CASE REPORT

Pancreatic Adenosquamous Carcinoma with Direct Gastric Invasion : Preoperative Diagnosis by Endoscopic Biopsy —A Case Report

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Abstract : Pancreatic adenosquamous carcinoma (PASC) is a rare and highly aggressive subtype of pancreatic cancer with a dismal prognosis, and its preoperative diagnosis remains challenging. We report the case of an 82-year-old man who presented with epigastric pain and appetite loss. Imaging studies revealed a large, partially necrotic mass in the tail of the pancreas that was contiguous with the posterior gastric wall, accompanied by multiple metastases to the liver, lungs, regional lymph nodes, and peritoneum. Upper gastrointestinal endoscopy identified a large, excavated ulcer within a submucosal tumor-like elevation, and biopsies from the ulcer margin confirmed the presence of squamous cell carcinoma. The pathological findings showed PASC. The patient was diagnosed with Stage Ⅳ PASC, and palliative care was selected in view of advanced dementia and disease extent. This case shows that PASC can present with direct gastric penetration, and it highlights the value of direct endoscopic biopsy of the invaded gastric site to secure a definitive preoperative histopathologic diagnosis. PASC should be considered in the differential diagnosis of pancreatic masses that exhibit gastric invasion and marked internal necrosis on imaging. J. Med. Invest. 73 : 286-290, February, 2026

Keywords **:** *PASC, gastric invasion, direct endoscopic biopsy*

INTRODUCTION

Pancreatic adenosquamous carcinoma (PASC) is classified in the 8th edition of the Japanese Classification of Pancreatic Carcinoma as a histological subtype of invasive pancreatic ductal carcinoma (1). It is defined by adjacent or admixed adenocarcinoma and squamous cell carcinoma components, where the squamous cell component should account for at least 30% of the neoplasm. And a case is practically classified in this category when only squamous cell carcinoma components can be found in the routine examination (1). PASC is relatively rare, accounting for 1–4% among all pancreatic cancers (2, 3). It has a poor prognosis owing to its rapid growth and marked invasiveness into adjacent organs, lymph nodes, vessels, and nerve plexuses (4, 5). Herein, we report a case of PASC that presented with direct gastric invasion, where the diagnosis was successfully established via endoscopic biopsy of the resulting gastric ulcer.

CASE

An 82-year-old man presented with a 3-day history of epigastric pain and loss of appetite. His past history included curative endoscopic submucosal dissection for early gastric cancer at the age 79. On admission, his height was 162 cm ; weight, 60 kg ; temperature, 37.3 °C ; blood pressure, 136/94 mmHg ; and pulse, 130/min. No conjunctival pallor, jaundice, or cervical lymphadenopathy was observed, and the chest and abdominal findings were unremarkable. Laboratory tests revealed mild anemia (hemoglobin level 11.1 g/dL) and elevated aspartate aminotransferase (AST : 41 IU/L), lactate dehydrogenase (LDH : 383 IU/L), alkaline phosphatase (ALP : 377 IU/L), gamma-glutamyl transpeptidase (γGTP : 78 IU/L), total bilirubin (T-Bil : 1.9 mg/dL), and C-reactive protein (CRP : 8.01 mg/dL) levels. Tumor markers were also elevated : carcinoembryonic antigen (CEA) 6.9 ng/mL (normal <4.5), Duke pancreatic monoclonal antigen type 2 (DUPAN-Ⅱ) 160 U/mL (normal <150), squamous cell carcinoma antigen (SCC) 11.8 ng/mL (normal <2.5), and especially carbohydrate antigen (CA19-9) at 375.7 U/mL (normal <37).

