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Case Report

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Rare Case of Metachronous Small-Bowel Metastasis from Pancreatic Cancer Presenting as Anemia Approximately 5 Years Postpancreatoduodenectomy

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Abstract

Aim: *Intraductal papillary mucinous neoplasm (IPMN) is a premalignant cystic neoplasm originating from the pancreatic duct, with a risk of progression to pancreatic cancer. Surgical resection of IPMN has favorable outcomes, yielding high overall and disease-free survival rates. However, the incidence of malignant change or metastasis after surgical resection requiring repeat surgery remains high. Intestinal metastasis from pancreatic cancer, particularly after primary surgery, is extremely rare. Systemic treatments, including chemotherapy and radiotherapy, are typically used. Nevertheless, although surgery is not generally indicated, emerging research shows that it can be possibly beneficial for some patients. Herein, we present a 56-year-old female patient diagnosed with IPMN-associated pancreatic cancer without lymph node metastasis, who successfully underwent reresection for jejunal metastasis at nearly 5 years after the initial pancreaticoduodenectomy.*

Background: *Intraductal papillary mucinous neoplasm (IPMN) is a premalignant cystic neoplasm originating from the pancreatic duct, with a risk of progression to pancreatic cancer. Surgical resection of IPMN has favorable outcomes, yielding high overall and disease-free survival rates. However, the incidence of malignant change or metastasis after surgical resection requiring repeat surgery remains high. Intestinal metastasis from pancreatic cancer, particularly after primary surgery, is extremely rare. Systemic treatments, including chemotherapy and radiotherapy, are typically used. Nevertheless, although surgery is not generally indicated, emerging research shows that it can be possibly beneficial for some patients*

Case: *A 56-year-old female with a history of stage III nasopharyngeal cancer (T2N1M0), treated with concurrent chemoradiotherapy in 2012, was diagnosed with IPMN-associated pancreatic cancer (pT1cN0M0) in 2019. The tumor was located in the pancreatic head and the patient underwent a pancreaticoduodenectomy without adjuvant therapy. In early 2023, the patient developed chronic anemia(hemoglobin 8–9 g/dL) without gastrointestinal bleeding. Despite unremarkable endoscopic and CT findings, a positron emission tomography-CT scan revealed a hypermetabolic lesion in the jejunum. Biopsy confirmed adenocarcinoma of pancreatic origin, consistent with metastasis. In January 2024, re-resection of the jejunal metastasis and biliary reconstruction were performed. The patient recovered uneventfully, and pathology confirmed pancreatic adenocarcinoma metastasis.*

Conclusion: *This case presents a rare occurrence of jejunal metastasis following pancreaticoduodenectomy for IPMN-associated pancreatic cancer. Successful re-resection of the metastatic lesion highlights the potential role of surgery in select cases of oligometastatic recurrence. While chemotherapy remains the standard treatment for metastatic pancreatic cancer, surgical intervention should be considered in patients with limited recurrence, particularly when complete tumor resection is feasible. Regular surveillance with imaging and tumor markers is essential for early detection of recurrence and improving long-term outcomes.*

1. Introduction

Intraductal papillary mucinous neoplasm (IPMN) is a premalignant cystic neoplasm originating from the pancreatic duct. Its risk of progression to pancreatic cancer ranges from 6% to 46%, and it is typically diagnosed in individuals aged 50–60 years. Surgical resection has favorable outcomes with higher overall survival rates and disease-free survival rates [1]. The indications for surgery include jaundice, an enhancing mural nodule measuring >5 mm, and a main pancreatic duct diameter measuring >10 mm, which indicate a higher risk of malignant transformation. However, the incidence rate of recurrence requiring repeat surgery during long-term follow-up (10 years) remains as high as 62% [2]. To date, the risk of metastasis after surgical resection for pancreatic cancer remains at 66%–80%. Metastases can occur locally (the pancreatic remnant or mesenteric root), regionally (the regional lymph nodes, soft tissue, or peritoneal cavity), or distantly (the other organs or lymph nodes), with the liver and lung being the most common sites of distant recurrence. The management strategies for metastatic pancreatic cancer lack standard protocols due to the absence of phase III trials or robust evidence-based studies. Nevertheless, regardless of the type of metastasis, systemic treatment such as chemotherapy and radiotherapy are generally utilized as these are considered systemic diseases. Surgery is not commonly indicated. However, recent research has shown that it can be possibly beneficial for some patients [3]. Intestinal metastasis is extremely rare, particularly with sporadic reports of reresection after primary surgery. Herein, we present a case of successful surgery for jejunal metastasis after pancreaticoduodenectomy for IPMN-associated pancreatic cancer.

