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Case Report

An intraductal papillary mucinous neoplasm associated tubular adenocarcinoma with sarcomatoid component: A case report ☆,☆☆

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ABSTRACT

Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are a risk factor for the development of adenocarcinoma. However, the presence of a component of sarcomatoid carcinoma in the malignant tumor has rarely been described in the literature. A 30-year-old Chinese woman was admitted to our hospital with vague abdominal pain and a poor appetite for 2 months. Computed tomography revealed a huge, unilocular, solid-cystic mass in the pancreatic body, and tail. The patient underwent an en bloc resection of the distal pancreatic tumor with splenectomy and regional lymphadenectomy. Pathologic examination revealed an IPMN associated tubular adenocarcinoma containing a component of sarcomatoid (spindle-shaped cell) carcinoma. Immunohistochemical results revealed that the mononuclear spindle-shaped cells were positive for both pan-cytokeratin and vimentin. There was no evidence of perineural or vascular infiltration, lymph nodal metastasis, or positive surgical margins. The patient developed local recurrence 3 months after surgery for which she received chemoradiotherapy at another hospital. Distant metastases were detected 6 months after the surgery and the patient expired 9 months after surgical resection. We *concluded* that the presence of sarcomatoid change in IPMN-associated pancreatic adenocarcinoma may indicate poor prognosis.

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Introduction

Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are a distinct pathologic entity of mucin-producing pancreatic tumors with malignant potential [1].

These tumors arise from the ductal epithelium of the main pancreatic duct or its branches. They are characterized by epithelial proliferation in a papillary pattern and mucin hypersecretion, leading to cystic dilatation of the involved pancreatic ducts [2]. The extent of cellular atypia in IPMNs varies from low-grade dysplasia to invasive carcinoma [3], with invasive carcinomas being observed in 40%-60% of resected IPMNs [4]. The 2 distinct histopathological subtypes of adenocarcinoma that are commonly found to be associated with IPMNs are colloid (mucinous non–cystic) and conventional (tubular) adenocarcinoma [5].

Sarcomatoid carcinoma of the pancreas (SCP) is a rare tumor that is characterized by the presence of both carcinomatous and sarcomatous elements [6]. According to the 2010 World Health Organization (WHO) classification of tumors, SCP is classified as an undifferentiated (anaplastic) carcinoma of the pancreas [7]. Histologically, *SCP* shows that malignant spindle-shaped cells are arranged in a storiform pattern with a coexisting epithelial cell component [6].

Here we report a rare case of IPMN associated tubular adenocarcinoma containing a component of sarcomatoid carcinoma which underwent R0 resection with lymphadenectomy. However, the patient succumbed to death, due to local recurrence, and metastasis, 9 months after surgery.

Case report

A 30-year-old Chinese woman was admitted to our hospital with vague abdominal pain and a poor appetite for 2 months. She denied nausea, vomiting, jaundice, fever, or weight loss. No abuse of ethanol or smoking was reported. She had no significant family history or other diseases. Physical examination revealed a palpable mass of about 7.0 cm × 6.0 cm in the left upper abdomen, with a smooth surface, and restricted mobility. Ultrasonography of the abdomen revealed a 12.0 cm × 10.0 cm macrocystic lesion located in the distal body and tail of the pancreas. The results of laboratory tests, including the complete blood count, liver function tests, kidney function tests and urinalysis, were within the normal range. The serum levels of tumor markers, namely carbohydrate antigen 19-9 (CA 19-9), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA) was normal, while *the level of cancer antigen 125 (CA125)* was 170.91 $U\ mL^{-1}$ (normal value, 0-35 $U\ mL^{-1}$).

Contrast-enhanced computed tomography (CT) of the abdomen demonstrated a large, unilocular, solid-cystic mass measuring 14.0 cm × 9.8 cm that was located in the body and tail of the pancreas. Inside the cyst, there were several mural nodules with homogeneous enhancement, *multiple nodular shadows with uneven size and irregular shape were seen in the capsule, and the density in some nodules was uneven* (Fig. 1). There was a compression of the superior mesenteric and splenic vein by the mass without infiltration. The main pancreatic duct was not well delineated. The CT scan of the chest and abdomen did not show any hepatic or pulmonary metastasis. With the provisional diagnosis of pancreatic cystic neoplasm, surgical excision was planned for the patient.

