Synchronous Pancreatic Acinar Cell Adenocarcinoma and Gastric Adenocarcinoma: a Case Report and Literature Review

Tian Fang
Jilin University First Hospital https://orcid.org/0000-0002-2267-7755
Tingting Liang
Jilin University First Hospital
Yizhuo Wang
Jilin University First Hospital
Chang Wang (wangchang@jlu.edu.cn)
Department of Oncology, First Hospital of Jilin University

Case Report

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Abstract

Background: Multiple primary malignant tumors are two or more malignancies in an individual without any relationship between the neoplasms. In recent years, increasing number of cases have been reported. However, Synchronous double primary gastric cancer and pancreatic acinar cell carcinoma are relatively rare to be reported. Further, most pancreatic tumors are consistent with pancreatic ductal adenocarcinomas, and other histologies are rare. We present the first case of synchronous pancreatic acinar cell adenocarcinoma and gastric adenocarcinoma.

Case presentation: A 69-year-old man came to our department with a history of vomiting, epigastric pain, and weight loss. Imaging revealed space-occupying lesions in the stomach and the tail of the pancreas, respectively. The patient underwent laparoscopic radical gastrectomy and pancreatectomy simultaneously. The pathologies of surgical specimens were completely different: the resected gastric specimen was a moderate to poorly differentiated adenocarcinoma, whereas the pancreatic tumor was consistent with acinar cell carcinoma. The patient was treated with six cycles of oxaliplatin and S-1 chemotherapy. As of March 2021, the patient was healthy without any recurrence or metastasis. After reviewing lots of literatures on simultaneous pancreatic and gastric cancers at home and abroad, we discuss the clinical characteristics of these rare synchronous double cancers. Most of the cases had undergone surgery and adjuvant chemotherapy, and all of the cases were pathologically confirmed by postoperative specimen.

Conclusions: Synchronous pancreatic acinar cell and gastric adenocarcinoma can occur and should be considered when tumors are found in these organs.

Introduction

Pancreatic carcinoma and gastric carcinoma are the second and fifth most common digestive system tumors, respectively [1]. Pancreatic cancer is one of the deadliest malignancies and is usually diagnosed at an advanced stage, leading to poor overall survival. Synchronous double gastric cancer and pancreatic cancer is very rare. This report describes a rare case of synchronous double pancreatic acinar cell adenocarcinoma (PACC) and gastric adenocarcinoma. This is the first case of double cancers related to PACC and gastric cancer. Furthermore, we review the literature of synchronous gastric and pancreatic tumors in the PubMed, Web of Science, CNKI, and Embase databases and discuss the principles of treatment and prognosis of synchronous pancreatic and gastric tumors.

Case Presentation

Chief complaints

A 69-year-old man came to our department with a history of vomiting, epigastric pain for 3 months, and weight loss about 5 kg.

History of present illness

The patient developed vomiting, epigastric pain 3 months previously.

History of past illness

The patient had no past illness.

Personal and family history

Two younger brothers of patient had lung cancer and throat cancer, respectively.

Physical examination

The patient's temperature was 36.3℃, heart rate was 65 beats per min, respiration was 17 breaths per min, and blood pressure 131/86 mmHg. Clinical abdominal examination showed that the abdomen was soft and flat, with obvious tenderness in the upper abdomen, no muscle tension, no rebound pain, and no abdominal mass was touched.

Laboratory examinations

Laboratory test results were almost normal. The results of blood, urine and stool tests were within the normal ranges. The carcinoembryonic antigen in tumor markers was slightly elevated (4.06 ng/mL; normal: < 3.4 ng/mL).

Imaging examinations

Gastroscopy revealed a large ulcer about 5.5 × 6.6 × 0.5 cm originating from the gastric fundus, and pathological biopsy revealed gastric adenocarcinoma. Abdominal contrast-enhanced computed tomography (CT) indicated uneven thickening in the antrum of the stomach with irregular mucosa and heterogeneous contrast enhancement on the antrum of the gastric wall, as well as a space-occupying lesion about 34 × 16 mm in the tail of the pancreas (Fig. 1). Because there were no definite contraindications, the patient underwent laparoscopic exploration, which revealed masses in the stomach and pancreas. After evaluating the resectability of the gastric and pancreatic tumors, the patient underwent laparoscopic radical gastrectomy, gastric vagotomy, pancreatectomy, and splenectomy (Fig. 2).