2. Case

A 56-year-old female patient with a history of stage III nasopharyngeal cancer (T2N1M0), which was treated with concurrent chemoradiotherapy in 2012, was diagnosed with IPMN-induced pancreatic cancer (pT1cN0M0) associated with invasive carcinoma in 2019. The tumor was located at the pancreatic head with tortuous dilatation of the main pancreatic duct. The patient underwent pancreaticoduodenectomy in 2019. Thereafter, she has been under regular follow-ups without any adjuvant therapy. The patient presented with anemia since 2023, with hemoglobin levels consistently at approximately 8–9 g/dL despite the absence of melena or hematochezia. Repeated upper gastrointestinal endoscopies, colonoscopies, and computed tomography (CT) scans revealed no abnormalities or evident metastases. The patient was diagnosed with iron deficiency anemia. Hence, treatment with oral iron supplementation was started, and she was admitted to the hematology ward every 3 months for intravenous iron therapy. During her hospital admission for further anemia assessment, positron emission tomography-CT scan revealed a hypermetabolic soft tissue lesion in the jejunum near the choledochojejunostomy anastomosis. Single-balloon enteroscopy was performed, and results revealed an ulcerative lesion in the jejunum near the choledochojejunostomy, with biopsy confirming adenocarcinoma, indicative of metastasis from the pancreas. A small-bowel series showed no signs of bowel obstruction. In January 2024, a repeat surgery was performed, involving the resection of the biliary limb from previous pancreaticoduodenectomy (Figures 1, 2, and 3).

Figure 1: Biliary Limb Resection, Including Resection of the Pancreticojejunostomy, Hepaticojejunostomy, and Jejunum

