Endoscopic ultrasound for detecting small pancreatic tumor missed by computed tomography

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Abstract
Pancreatic cancer is the eighth leading cause of cancer-related deaths in Taiwan. Pancreatic cancer has a poor prognosis. Diagnosis of early-stage pancreatic cancer, which can be defined based on resectability, size, or curability, will improve survival. Diagnostic tools for pancreatic cancer include transabdominal ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS). We report the case of a 48-year-old man who presented with progressively yellowing skin. An initial CT imaging study did not reveal the pancreatic lesion. Further imaging with EUS was performed to search for the organic lesion causing an abrupt distal common bile duct stricture, and a heterogeneous hypoechoic tumor located at the uncinate process was identified. The patient underwent a Whipple operation because malignancy could not be ruled out. The final pathological result was moderate to poorly differentiated adenocarcinoma.

1. Introduction
Pancreatic cancer has been the eighth leading cause of cancer-related deaths in Taiwan in recent years. In most cases, the outcome of pancreatic cancer is poor. The clinical manifestations of pancreatic tumors are epigastralgia, jaundice, steatorrhea, body weight loss, vomiting, anorexia, and asthenia. Initial clinical presentations, such as painless jaundice and new onset diabetes, may be early signs of a pancreatic head tumor.

Diagnostic tools for pancreatic cancer include transabdominal ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS). In recent years, improvements in the imaging technologies mentioned above have helped in the early detection of pancreatic cancer. The high sensitivity and specificity of EUS plays an important role when trying to identify a small pancreatic tumor. It also helps in obtaining tissue samples via fine needle aspiration.

In this case, the initial CT image did not reveal the pancreatic head tumor. We share our experience of using EUS for detection of a small pancreatic head tumor. We confirmed the diagnosis of pancreatic head adenocarcinoma after surgical intervention.

2. Case report
A 48-year-old man had a medical history of hypertension and diabetes mellitus controlled with an oral hypoglycemic agent combined with insulin for 2 years. He developed progressively yellowing skin over the course of 1 week. He complained of postprandial abdominal fullness with dull pain, tea colored urine, and diarrhea with light bright oil muddy stool in the last week. He denied the presence of fever, clay-colored stool, and recent body weight loss.

Biochemistry data revealed hyperbilirubinemia (total bilirubin level: 13 mg/dL, direct bilirubin level: 8.0 mg/dL), elevated alkaline phosphatase (ALK-P: 688 IU/L) level, elevated r-glutamyl transpeptidase (r-GT: 1842 IU/L) level, and an abnormal liver function test (aspartate transaminase [AST] level: 230 IU/L, alanine
transaminase [ALT] level: 395 IU/L). The patient’s serum sample tested negative for hepatitis B and hepatitis C. Echography showed a gallbladder (GB) stone and common bile duct (CBD) dilatation. Conventional abdominal CT with and without contrast also confirmed the presence of GB stones and CBD dilatation. It did not reveal any abnormal pancreatic head lesion (Fig. 1).

Endoscopic retrograde cholangiopancreatography (ERCP) was performed under the indication of obstructive jaundice. The fluoroscopy showed proximal CBD dilatation with an abrupt distal CBD stricture. One plastic stent (8.5 Fr, 9 cm) was placed in the distal CBD (Fig. 2A). A biopsy was obtained from the edematous change of the papilla with villous appearance (Fig. 2B). The final pathological result was chronic inflammation.

The patient’s serum tumor marker levels were as follows: carcinoembryonic antigen (CEA) 1.71 ng/mL (normal range < 5.00 ng/mL) and CA 19-9 283.90 U/mL (normal range < 37.00 U/mL). The immunoglobulin subclass 4 level was within the normal range.

Because of high suspicion of malignancy, we chose endoscopic ultrasound (EUS) instead of MRI of the pancreas to detect the organic lesion that caused the distal CBD stricture because initial abdominal CT did not show any suspicious lesion in the pancreas. In addition, tissue sample could be obtained using EUS fine needle aspiration if any suspicious lesions are found. EUS revealed pancreatic duct dilatation in the head portion and one heterogeneous hypoechoic tumor of about 2.68 × 2.34 cm located at the uncinate process (Fig. 3). Fine needle aspiration from the uncinate process tumor was performed. The final cytology report showed negative results for malignancy.

MRI was performed to view the irregular enhanced lesion at the uncinate process of the pancreas on the arterial phase. Diffusion weighted images also showed relatively high signal intensity in the uncinate process (Fig. 4). A high malignancy potential of the pancreatic uncinate process was suspected from the imaging results.

We performed a Whipple operation with findings of a hard pancreatic tumor, which compressed to the distal CBD with dilatation. On gross appearance, it was a circumferential sclerotic tumor, measuring 2.5 × 2.5 × 1.5 cm in size, involving the pancreatic head. The margins of the peripancreatic tissue were free of tumor. Microscopically, vascular invasion was absent. Two out of 21 lymph nodes showed metastatic adenocarcinoma. It was proven to be a moderately to poorly differentiated pancreatic head adenocarcinoma (Fig. 5). According to the American Joint Committee on Cancer 7th Edition Staging, the pathologic TNM stage was T2N1M0, Stage IIb. After surgical intervention, the patient received systemic chemotherapy with gemcitabine.