Non-contrast chest-abdomen-pelvis computed tomography revealed an approximately 7 cm iso-dense, internally heterogeneous mass with calcification in the pancreatic tail, abutting the upper posterior wall of the stomach, with adjacent lymph node enlargement. Additionally, an approximately 8 cm mass, iso-dense periphery and a low-density center, was identified in the right hepatic lobe. And an irregularly shaped mass within the abdominal cavity was also noted (Figure 1A). In addition, scattered nodules were noted in both lungs (Figure 1B). Abdominal magnetic resonance imaging (MRI) revealed that the pancreatic tail mass was iso-intense on T1-weighted imaging (Figure 2A), hyper-intense on T2 fat-suppressed imaging (Figure 2B), and iso-intense with peripheral high intensity on diffusion-weighted imaging (Figure 2C). The MRI signal within the tumor was heterogeneous, suggesting the possibility of necrosis or fibrosis within the tumor. The pancreatic tumor was continuous with the posterior wall of the upper gastric body (Figure 2A, 2B). Particularly on T2 fat suppressed imaging images, the high signal intensity extended into the gastric wall lumen, indicating potential gastric wall invasion and penetration (Figure 2B). Liver metastases were identified throughout the liver, with tumors ranging from 1 cm to 8 cm in size. On T1-weighted

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images, they appeared as low signal intensity. The 8 cm tumor in the right lobe showed low signal intensity peripherally and isointense internally (Figure 2A). On T2 fat-suppressed images, the interior exhibited strong high signal intensity, suggesting a fluid content (Figure 2B). On diffusion-weighted images, the tumors demonstrated high signal intensity, with the right lobe tumor particularly exhibiting a doughnut-shaped morphology (Figure 2C). In addition, lymph node enlargement adjacent to the pancreatic tumor and an irregularly shaped mass was found in the abdominal cavity (Figure 1A, 2A), indicating lymph node and peritoneal metastases.

Upper gastrointestinal endoscopy revealed a submucosal tumor-like elevation on the posterior wall of the upper gastric body with a large excavated ulcer (Figure 3A, B). Biopsy specimens from the gastric ulcer margin showed strongly atypical cancer cells with keratinization and intercellular bridges on HE staining. They demonstrated findings consistent with squamous cell carcinoma, with no adenocarcinoma components observed (Figure 4A, B). In immunohistochemistry, tumor cells showed strong immunoreactivity for p40, suggesting squamous cell carcinoma. No adenocarcinoma component was observed (Figure 4C). A few number of tumor cells were immunoreactive with CA19-9 (Figure 4D).

Although only squamous cell carcinoma components were detected in the biopsy from the gastric ulcer, based on the definition in the 8th edition of the Japanese Classification of Pancreatic Carcinoma (1) and the imaging findings, the patient was diagnosed as PASC of the pancreatic tail with direct gastric wall invasion and distant metastases to the liver, lungs, lymph nodes, and peritoneum (clinical stage T3N1aM1, Stage IV). Given his advanced dementia, a palliative approach was selected. He was transferred to a long-term care hospital on hospital day 28 and died on hospital day 58.