Upon laparotomy, the mass was found to be located in the body and tail of the pancreas with displacement of the surrounding organs, including the gastric fundus and spleen, without invasion. There were dense adhesions around the tumor. During the dissection, the cyst got accidentally opened and approximately 1000 mL of clear viscous mucoid liquid was drained from the cystic mass. An en bloc resection of the distal pancreatic tumor was performed with splenectomy and regional lymphadenectomy. The operative time was 220 minutes and the intraoperative blood loss was 300 mL. *The* postoperative course was uneventful. The duration of hospital stay was 13 days. The amylase level of the cyst liquid was 6153 $U\ L^{-1}$.

Macroscopically, a 9 cm well-circumscribed tumor with soft texture and reddish surface was located in the pancreatic body and tail. On cut-section, the lesion showed unilocular macrocystic space communicating with the dilated main pancreatic duct. There were several solid mural nodules fastened to the capsule wall. Microscopically, IPMN associated tubular adenocarcinoma was present and showed protrusion in to the involved pancreatic duct (Fig. 2A). The spindle-shaped cells were observed at the periphery of the IPMN (Fig. 2A). In the solid mural nodules, there was storiform arrangement of the mononuclear spindle-shaped cells (Fig. 2B). The surgical margins were free of tumor cells. There was no perineural, vascular or lymph nodal invasion. The immunohistochemical results showed that the mononuclear spindle-shaped cells were positive for pan-cytokeratin (Fig. 3A) and vimentin (Fig. 3B), while they were negative for *chromogranin A (CgA), and synaptophysin (Syn)*. The proliferative index (Ki-67) of the spindle-shaped cells was high (approximately 60%). The final pathologic diagnosis was IPMN associated tubular adenocarcinoma with co-existent sarcomatoid (spindle-shaped cell) carcinoma.

After 3 months of follow-up, on a routine check-up with systemic position emission tomography (PETCT) scan, we found local recurrence, and metastasis in the small bowel mesentery. The patient received palliative gemcitabine therapy (1000mg m^{-2} weekly for 2 weeks and repeated every 4 weeks) at another hospital. CT scan performed 6 months following surgery showed development of liver and duodenum metastases. The patient succumbed to the disease 9 months after the surgery.

Discussion

Sarcomatoid (spindle cell) carcinoma is one of the histologic variants of the anaplastic carcinoma of the pancreas [8]. The other 2 histologic variants are pleomorphic cell type and giant cell type carcinoma [8]. The clinical symptoms of SCP are non–specific, including weight loss, fatigue, anorexia, abdominal pain, nausea, and vomiting [9]. These symptoms are similar to those seen in patients with conventional pancreatic adenocarcinoma (PDAC). Radiologically, SCP usually appear as large,

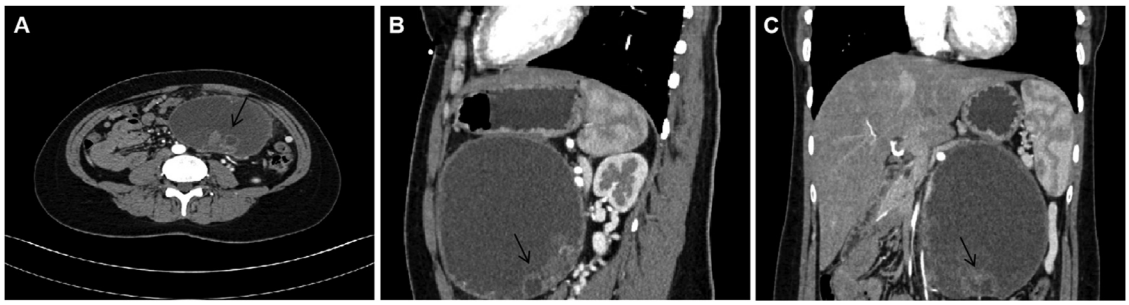

Fig. 1 – (A) Axial, (B) sagittal, and (C) coronal abdominal contrast-enhanced CT scan demonstrating a large pancreatic solid-cystic mass, there were multiple nodules in the capsule, the shape was irregular, and the density in some nodules was uneven (indicated by arrows).