Further diagnostic work-up

The resected stomach lesion was 5 × 5 × 1.5 cm, and the Lauren classification was the intestinal type. The pathology of the resected specimen from the stomach confirmed moderately to poorly differentiated adenocarcinoma (pStage IIIB, T4aN2M0 per the American Joint Committee on Cancer [AJCC] seventh edition criteria) (Fig. 3A). The tumor had invaded the serous membrane but did not involve adjacent structures. Perineural and vascular infiltration were observed. Regional nodes were positive (4/32), and the resection margins were free of tumor cells. The cancer cells did not infiltrate the omentum, and there was no metastasis in the omentum lymph nodes.

Immunohistochemistry indicated positivity for pan-cytokeratin and villin and partial positivity for CK7 (Fig. 3B). The tumor was negative for HER-2 (4B5) and CK20. The Ki-67 positivity was about 50% in a high-power field.

The volume of the resected pancreatic specimen was 4.1 × 2.2 × 1.5 cm. The pathology was consistent with PACC (pStage III, T3N1M0 per the AJCC seventh edition criteria) (Fig. 4A, B). Perineural infiltration was observed, but there was no vascular infiltration. Regional nodes were negative, and the resection margins were free of tumor cells.

Immunohistochemistry indicated positivity for CAM5.2, CK19, CK7, and membranous expression of beta-catenin and scattered positivity for carcinoembryonic antigen. The Ki-67 positivity was 30% in one high-power field (Fig. 4C-4F). The tumor was negative for vimentin, chromogranin A, synaptophysin, CD10, and CD56.

FINAL DIAGNOSIS

The final diagnosis of the presented case was synchronous moderately to poorly differentiated gastric adenocarcinoma (pStage IIIB, T4aN2M0) and PACC (pStage III, T3N1M0).

TREATMENT

The patient underwent laparoscopic radical gastrectomy, gastric vagotomy, pancreatectomy and splenectomy. One month after the operation, chemotherapy consisting of oxaliplatin and S-1(SOX) was initiated. The patient was treated with six cycles of chemotherapy.

OUTCOME AND FOLLOW-UP

As of March 2021, the patient was healthy without any recurrence or metastasis by imaging examination.

Discussion

The present case of synchronous double primary cancer of pancreas and gastric was confirmed by postoperative pathological and immunohistochemical analyses. The reason why we reported this case is that the incidence of synchronous gastric

adenocarcinoma complicated with PACC is rare, especially the incidence of PACC alone is relatively low, accounting for approximately 1%-2% of exocrine pancreatic neoplasms [2].

Previous studies have shown an incidence of gastric cancer with a synchronous second primary cancer of 1.0–5.0% [3–5]. Gastric carcinoma associated with pancreatic carcinoma accounts for 5% of all cases of gastric carcinoma associated with carcinoma of other organs, ranking forth [3]. Correspondingly, the most common synchronous tumor associated with pancreatic cancer was gastric cancer [6]. The overall survival of pancreatic cancer patients with stomach cancer (33.9 months) was significantly better than that of patients with only pancreatic cancer (17.0 months) [6]. This may be due to the fact that patients with pancreatic cancer are at an early stage when synchronous double cancers are diagnosed.

After reviewing lots of literatures on simultaneous pancreatic and gastric cancers at home and abroad, we found out synchronous double tumors involving the two organs are rare, among which PACC is even rarer. Details of reported cases are shown in Table 1 [7–20], including our case. The average age at diagnosis is 67 years (range 42–77 years), and men are twice as likely to be diagnosed with synchronous pancreatic and gastric cancer than women. Pancreatic ductal adenocarcinoma (PDAC) is the most common pancreatic tumor in these cases. PACC accounts for 11.1% (2/17) among the 17 synchronous double cancer cases, while PDAC accounts for 70.6% (12/17). The remaining 3 cases did not mention the pathological type. The most common tumor location is the head of the pancreas, accounting for 66.7% of cases (10/15). Two cases of tumors in the body of the pancreas and three cases of tumors located in the tail of the pancreas have been described. In two cases, the tumor location was not reported. Eleven patients (64.7%) underwent surgery for the double tumors. All of these cases were pathologically confirmed by postoperative specimen and none were diagnosed before surgery, which was consistent with our case. That these patients were able to undergo curative resection may indicate that these patients are diagnosed at earlier stages and are likely to have better prognoses than patients with only pancreatic cancer. This also highlights that synchronous double tumors do exist, and a second tumor should not necessarily be considered metastasis from another organ, which could lead to misdiagnosis and the abandonment of surgical resection.