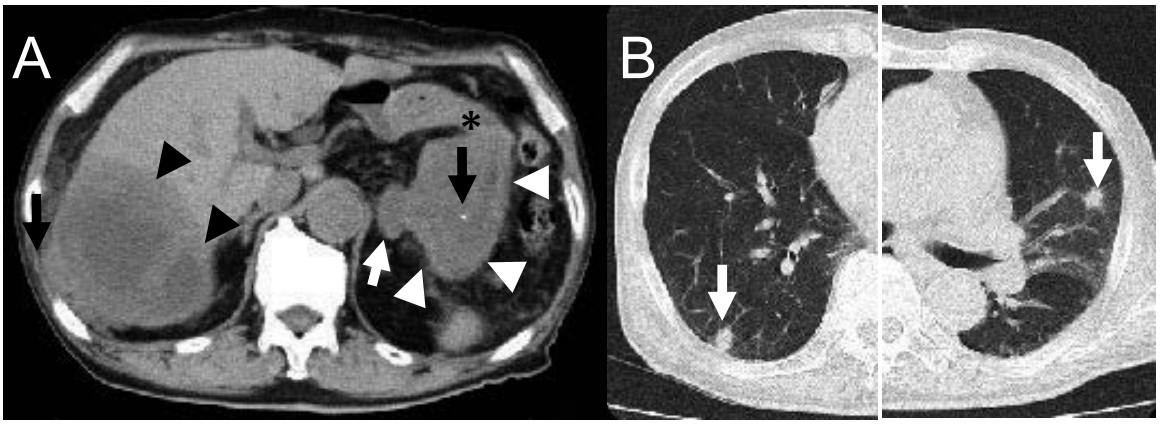

Figure 1. Abdominal computed tomography (CT) revealed a tumor (white arrowhead) of iso-density but heterogeneous internal structure, contiguous with the stomach (*) at the pancreatic tail, containing internal calcifications (black arrow). Additionally, it was associated with lymph node enlargement (white arrow), iso-density metastasis with low-dense central area in the right lobe of the liver (black arrowhead), and an irregularly shaped mass within the abdominal cavity (black arrow) (A). Chest CT demonstrated high-density bilateral pulmonary metastases (white arrows) (B).

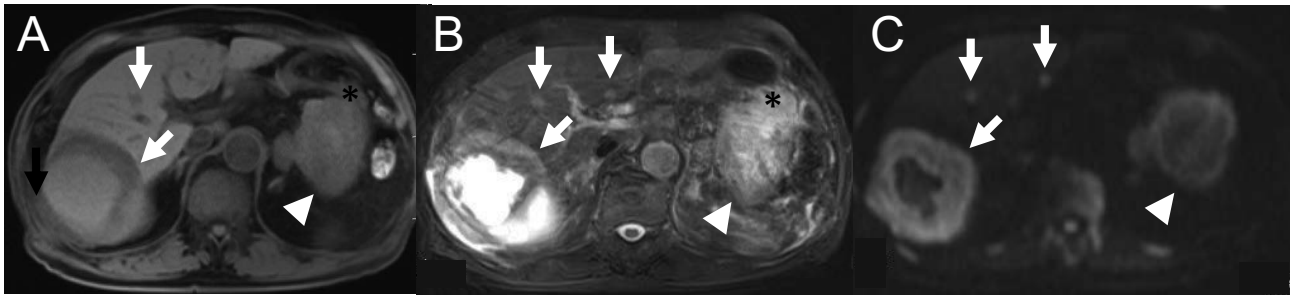

Figure 2. Abdominal magnetic resonance imaging (MRI) showed a pancreatic mass (white arrowhead) with internal heterogeneity, appearing iso-intense on T1-weighted images (A), hyper-intense on T2 fat-suppressed images (B), and low-intense with peripheral hyperintensity on diffusion-weighted images (C). It was in contact with enlarged lymph nodes and contiguous with the posterior wall of the upper gastric body (*) (A, B). Metastatic liver tumors (white arrow) were noted throughout the liver, appearing as low signal intensity on T1-weighted images (A), and high signal intensity on T2 fat-suppressed images (B) and diffusion-weighted images (C). The interior of an 8 cm tumor in the right hepatic lobe showed iso-signsl sintensity on T1-weighted images (A), and high-signal intensity on T2 fat-suppressed images (B), suggesting the presence of a liquid component. Furthermore, an irregularly shaped mass (black arrow) was noted within the abdominal cavity (A), showing peritoneal metastasis.