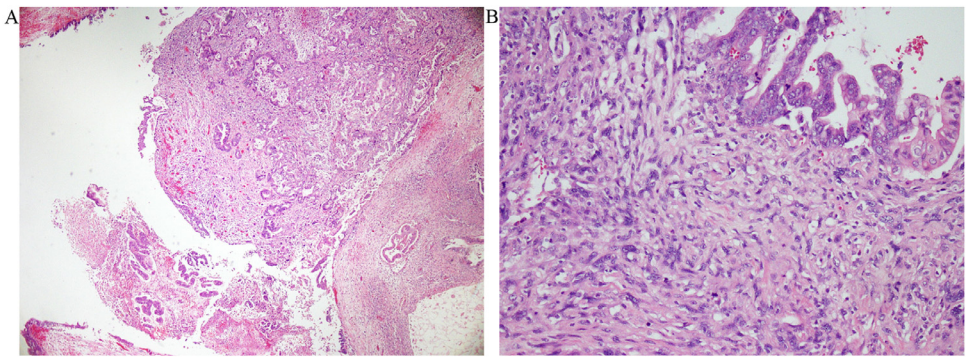

Fig. 2 – Microscopic appearance of the tumor: (A) IPMN associated tubular adenocarcinoma and scattered spindle-shaped cells (hematoxylin and/or eosin staining, 100 ×). (B) The mononuclear spindle-shaped cells in the solid mural nodules (hematoxylin and/or eosin staining, 200 ×).

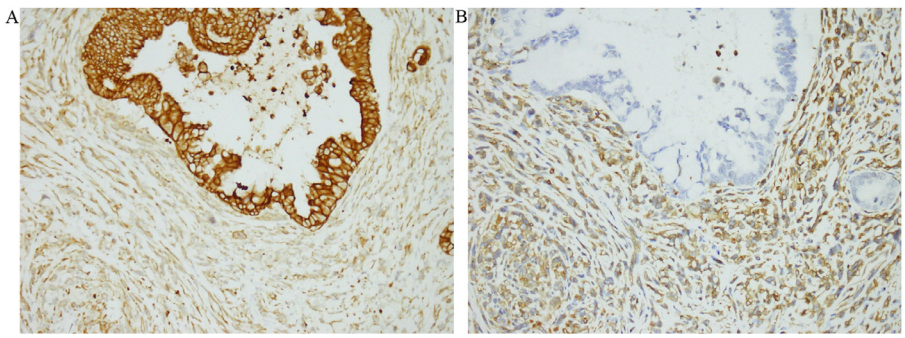

Fig. 3 – Immunohistochemistry: (A) The intraductal tubular adenocarcinoma cells and mononuclear spindle-shaped cells showing positive staining with epithelial marker pan-cytokeratin (200 ×). (B) Mononuclear spindle-shaped cells are immunoreactive for the mesenchymal marker vimentin, while intraductal tubular adenocarcinoma cells are negative for vimentin (200 ×).

exophytic, moderately hyper-vascular tumors with extensive areas of necrosis [10]. Hence, preoperative diagnosis of SCP is difficult. A definite diagnosis of SCP can be made only following histopathological examination. On immunohistochemistry, the spindle-shaped tumor cells are found to stain positively for *creatine kinase* (CK), S-100 protein, α1-chymotrypsin, α1-antitrypsin, anti–CA19-9 and *smooth muscle actin* (SMA) and no staining for vimentin [11]. However, in the present case, the malignant spindle cells were densely arranged in a storiform pattern in the solid mural nodules and were positive for both vimentin (mesenchymal maker) and pan-cytokeratin (epithelial maker), while the intraductal tubular adenocarcinoma cells were only positive for pan-cytokeratin.