Table 1
Reported cases of synchronous gastric and pancreatic tumors.

Author, year	Age	Gender	Gastric tumor location	Gastric histology	Pancreatic tumor location	Pancreatic histology	Treatment
Eriguchi N et al. (2000)[7]	76	male	upper gastric angle	Moderately differentiated tubular adenocarcinoma	Not mentioned	Well to moderately differentiated tubular adenocarcinoma	surgically treated
Kubota E et al. (2009) [8]	67	male	Not mentioned	Moderately differentiated adenocarcinoma	Not mentioned	Absence of pancreatic histology	Chemotherapy:S-1, paclitaxel and lentinan
Meng L et al. (2010) [9]	42	male	gastric antrum	gastric GIST	pancreatic head	pancreatic GIST	surgically treated
SHEN Z.L et al. (2010)[10]	72	female	major gastric curvature	gastric GIST	the head of the pancreas	poorly differentiated PDAC; malignant fibrous histiocytoma	surgically treated
Muroni M et al. (2010)[11]	73	None	gastric antrum and pyloric portion	moderately differentiated adenocarcinoma	uncinate portion of the pancreas	poorly differentiated PDAC	surgically treated
Dasanu CA et al. (2011)[12]	75	male	Not mentioned	GIST	the head of the pancreas	moderately to poorly differentiated carcinoma	surgically treated
Kourie HR et al. case 1 (2012) [13]	56	male	anterior part of the antrum	Poorly differentiated adenocarcinoma with independent mucus-secreting cells	the head of the pancreas	Necrotic ductal adenocarcinoma	Chemotherapy: Folfirinox
Kourie HR et al. case 2 (2012)[13]	62	male	gastric wall of the greater curvature	Gastric adenocarcinoma with mucinous component	tail of the pancreas	Tubular adenocarcinoma (ck7+; ck20-; ck19+)	Chemotherapy: Folfirinox
Ohtsubo K et al. (2013)[14]	77	male	in the middle of stomach	Adenocarcinoma stage IB, T2bN0M0	pancreatic head	Adenocarcinoma stage IIA, T3N0M0	treated with chemotherapy:S-1
Baba H et al. (2015) [15]	70	male	The fundal region and greater curvature of the stomach	low grade gastric calcified stromal tumor (GIST)	the head of the pancreas	adenocarcinoma	surgically treated
Ghothim M et al. case 1 (2015) [16]	73	male	The antrum of the stomach	adenocarcinoma (pT1N1M0 stage IB, G2)	the head of the pancreas	ductal pancreatic cancer. (pT2N1M0, stage IIB, G3)	surgically treated; gemcitabine in six cycles

GIST = Gastrointestinal Stromal Tumors; PDAC = Pancreatic ductal adenocarcinoma; ACC = acinar cell carcinoma.

Author, year	Age	Gend-er	Gastric tumor location	Gastric histology	Pancreatic tumor location	Pancreatic histology	Treatment
Ghothim M et al. case 3 (2015) [16]	74	male	The antrum of the stomach	gastric adenocarcinoma diffuse type (pT2bN2M0, G3)	pancreatic head	papillary mucinous carcinoma (pT2N0M0, stage IB, G1)	Surgically treated; Radiotherapy and chemotherapy
Fiore M et al. case 1(2015)[17]	63	male	Not mentioned	gastric GIST (T2N0)	pancreatic head	adenocarcinoma (T2N0)	surgically treated
Santos-Fernández J et al. (2015)[18]	64	female	prepiloric antral ulcer	well differentiated gastric adenocarcinoma (T1N0M0)	pancreatic tail	pancreatic adenocarcinoma (T3N1M1)	Not mentioned
Arabadzhie-va E et al. (2016)[19]	60	female	in the pyloric area	gastric GIST	pancreatic body	pancreatic neuroendocrine tumor	surgically treated
Yonenaga Y et al. (2016)[20]	63	male	antrum of the stomach	ACC of gastric	the body of the pancreas	ACC of pancreas	Chemotherapy
Our case (2021)	69	male	antrum of the stomach	gastric adenocarcinoma	the tail of the pancreas	ACC of pancreas	surgically treated;Chemotherapy

