively, these lesions were anechoic, large, cystic, multilobulated, with well-defined boundaries and an irregular solid component and a septum on the inside. Cystic changes observed in the tumours were considered degenerative, accompanied by extensive cystic necrosis.

EUS is a good diagnostic test for evaluating lesions associated with the pancreas and the entire pancreatic duct, solid components of the cystic lesions and infiltration into pancreatic parenchyma, more rapidly than possible with conventional imaging modalities.[12] As a stand-alone test, it is difficult to assess the malignant potential of lesions using EUS and to make an accurate differential diagnosis, EUS-guided FNAis preferred. This would allow a sampling of cystic fluid and tissue from septal or intramural cysts. In addition, several tests can be performed to evaluate diverse tumour markers such as CEA, CA72–4, CA125 and CA19–9 using the cystic fluid obtained from cystic lesions.[13] Generally, if the CEA level in cystic fluid is less than 5 ng/dL, it is considered to be benign and if it is more than 800 ng/dL, a mucinous cystic neoplasm is suspected.[14] With

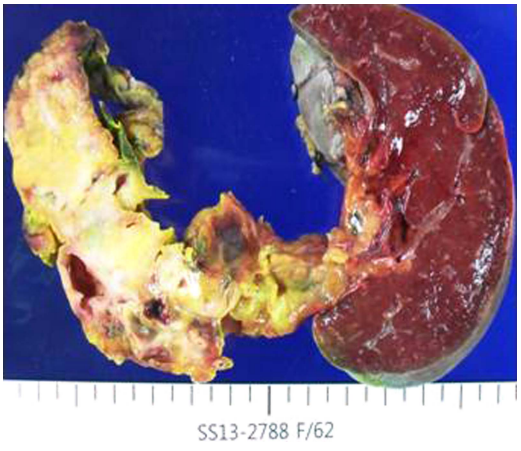

Figure 4 The cut section of the specimen showing the tumour in the distal pancreas that was greyish-white and granular with focal necrosis and peripheral cystic spaces. Findings of the splenic capsule and parenchyma were unremarkable on gross appearance.

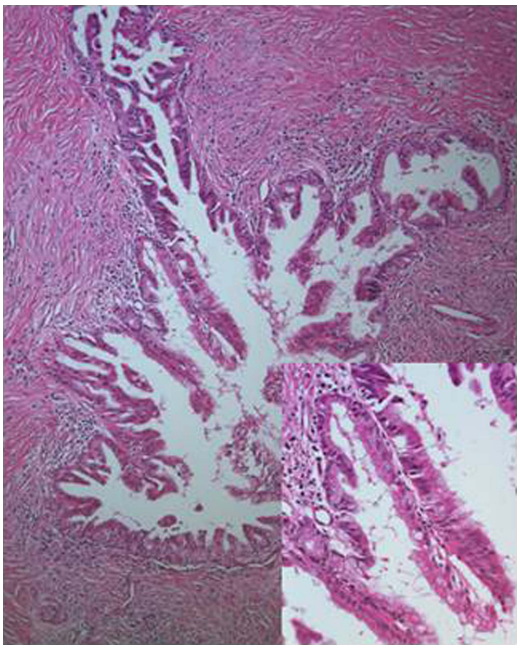

Figure 5 The solid portion of the tumour was composed of complex tubular glands with a desmoplastic stromal response (H&E, staining ×100). Inset, ductal adenocarcinoma arising from a large gland (H&E, ×100).

regard to the limitations of EUS-guided FNA, it is difficult to obtain a large quantity of cells routinely, which raises the probability of false-negative results on histopathological examination.[2] In our case, a diagnosis of mucinous cystic neoplasm was considered because of the high CEA level in the cystic fluid (more than 1000 ng/dL), there were no malignant cells on histopathology and characteristic findings on EUS. Accordingly, it is difficult to distinguish between benign and malignant pancreatic cystic neoplasms using EUS-FNA alone and so a diagnosis should be made by assessing results from diverse imaging tests, laboratory examinations and biopsy.

In cases of pancreatic cystic lesions wherein the preoperative diagnosis is unclear in the presence of symptoms, surgical removal is recommended and particularly in cases of mucinous

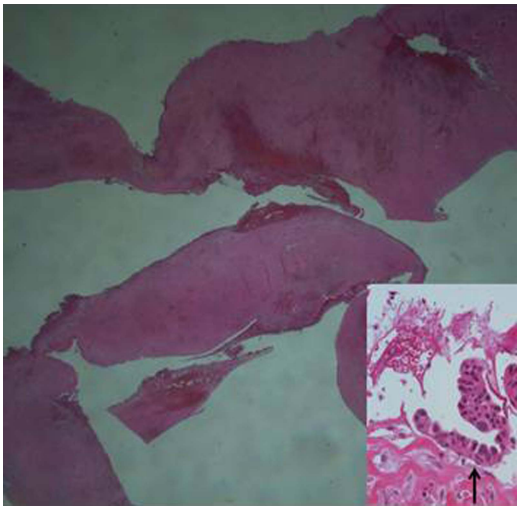

Figure 6 Histological examination of the cyst wall shows malignant columnar epithelial cells (H&E, ×40). Inset, pleomorphic cells (arrow, H&E, ×400).

cystic neoplasms and intraductal papillary mucinous neoplasms with the possibility of malignant degeneration, complete surgical removal should be considered.[12] In cases of patients diagnosed with pancreatic cystic lesions wherein the cystic change is associated with a solid tumour, the possibility of malignancy can be obscured and therefore, a thorough evaluation should be conducted.[15] Accordingly, when differential diagnosis of a pancreatic cystic lesion is made, all available clinical and histopathological tools should be used to arrive at an accurate diagnosis, and particularly special attention is needed in cases of small cystic lesions which can be easily overlooked.

Learning points

- The appearance and pathophysiology of cystic changes accompanying solid cancers of the pancreas are diverse and may resemble features of benign cystic lesions of the pancreas; therefore, differentiation between these conditions is needed.
- Endoscopic ultrasound is a useful method for the diagnosis of cystic lesions of the pancreas, but it has low specificity and the results are prone to subjective differences. An accurate diagnosis of cystic lesions of the pancreas involves good physician judgement by systematic evaluation of all available diagnostic tests and methods, including imaging and laboratory examinations.
- Endoscopic ultrasound-guided fine needle aspiration and histological examination are important for the differential diagnosis of pancreatic cystic lesions, but physicians should be aware of the possibility of false-negative or false-positive results.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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