Anaplastic pancreatic carcinoma growing within the main pancreatic duct complicated by a large pseudocyst

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Abstract
A 71-year-old woman with epigastric pain and fever visited our hospital. She had elevated levels of serum amylase and C-reactive protein, and computed tomography revealed a large, 20 cm diameter, pancreatic cyst. A low-density nodule was also identified in the head of the pancreas with mild dilation of the distal main pancreatic duct (MPD). The patient was diagnosed with pancreatic ductal carcinoma complicated by a pancreatic pseudocyst (PPC). After drainage of the cyst, a pancreatoduodenectomy was safely performed. Histological examination revealed anaplastic pancreatic carcinoma (APC) composed of spindle cells and osteoclast-like giant cells. The tumor occupied the lumen of the MPD and acute and chronic obstructive pancreatitis was evident. Although her postoperative course was uneventful, the tumor recurred as multiple liver metastases three months after surgery, and she died of disease progression four months after surgery. PPCs are often caused by alcohol use, biliary tract disease, or blunt trauma. However, PPCs caused by APC is rarely seen. Although extremely rare, pancreatic cancer or APC should be considered as a cause of PPCs. A spindle cell component to the tumor seems to be associated with a dismal prognosis, while growth within the pancreatic duct is reported to carry a better prognosis.

Keywords: anaplastic pancreatic carcinoma, chronic obstructive pancreatitis, main pancreatic duct, pancreatic pseudocyst

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Introduction

Anaplastic pancreatic carcinoma (APC), a subtype of pancreatic infiltrating ductal adenocarcinomas, is rare but clinically important disease because of its aggressive nature. The incidence of APC, estimated from nationwide statistics in the United States, is around 5% of the pancreatic duct adenocarcinoma (PDA), and overall survival for APC is significantly worse than for PDA, unless the tumor is surgically resected1,2. Published case reports have demonstrated several distinctive growing patterns of APC, such as predominant growth into the portal vein and main pancreatic duct (MPD)3,4. Herein, we would like to describe a case of APC predominantly growing into the main pancreatic duct (MPD) and causing a large pancreatic pseudocyst (PPC) and chronic obstructive pancreatitis.

Case Report

A 71-year-old woman visited our hospital for epigastric pain and fever. There was no history of heavy alcohol use or abdominal trauma. Laboratory examination results showed elevated levels of serum pancreatic amylase (1,139 U/L) and C-reactive protein (15.6 mg/dl). Abdominal enhanced computed tomography revealed a large PPC of 20 × 10 × 10 cm, compressing the stomach (Fig. 1a, b). A low-density nodule on computed tomography and a hypo-echoic nodule on endoscopic ultrasonography, 20 mm in size, was also identified in the head of the pancreas, with mild dilation of the distal MPD (Fig. 1c).

The patient was diagnosed with a pancreatic tumor, complicated with PPC. Due to the technical difficulty of endoscopic retrograde pancreatic duct drainage, endoscopic ultrasonography-guided pseudocyst drainage was performed. As the cyst shrank and the drainage tube deviated from the cyst, endoscopic retrograde cholangiopancreatography and tube placement in the MPD was performed for further differential diagnosis and treat-
The patient then underwent pancreatoduodenectomy. The pseudocyst was not yet macroscopically observed and adhesions around the omental bursa were easily dissected. Peritoneal lavage cytology was negative for cancer cells. On macroscopic observation of resected specimen, the expansive, round, 21 mm in size, tumor occupying the lumen of the MPD was observed (Fig. 2). Microscopically, the tumor was composed of two distinctive types of cells; the anaplastic mononuclear spindle cells and the osteoclast-like reactive multinuclear giant cells (Fig. 3a), leading to the diagnosis of APC growing within the MPD (Fig. 3b). The anaplastic spindle cells were dominant, while osteoclast-like giant cells accounted for about 40% depending on the site of the tumor. The invasive ductal adenocarcinoma was occasionally distributed in the APC tumor tissue (Fig. 3c). Most of the extraductal tissue showed the features of chronic obstructive pancreatitis (Fig. 3d). Immunohistochemically, the osteoclast-like giant cells were positive for anti CD68, (Fig. 3e), while both types of tumor cells were positive for vimentin. Approximately 60% of the anaplastic spindle cells were positive for MIB-1, while osteoclast-like giant cells were negative (Fig. 3f).