GIST = Gastrointestinal Stromal Tumors; PDAC = Pancreatic ductal adenocarcinoma; ACC = acinar cell carcinoma.

The clinical manifestations of PACC are related to the location and size of the tumor. Unlike patients with PDAC, patients with PACC present with nonspecific symptoms, including abdominal discomfort, weight loss, weakness, nausea, vomiting, melena, and diarrhea [21]. Further, clinical symptoms common in PDAC, such as painless obstructive jaundice, are uncommon in PACC [22].

Endoscopic ultrasonography (EUS) and imaging findings such as CT and magnetic resonance imaging (MRI) are helpful to assist with achieving a correct preoperative diagnosis for double cancers [23]. CT is a valuable tool for the accurate preoperative evaluation of the local extent of gastric cancer and EUS can be used for histopathological confirmation [24]. PACC is typically completely solid when small and contains cystic or necrotic areas when large and generally lacks the dilatation of the biliary or pancreatic duct on CT [25]. However, it is difficult to diagnose PACC on the basis of radiological findings alone. EUS-guided fine-needle aspiration (EUS-FNA) has a very high sensitivity (> 85%) and specificity (> 95%) for diagnosis of malignancy in a solid pancreatic mass compared to cross-sectional imaging (CT/MRI) [26]. Whereas the position of the pancreas is relatively deep and it is also difficult to take a EUS-FNA. An experienced radiologist can give a preliminary imaging diagnosis of PDAC, which tends to be hypovascular, suggesting hypoechoic on imaging [27]. However, it is difficult to distinguish whether the primary tumor has metastasized to other organs in imaging, because tumors can also metastasize through the hematogenous or the lymphatic pathway in addition to direct invasion. If necessary, preoperative pathology must be performed to opt for the correct surgical approach. The present case of abdominal CT revealed a 41mm heterogenous mass with a clear boundary in the tail of the pancreas, which is suggestive.

The prevalence of pancreatic metastasis of gastric cancer is extremely rare. There were only 12 cases of isolated pancreatic metastasis in gastric cancer in the previous literature [28]. Correspondingly, metastatic gastric tumor secondary to pancreatic carcinoma is an unusual clinical event. There were only 7 cases of gastric metastasis of pancreatic cancer in the previous literature [29–35]. All of these cases, the histopathology and immunohistochemical of primary cancer and metastatic cancer are consistent. This is completely different from our case. In terms of histopathology, the two resected specimens were different, showing that adenocarcinoma in the stomach and acinar cell carcinoma in the pancreas. Moreover, immunohistochemical studies showed differences in staining at the two sites. Finally, we concluded that both of them were primary tumors, not metastatic tumors.

PACC is associated with a better prognosis than PDAC but a worse prognosis than pancreatic neuroendocrine tumors [36]. Metastatic PACCs are generally not curable and are treated with systemic chemotherapy [36]. The treatment regimens have not yet been standardized. Most of the treatment regimens used are the same as those used for PDAC or colorectal cancer [36]. Simultaneous removal of double primary carcinomas should be attempted, radiotherapy and chemotherapy should also be considered for patients who need adjuvant treatment decided by both disease stage [37]. If it is necessary to adjuvant treatment, try to choose an antineoplastic therapy that takes both into account. In our case, whether gastric adenocarcinoma or PACC, the optimal chemotherapy regimens are SOX.