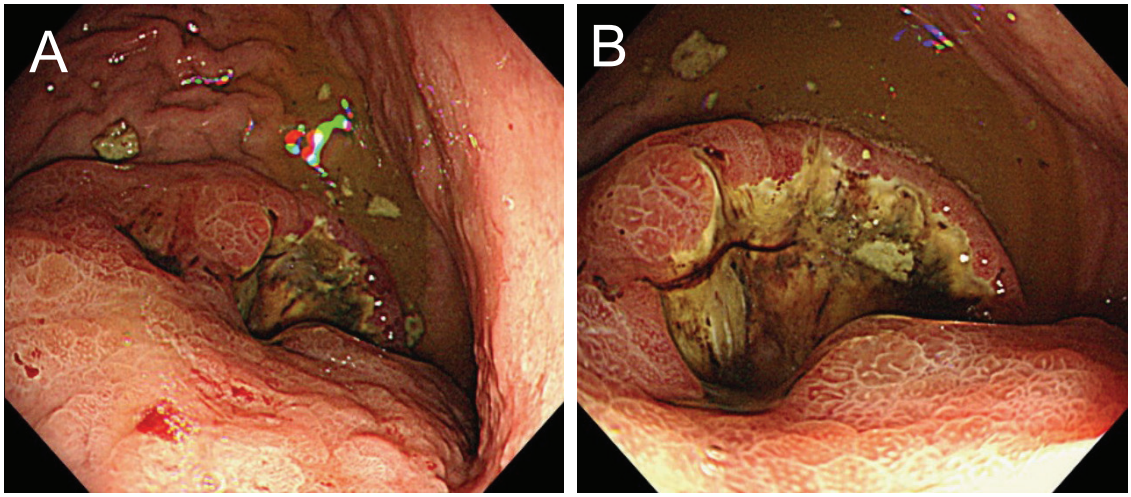

Figure 3. Upper gastrointestinal endoscopy revealed submucosal tumor-like elevation on the posterior wall of the upper gastric body with a large, excavated ulcer on the posterior wall of the upper gastric body (A, distant view ; B, close-up view).