There were neither lymph node metastases pN0(0/28), nor distant metastases. The tumor was classified as T2, N0, M0 Stage II, according to the TNM Classification of Malignant Tumors, Eighth Edition, UICC. The patient was discharged 17 days postoperatively, with no short-term complications. However, 3 months after surgery, the tumor recurred with multiple liver metastases, which were not proven by pathological diagnosis, and the patient died 4 months after surgery.

Fig. 1 Imaging diagnosis of the pancreas tumor.

a. Abdominal computed tomography (CT) shows the head of the pancreas (red arrow).
b. Coronal CT view. A huge pancreatic pseudocyst (PPC) measuring 20 × 10 cm at the largest diameter is shown.
c. Endoscopic ultrasonography shows a low-density tumor in the head of pancreas (green arrow).
d. Enhanced abdominal CT shows a remarkably shrunken PPC (blue arrow). Endoscopic retrograde pancreatic duct drainage tube is placed (yellow arrow).
Fig. 2 Serial horizontal sections of pancreatoduodenectomy specimen.

a. Along the open cut of dilated distal bile duct (DBD) from hepatic cut end side (HCES), ampullary bile duct (ABD), and peripancreatic tissue (PP) are sown.

b. Fig. 2b and c are serial horizontal sections from HCES (no.1) to ACC (no.9). The sections are stained with hematoxylin and eosin (H.E. staining in 2c). The expansive, round, 21mm in size, tumor, occupies the lumen of the MPD (arrows). Mild irregular dilatation of MPD is observed in no.9 of 2b, without tumor invasion. Within the tumor tissue, small blackish round foci are probably the traces due to the previously performed indwelling of 5Fr. stent into MPD (arrowhead).

c. From no.2 to no.6 sections, intraductal growth of APC becomes more evident. The involved MPD shows the bifurcation in no.3 and 4 and the diameter of lumen reaches to 13 mm in serial section of no.6. On the other hand, in the following lower-sided sections (from no.6 to no.8), the involved MPD are gradually decreased in size.

Abbreviation, OP: chronic obstructive pancreatitis, W: well-preserved pancreatic parenchyma, D: duodenum.
Fig. 3 Histopathology of the APC. A-D: HE stain, E: immunohistochemical staining for anti CD68, F: immunohistochemical staining for anti MIB-1

a. The APC is composed of the anaplastic spindle cells and osteoclast-like giant cells. bar: 20 µm.
b. The partially circumscribed crescent-shaped narrow space (CSS) is frequently seen, by significant intraductal growth of APC, between the proper wall of MPD and APC expanding MPD. Their surfaces are covered by non-neoplastic single-layered, cuboidal to cylindrical, epithelial cells. bar: 20 µm.
c. The invasive ductal adenocarcinoma is occasionally distributed in the APC tumor tissue. bar: 20 µm.
d. Extraductal tissue (OP) shows the features of chronic obstructive pancreatitis. bar: 200 µm.
e. Immunohistochemically, osteoclast-like giant cells are positive for CD68, on the other hand, neoplastic spindle cells are negative. bar:20 µm.
f. For MIB-1, the former cells are almost negative, while the latter type of cells are about 60% positive. bar: 20 µm.
Discussion

The present case demonstrates two unusually clinical features. First, the APC was accompanied by a large PPC and severe chronic obstructive pancreatitis. The latter was seen around the MPD in which the lumen was almost occupied by APC invasion. It is well known that pancreatic cancer is a rare etiology of acute pancreatitis, accounting for only 1.2% of cases\(^{5}\).

Furthermore, pancreatic carcinoma rarely occurs in association with PPCs. To our knowledge, only nine cases of pancreatic carcinoma with PPCs have been reported in the English literature (Table 1)\(^{6-13}\). In eight cases of them, the pathological findings revealed pancreatic ductal adenocarcinoma, while one case was associated with poorly differentiated invasive ductal adenocarcinoma with osteoclast-like giant cells. When the MPD is obstructed by encasement or intraductal tumor growth, we assume the occurrence of chronic obstructive pancreatitis, especially in the distal pancreatic portion to the obstruction.