Above, we have ruled out the possibility of gastric and pancreatic malignant tumors metastasizing to each other. But is there a pathological type similar to acinar cell carcinoma (ACC) in gastric? Reviewing literatures of databases, we found that ACC could arise in the gastric as a polypoid submucosal tumor in the routine diagnostic field of gastric endoscopy [38]. By summarizing the six case reports published so far [38–41], we concluded that the diagnosis and treatment of ACC of gastric are basically consistent with that of PACC. On the one hand, immunohistochemical staining is the same as PACC showing strong positive reactions for antitrypsin and antichymotrypsin [42]. On the other hand, the main treatment method is surgery to prolong overall survival. The pathology of gastric cancer in our case was not this special type, it was a common gastric adenocarcinoma.

Conclusions

The case we reported about synchronous PACC and gastric cancer is rare and suggests that when treating patients with malignant tumors, the possibility of developing a simultaneous double primary malignancy should be considered. Imaging can find out space-occupying lesions but it is difficult to distinguish whether it is double primary or metastasis cancers. The golden criterion is the diagnosis of pathology. Simultaneous removal of resectable multiple primary carcinomas should be attempted, adjuvant treatment including radiotherapy and chemotherapy should also be considered. For those patients who are already in advanced stages at the time of diagnosis can be treated with chemotherapy and radiotherapy to improve the quality of life and prolong overall survival. In a word, the incidence of synchronous multiple primary malignancies does not necessarily signify an unfavorable prognosis, as long as satisfactory diagnosis and effective treatment are performed. More clinical experience needs to be accumulated in future.

Abbreviations

AJCC: American Joint Committee on Cancer; ACC: Acinar cell carcinoma;

PDCA: Pancreatic ductal adenocarcinoma; PACC: Pancreatic acinar cell carcinoma

CT: Computed tomography; MRI: magnetic resonance imaging

SOX: oxaliplatin and S-1; EUS: Endoscopic ultrasonography

EUS-FNA: EUS-guided fine-needle aspiration

Declarations

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Availability of data and materials

All data generated or analyzed during this case are included within the article.

Ethics approval and consent to participate

The need for ethics approval and consent was waived, since a consent for publication was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Written informed consents were obtained from the patients or family of the patient for publication of this Case series and any accompanying images.

Authors' contributions

W.C. proposed the study, interpreted the data, and revised and finalized the manuscript. F.T., L.T.T, and W.Y.Z. collected, analyzed and interpreted the data and drafted the manuscript. All authors issued final approval for the version to be submitted.

