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

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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°C, 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                        | Gastric tumor location | Pancreatic tumor location | Pancreatic histology                                         | Treatment                                                                 |
|-------------------------------|-----|--------|------------------------|------------------------------------------|------------------------|---------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------|
| Eriguchi N et al. (2000)[7]   | 76  | male   | upper gastric angle    | Moderately differentiated tubular adenocarcinoma | Not mentioned          | 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                                    | 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                                              |
| Ohsubo 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 | Gender | 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 |
| Arabadzhieva 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;  
PDAC: 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).

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