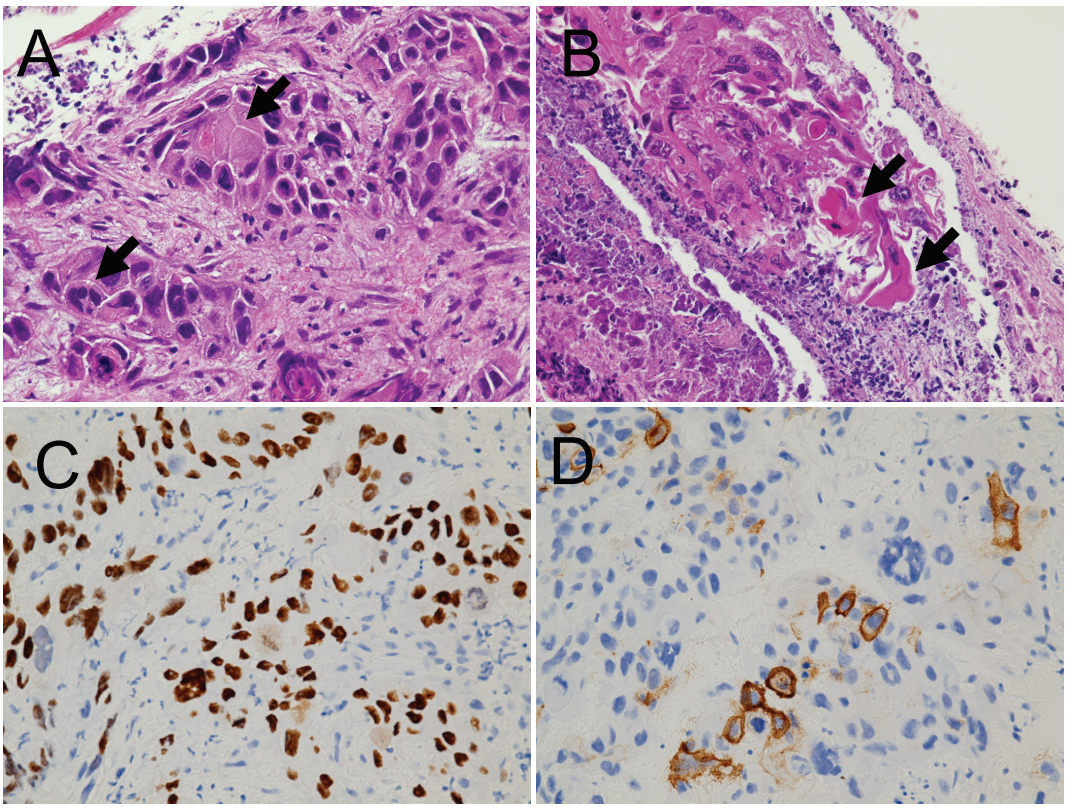

Figure 4. Pathological findings in H&E staining (A, B) from the gastric ulcer revealed highly atypical carcinoma cells with intercellular bridges (A, arrow) and keratinization (B, arrow), consistent with squamous cell carcinoma. Immunohistochemistry revealed strong p40 immunostaining in tumor cells (C), and partial staining of tumor cells was observed with CA19-9 immunostaining (D). (A, B : H&Ex40, C : p40x40, D : CA19-9x40)

DISCUSSION

This case involved gastric intraluminal penetration by a pancreatic tumor, with endoscopic biopsies from the ulcer demonstrating strongly atypical squamous cell carcinoma tissue with keratinization and intercellular bridges, establishing the diagnosis of PASC.

Macroscopically, PASC tends to exhibit expansive growth and, with rapid tumor enlargement, frequently develops internal necrosis, hemorrhage, and cystic changes. Charbit *et al*. (6) reported that the doubling time of squamous cell carcinoma is half of that of adenocarcinoma in human tumors. Based on this, squamous cell carcinoma is considered to be more apt to be necrotic than adenocarcinomas, because angiogenesis for blood supply cannot catch up with the growth of the tumor (7). The rapid growth of squamous components in PASC is presumably related with bleeding or cystic and necrotic transformations of the tumor (8). And these features may help differentiate PASC from conventional pancreatic ductal adenocarcinoma (PDAC). The characteristics of an imaging diagnosis are rich vessel proliferation and cystic transformation accompanied by internal necrosis, as well as calcification. CT and MR imaging features could be a useful clue for diagnosing PASC (9). Contrast-enhanced CT of PASC revealed contrast enhanced margins accompanied by non-contrast-enhanced lesions inside, suggesting hemorrhage or necrosis changes. This finding is effective for differentiating PASC from pancreatic ductal carcinoma (8, 9). In addition, it is a characteristic of adenosquamous cell carcinoma that T2-weighted MRI shows a high-intensity signal in the tumor (10). In our case, the interior of the pancreatic tail tumor appeared as an area of iso-density on plain CT, but was internally heterogeneous, suggesting necrotic changes within the tumor (Figure 1A). MRI revealed that the pancreatic tumor exhibited a heterogeneous hyperintense signal on T2 fat-suppressed images, and metastatic lesions throughout the liver also exhibited high signal intensity, but the center of the 8 cm tumor in the right lobe of the liver exhibited a homogeneous, intense high signal intensity (Figure 2B). These findings may also reflect necrotic changes in the pancreas, cystic changes associated with rapid proliferation of the liver tumor, necrosis, or old hemorrhagic changes, consistent with typical findings of PASC.

Biologically, the squamous component has been implicated in faster growth and higher malignancy. Its growth rate is nearly twice that of the adenocarcinoma component, with a shorter doubling time leading to expansile growth and larger tumor size at detection compared with adenocarcinoma (6). At the molecular level, PASC is less differentiated than adenocarcinoma, exhibits more genomic abnormalities and marked genomic instability, and shows greater intratumoral heterogeneity, including the pathological transition from adenocarcinoma to squamous components (11). In addition to KRAS mutations in adenocarcinoma and squamous carcinoma cells, multiple genetic alterations, such as those in p53 and SMAD4, have been implicated in PASC pathogenesis (11, 12).