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Figures

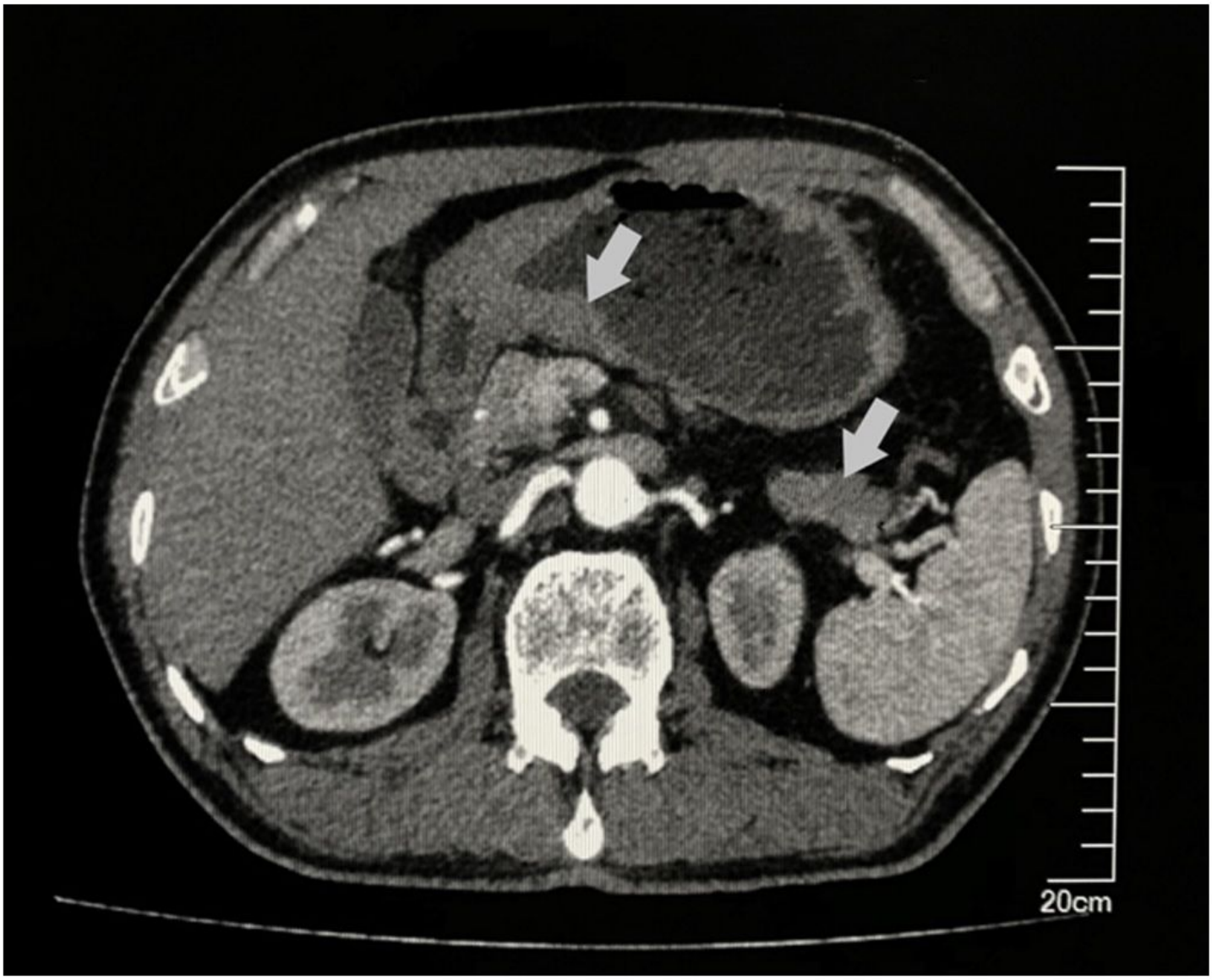

Figure 1

On contrast-enhanced CT of stomach, white arrow on the left showed uneven thickened with irregular mucosa and heterogeneous contrast enhancement on the antrum of gastric wall; white arrow on the right indicated a space-occupying lesion about 34*16mm in the tail of the pancreas.