Second, the prognosis of our patient was dismal. The literature suggests that undifferentiated carcinoma of the pancreas (anaplastic pancreatic carcinoma, APC) involving intraductal growth is associated with a better prognosis, and considered to be a sign of early stage disease\(^{14}\). However, the histopathological type of APC is another important factor related to the prognosis; studies suggest that osteoclast-like cells, which are multinuclear reactive histiocytic cells and immunohistochemically positive for CD68, are the cell subtype related to a better prognosis\(^1,2\); while other cell type which are atypical mononuclear spindle cells and show, immunohistochemically high labeling with MIB-1. This type of cells seems to be related to a poorer prognosis. Indeed, multiple liver metastases and aggressive disease progression were observed in the present case, despite the complete resection of the APC harboring the spindle-like cells.

In conclusion, here we report a very rare case of APC accompanied by a PPC and preferential tumor growth within the lumen of the MPD. Pancreatic cancers, including APC, should be considered as a less common cause of PPCs.

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References


Table 1. The nine cases of the pancreatic carcinomas with the pancreatic pseudocysts, reported in the English literature (1994–2016).

<table>
<thead>
<tr>
<th>Author, Year [ref. No.]</th>
<th>Age</th>
<th>Gender</th>
<th>Size of tumor (mm)</th>
<th>Size of cyst (mm)</th>
<th>Drainage</th>
<th>Treatment</th>
<th>Pathological findings</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimura, 1994 (6)</td>
<td>60</td>
<td>M</td>
<td>8 × 8</td>
<td>30</td>
<td>Not performed</td>
<td>DP</td>
<td>PDAC</td>
<td>NA</td>
</tr>
<tr>
<td>Kimura, 1994 (6)</td>
<td>57</td>
<td>M</td>
<td>30 × 20</td>
<td>110 × 70</td>
<td>Not performed</td>
<td>DP</td>
<td>PDAC</td>
<td>8 months, dead (with recurrence)</td>
</tr>
<tr>
<td>Ohmura, 2000 (7)</td>
<td>83</td>
<td>F</td>
<td>65 × 32</td>
<td>115 × 58</td>
<td>Penetration into the stomach</td>
<td>DP, TG</td>
<td>PDAC 17 months, alive (without recurrence)</td>
<td></td>
</tr>
<tr>
<td>Inagi, 2006 (8)</td>
<td>44</td>
<td>M</td>
<td>18 × 15</td>
<td>100</td>
<td>Cystectomy</td>
<td>DP</td>
<td>PDAC</td>
<td>8 months, dead (peritonitis carcinomatosa)</td>
</tr>
<tr>
<td>Yamaguchi, 2007 (9)</td>
<td>72</td>
<td>M</td>
<td>40</td>
<td>220</td>
<td>Percutaneous</td>
<td>TP</td>
<td>poorly differentiated ductal adenocarcinoma</td>
<td>3 months, dead (peritonitis carcinomatosa)</td>
</tr>
<tr>
<td>Sugiyama, 2012 (10)</td>
<td>60</td>
<td>F</td>
<td>NA</td>
<td>45</td>
<td>Not performed</td>
<td>PD</td>
<td>PDAC</td>
<td>NA</td>
</tr>
<tr>
<td>Ohkura, 2015 (11)</td>
<td>63</td>
<td>F</td>
<td>NA</td>
<td>52 × 32</td>
<td>Not performed</td>
<td>Insoluble (locally advanced)</td>
<td>PDAC</td>
<td>NA</td>
</tr>
<tr>
<td>Fujiwara, 2016 (12)</td>
<td>53</td>
<td>M</td>
<td>7</td>
<td>38</td>
<td>Not performed</td>
<td>ENPD</td>
<td>PDAC</td>
<td>12 months, alive (without recurrence)</td>
</tr>
<tr>
<td>Hoshimoto, 2016 (13)</td>
<td>61</td>
<td>M</td>
<td>20</td>
<td>38</td>
<td>Not performed</td>
<td>ENPD</td>
<td>PDAC</td>
<td>4 months, dead (liver metastases)</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not available; EUS, endoscopic ultrasonography; ENPD, endoscopic nasopancreatic drainage; DP, distal pancreatectomy; TG, total gastrectomy; TP, total pancreatectomy; PD, pancreatectoduodenectomy; PDAC, pancreatic ductal adenocarcinoma; APC, anaplastic pancreatic carcinoma; por, poorly differentiated ductal adenocarcinoma.