Metastatic gastric tumors from pancreatic cancer are rare. Oda *et al*. reported that the incidence of gastric metastasis from solid malignant tumors excluding direct invasion was 5.4%, but gastric metastasis excluding direct invasion from pancreatic cancer was observed in only 2 of 209 autopsy cases (13). On the other hand, PASC more frequently involves invasion into adjacent organs and blood vessels, has a higher frequency of lymph node metastasis (5), and direct invasion into the stomach and transverse colon has also been reported (8). Furthermore, Cedeno Kelly *et al*. reported that PASC in the tail of the pancreas can cause gastric wall infiltration and splenic infarction, while PASC in the head of the pancreas can cause obstructive jaundice and pancreatitis (14). Therefore, direct invasion of the gastric wall is suspected to be a frequent pathological condition in pancreatic tail PASC, potentially leading to easier preoperative histological diagnosis of PASC than the gastric lumen. However, there are very few reported cases of pancreatic adenosquamous carcinoma diagnosed preoperatively by histological examination of the site of gastric wall invasion. A search of PubMed and the Japanese database "Igakutyuozassi" using the keywords "pancreatic adenosquamous carcinoma" and "pancreatic squamous cell carcinoma" up to 2025 revealed only five reported cases of pancreatic adenosquamous carcinoma diagnosed preoperatively by gastric biopsy of the site of gastric wall invasion : Sekoguchi *et al*. (10), Hayashibe *et al*. (15), Takeuchi *et al*. (8), Kudo *et al*. (16), and Kim *et al*. (17, 18). The preoperative diagnosis of PASC is difficult, and many cases are diagnosed during surgery or autopsy. Nonetheless, histopathological diagnosis by biopsy of the invasion sites in other organs or endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has been reported (19). Obtaining a pathological diagnosis before treatment is crucial in pancreatic cancer care. The 2025 Japanese Pancreatic Cancer Clinical Practice Guidelines consider EUS-FNA a useful diagnostic modality for pancreatic masses ; however, its limitations include false negatives/positives, reduced accuracy in small lesions, and the risk of needle tract seeding (20). As an alternative, direct biopsy of tumor-invaded sites in the stomach or duodenum is a viable option (20). When imaging shows growth morphology characteristic of PASC or when gastric/duodenal invasion is present, PASC should be considered, and a direct biopsy of the invaded gastrointestinal site may be valuable.

The prognosis of PASC is poor, regardless of tumor size. Smoot *et al*. reported a median overall survival of 14.4 months after R0 resection, 8 months after R1 resection, and 4.8 months without surgery (4). In Japan, Imaoka *et al*. reported that the median overall survival was 15.7 months for PDAC compared with 8.3 months for PASC ($p = 0.026$) (21). Surgical resection is the first-line option when distant metastasis is absent ; however, many patients are ineligible for surgical resection owing to advanced disease, as in the present case. Chemotherapy generally follows the PDAC regimens, including S-1 monotherapy, S-1 plus gemcitabine, S-1 plus platinum agents, and paclitaxel-containing combinations. Auvray Kuentz *et al*. reported that FOLFIRINOX (FX) and gemcitabine-nab paclitaxel (GN) may be effective as first-line treatment regimens for advanced PASC (22). Immunotherapy is gaining attention as a promising option. In particular, the squamous cell carcinoma component may express high programmed death-ligand 1 (PD-L1) expression, raising the possibility of therapeutic effects of immune checkpoint inhibitors on PASCs (23).

In recent years, advances in chemotherapy for pancreatic cancer have led to an increasing number of reports of so-called conversion surgery, which enables resection even in cases of pancreatic cancer previously deemed unresectable at diagnosis. The usefulness of neoadjuvant therapy in pancreatic adenosquamous carcinoma (PASC) remains unclear. However, Walsh *et al*. reported that in patients with stage I-III PASC who underwent curative surgical resection, those who received neoadjuvant therapy before surgery had a significantly longer median overall survival compared with those who underwent surgery first (20.7 months vs. 15.9 months, $p = 0.03$) (24). Neoadjuvant therapy may improve the prognosis of PASC patients, and the importance of preoperative diagnosis of PASC is likely to increase in the future.

In conclusion, when pancreatic tumors exhibit characteristic findings such as internal necrosis and cyst formation, PASC should be included in the differential diagnosis. In cases with suspected gastric invasion that involves the luminal surface of

the gastric mucosa, a direct endoscopic biopsy of the invaded site can be an effective method for establishing a definitive preoperative diagnosis.

CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflicts of interest in association with the present study.

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