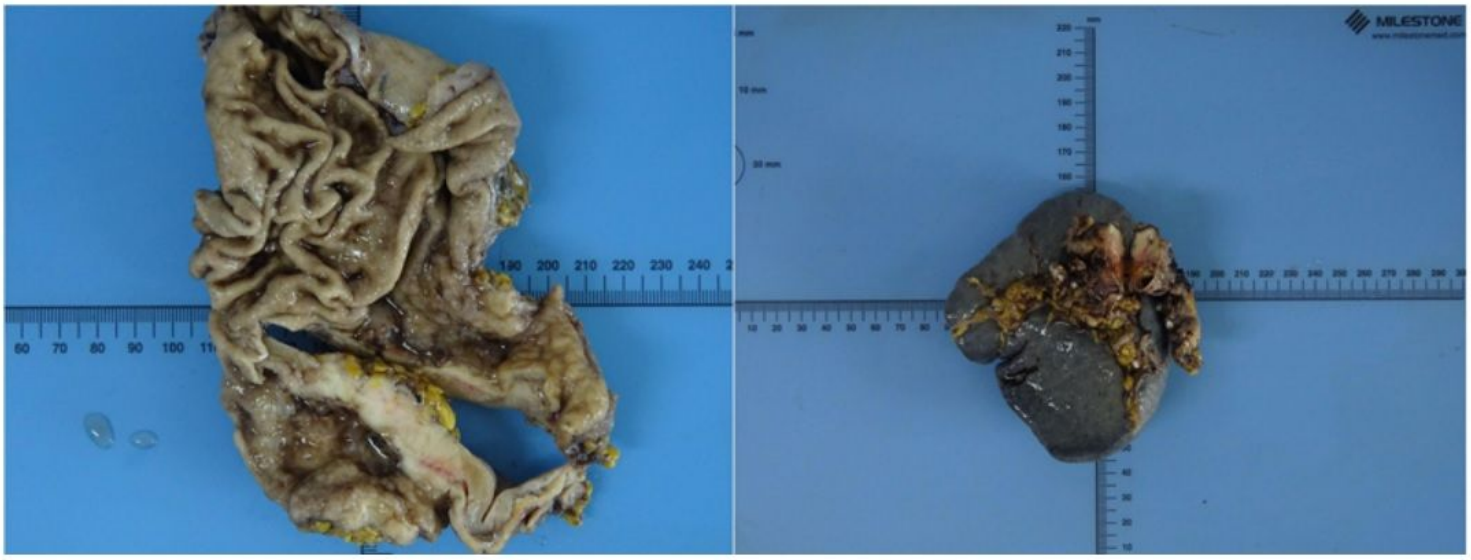

Figure 2

Specimen of resection (the left is gastric tumor and the right is pancreatic tumor)

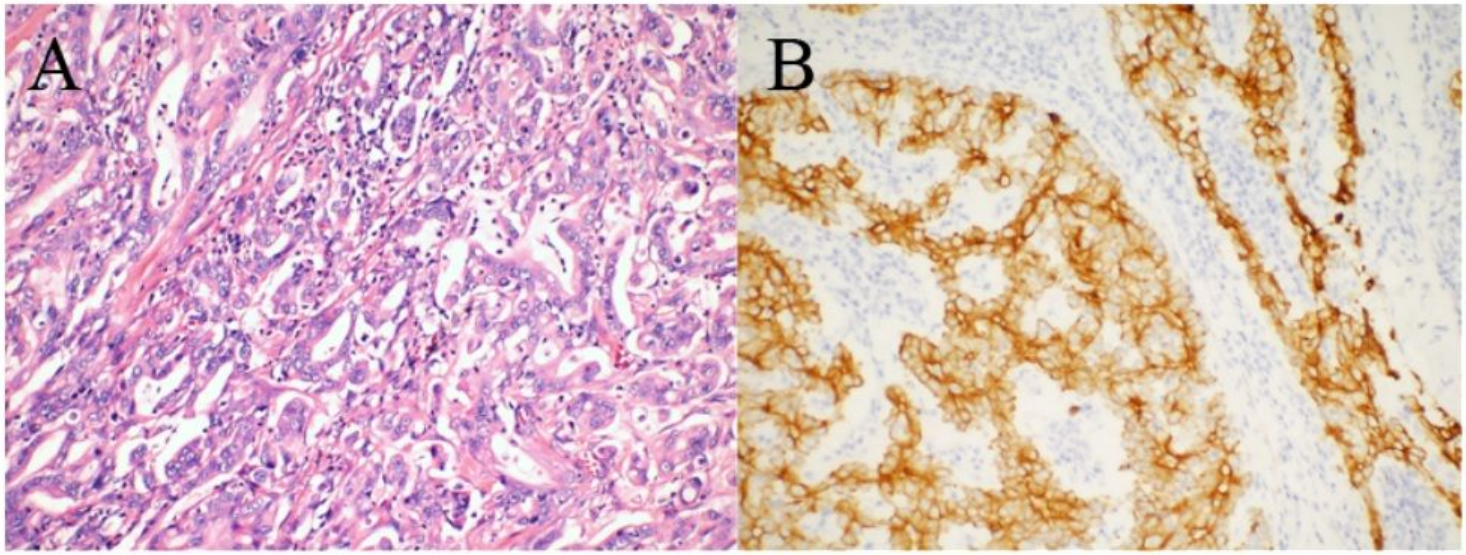

Figure 3

Microscopic examinations. Routine histology, stained using hematoxylin-eosin (H&E), shows gastric adenocarcinoma (A, ×200). Immunohistochemical staining of gastric tumor cells is partial positive for Cytokeratin 7 (B, ×200)