The coexistence of anaplastic carcinoma with IPMN is very rare with only ten reported cases, including our case, in the English *literature [3,4,12]. Poultsides et al. [4] reported that 3 of the*

5 *patients were female with a median age of 72 years*. The case reported by Fujii *et al*. [12] was giant cell type, and this present case was spindle cell type. The histologic subtypes of the other 8 cases were not described in the literature.

The etiology of sarcomatoid (spindle cell) carcinoma arising in the setting of IPMN has not been elucidated. However, the process of epithelial-mesenchymal transition (EMT) may explain the development of spindle cells in IPMN. Moreover, during the malignant progression of PDAC and cholangiocarcinoma, epithelial tumor cells lose their restricted phenotypes, epithelial characteristics and acquire motile behavior, thereby promoting metastases [13,14]. However, the mechanism of the formation of SCP, and its metastasis with or without IPMN is poorly understood.

Previous reports have shown that the 5-year survival rate of patients with resectable IPMN associated invasive pancreatic carcinoma varies between 22% and 45% [15–17], which is typically greater than the 10%-25% 5-year survival rate observed in resectable PDAC [18–20]. However, the better outcomes in IPMN associated adenocarcinoma are observed with colloid carcinoma or tubular carcinoma. Patients with IPMN associated anaplastic carcinoma have a poor prognosis with a median survival of 9 months after resection, which is similar to PDAC [4].

Although the median survival time after surgery is low, radical pancreatic resection still remains the mainstay treatment for sarcomatoid (spindle cell) carcinoma. *To evaluate the residual tumor grade after pancreatectomy, the transection, and circumferential resection margins (CRM) were analyzed [21]. The transection margins include the pancreatic duct margin, the bile duct margin, the proximal duodenal and/or stomach margin, and the distal duodenal margin. The CRM include the anterior surface, the medial margin, and the posterior pancreatic surface or resection margin (RM) [22]. A clear (R0) resection margin is defined as tumor cells* $\geq$ *1 mm away from any margin or surface (R0* $>$*1 mm) [23], American Joint Committee on Cancer (AJCC) now defines R1 as cancer cells within 1 mm of the margin [24]*. Strobel *et al*. [25] suggested that the median survival was significantly better after R0/R1 resection than after palliative surgery (7.1 vs 2.3 months). Adjuvant therapy (chemotherapy with or without radiotherapy) for resected IPMN associated invasive carcinoma has been found to be associated with improved overall survival compared with surgery alone, especially for those with higher stage, positive lymph node, and poorly differentiated tumors [26].

In summary, sarcomatoid carcinoma of the pancreas is a rare subtype of anaplastic carcinoma that is associated with a poor prognosis. Surgical resection remains the mainstay treatment in such cases. Additionally, a large tumor size, and the presence of mural nodules in a cystic pancreatic tumor on cross-sectional imaging may indicate malignant transformation.

Patient consent statement

Informed consent for publication of the dataset from the participant was obtained. The data did not contain any direct or indirect identifiers of the participant, publication of such data does not compromise anonymity or confidentiality or breach local data protection laws.

Availability of data and materials

All data generated and analyzed during this study are included in this published article.

Authors' contribution

Chuanhang Zang and Zhexuan Ye performed the operation, gathered tissue samples, and fellow-up data of the patient. Shuai Li, Bo Chi, and Shuai Chen performed the histologic examination. Chuanhang Zang was major contributors in writing the manuscript. All authors read and approved the final manuscript.

Patient consent

The study was approved by ethics committee of the first hospital of Jilin university, consent to participate was obtained.

Publication of clinical datasets

Informed consent for publication of the dataset from the participant was obtained. The data did not contain any direct or indirect identifiers of the participant, publication of such data does not compromise anonymity or confidentiality or breach local data protection laws.

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