### 3. Discussion

Pancreatic cancer is the eighth leading cause of cancer-related deaths in Taiwan. The most common initial clinical presentation of pancreatic exocrine tumors is pain, jaundice, and weight loss. The initial clinical presentation depends on the location of the pancreatic tumor. Jaundice, steatorrhea, and weight loss are more common symptoms in patients with pancreatic head tumors compared with in those with tumors in the body or tail. Around 60 to 70 percent of exocrine pancreatic cancers are located in the head portion of the pancreas, while only 20 to 25 percent are found in the body or tail. Pancreatic head tumors with an initial presentation of painless jaundice tend to have a more favorable prognosis, making surgical intervention desirable.

The present patient had a medical history of diabetes mellitus diagnosed less than 2 years ago. New onset diabetes mellitus can be an early sign of pancreatic head adenocarcinoma.

Transabdominal ultrasonography is the first-line imaging study used in patients with suspected biliary obstruction of unknown etiology. Transabdominal ultrasonography is readily available, inexpensive, and does not use ionizing radiation. However, it is not a suitable screening tool for detection of pancreatic masses due to its relatively low sensitivity. A pancreatic carcinoma typically appears as a focal hypoechoic hypovascular solid mass with irregular margins. In one study, the sensitivity for detection of pancreatic masses has been reported to range from 67 to 90% because of high operator dependence.

Multi-detector computed tomography (MDCT) is widely available and is the best-validated imaging modality for the evaluation of a patient with a suspected pancreatic mass. The typical image of pancreatic adenocarcinoma on MDCT is an ill-defined hypo-enhancing mass. The sensitivity of MDCT for the detection of pancreatic adenocarcinoma is as high as 89–97%. However, the shortcoming of MDCT is its low sensitivity for small lesions (less than 1.5 cm) of pancreatic tumors. The detection rate of small lesions in pancreatic head by MDCT is only 67% in this study.

In another study, the sensitivity was 100% for tumors >2 cm, but only 77% for tumors ≤2 cm in size. In the present case, the initial abdominal CT did not reveal the primary tumor in the pancreatic head, perhaps because of its size.

In an early meta-analysis, diagnosing cancer of the pancreas by ERCP with the “double duct” sign had a sensitivity of 92% and specificity of 96%. In the present case, mild proximal CBD dilatation with an abrupt distal CBD stricture was detected by ERCP. The most common malignant cause of obstructive jaundice in middle-aged adults in North America is cancers of the pancreatobiliary tract.
Thus, EUS was performed to search for the possible organic cause of abrupt distal CBD disruption. EUS provides better image resolution compared with trans-abdominal ultrasonography because of the small distance between the echoendoscope and the pancreas through the gastric or duodenal wall. It also helps in obtaining tissue samples from suspicious lesions via EUS guided fine needle aspiration (EUS-FNA). In one meta-analysis, the sensitivity of EUS-FNA for pancreatic cancer was 92% and the specificity was 96%. In a previous imaging study, for diagnosis of pancreatic cancer less than 10 mm in size and pancreatic duct dilatation, the tumor detection rate was higher on EUS than on CT or other modalities, and EUS-guided fine needle aspiration was helpful in confirming the histologic diagnosis.

Fig. 2. (A) Endoscopic retrograde cholangiopancreatography showed proximal CBD dilatation with distal CBD stricture (Arrow). (B) Edematous change with villous appearance of papilla is detected by side view endoscope (Arrow).

Fig. 3. (A) The CBD is measured about 3.9 mm with stent in situ (Arrow). (B) One heterogeneous hypoechoic tumor about 2.68 × 2.34 cm located at uncinate process (Arrow).

Fig. 4. Axial arterial-phase gadolinium-enhanced T1-weighted fat-suppressed gradient recalled echo MR image showed central hypointensity irregular mass with peripheral enhancement in uncinate process of pancreas (Small arrow). P: Pancreatic head (Large arrow), C: Common bile duct (Middle arrow) A: Superior mesentery artery, V: Superior mesentery vein.

Fig. 5. Microscopic photo showing moderate to poorly differentiated invasive adenocarcinoma with marked desmoplastic stromal reaction. Tumor cell nuclei are hyper-chromatic with nuclear pleomorphism. (Arrow, H&E stain, magnification ×40).
MRI also provides high sensitivity and specificity for detection of pancreatic cancer. It has become widely used in the diagnosis of pancreatic pathologies because of its very high soft-tissue contrast resolution, with an accuracy in the detection and staging of adenocarcinoma of 90–100%. MR cholangiopancreatography also provides images of pancreatic ductal system abnormalities. Furthermore, diffusion-weighted imaging (DWI) may provide further information about a wide variety of solid and cystic lesions of the pancreas and enable detection of solid pancreatic tumors with a high cellularity or fibrosis.

In conclusion, diabetes mellitus diagnosed less than 2 years prior was suggestive of an early sign of pancreatic head adenocarcinoma. However, the sensitivity of abdominal CT for detecting pancreatic head tumors smaller than 2 cm is low. MRI of the pancreas is another alternative to view detailed images of pancreatic anatomy. Moreover, it has a higher sensitivity for pancreatic tumors, but it does not enable tissue sampling. In the present case, the benefit of EUS is that not only does it provide us with a high detection rate for small lesions of the pancreatic head tumor but also enables tissue sampling via FNA. Although FNA was negative in this patient, EUS and MRI were both important to evaluate possible pancreatic tumors.

Conflict of interest

None.

References