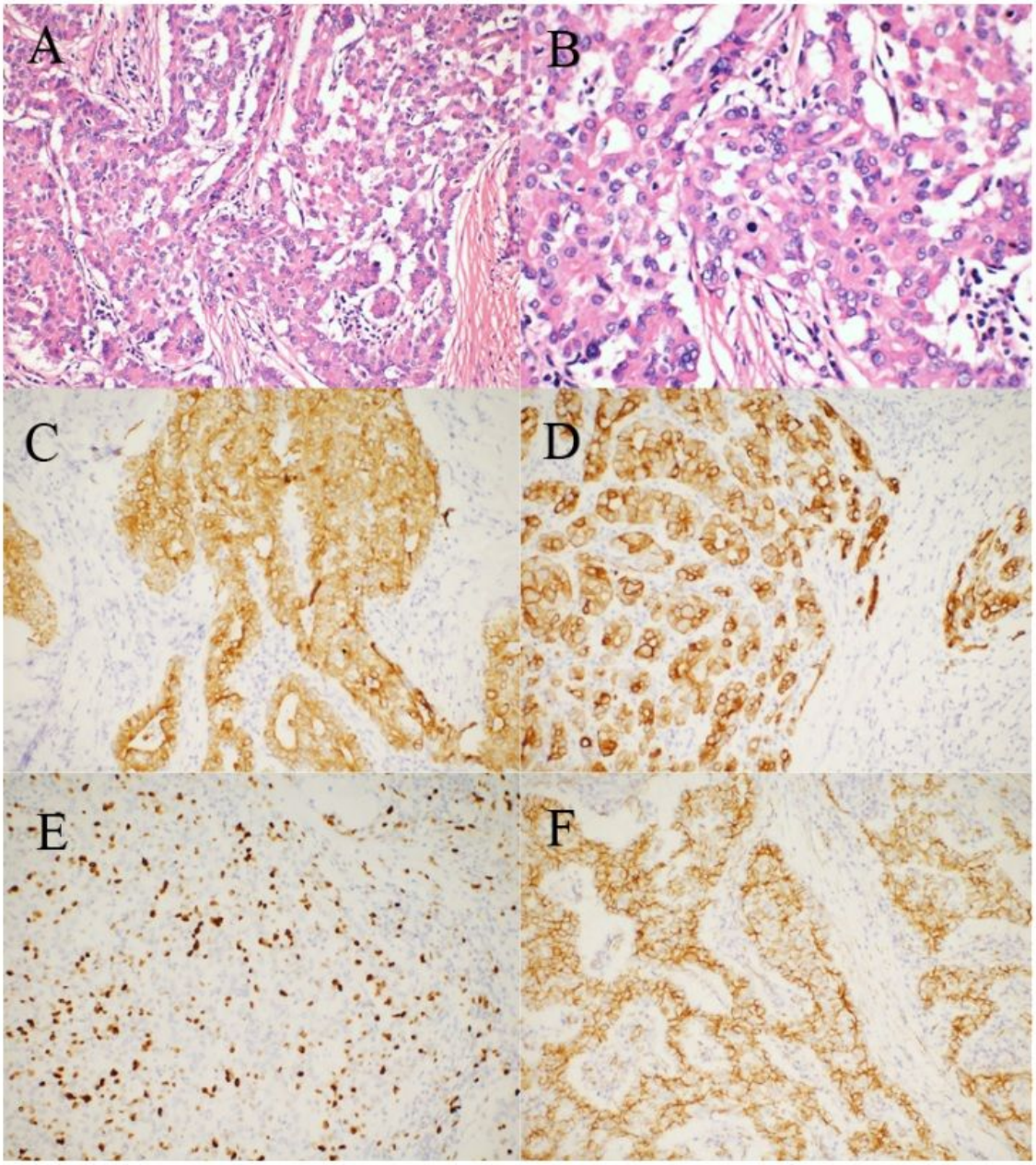

Figure 4

Microscopic examinations. Routine histology, stained using hematoxylin-eosin (H&E), shows pancreatic acinar cell adenocarcinoma (A, ×200); Nuclear division in pancreatic acinar cell carcinoma (B, ×400). Immunohistochemical staining of pancreatic tumor cells: CAM5.2 expression in pancreatic tumor (C, ×200); CK19 expression in pancreatic tumor (D, ×200); Ki-67 partial expression in pancreatic tumor (+30%) (E, ×200); membranous expression of beta-catenin in pancreatic tumor (F, ×200).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklist.pdf