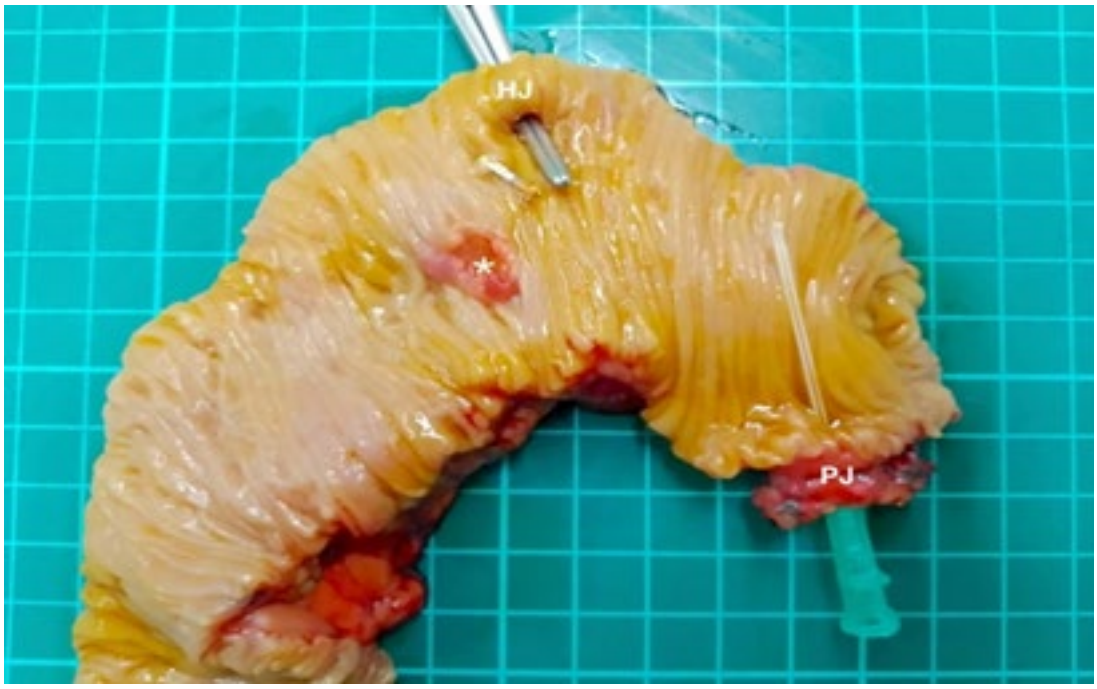

Figure 2: Resected Lesion. Metastatic Ulcerative Lesion (Asterisk). HJ Hepaticojejunostomy, PJ Pancreaticojejunostomy

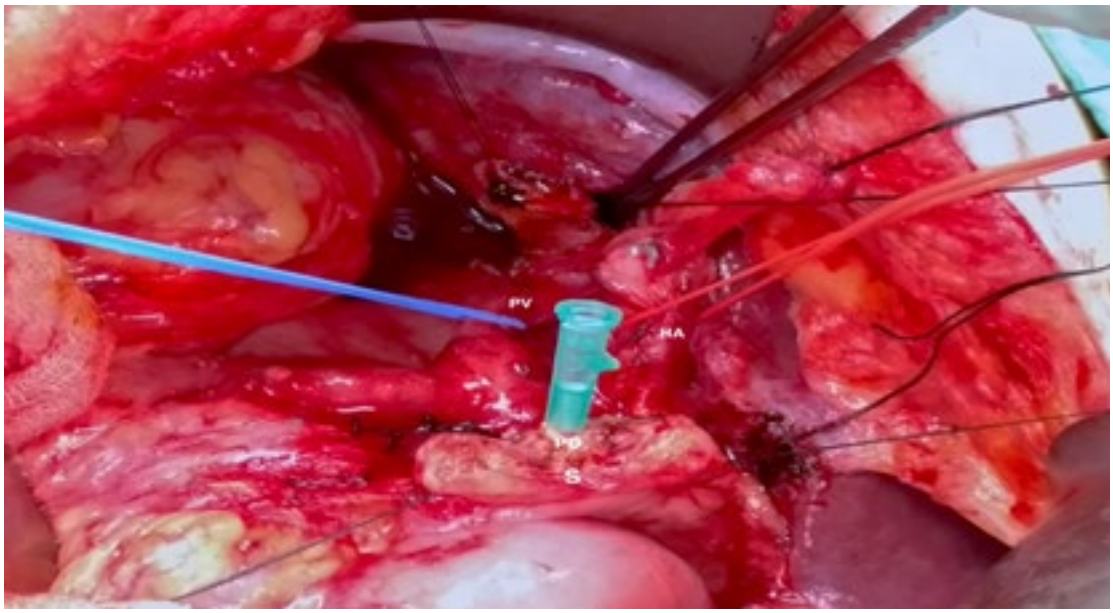

Figure 3: Pancreatic Duct and Stump Exposure during the Surgery. The Portal Vein Was Tagged With A Blue Vessel Loop And The Hepatic Artery With A Red Vessel Loop. The Pancreatic Duct Was Pinned By A Needle Catheter S stump

Intraoperative frozen section analysis of the resected margins confirmed the absence of metastatic disease. The biliary limb was reconstructed with three anastomoses (end-to-side pancreaticojejuno stomy, end-to-side hepaticojejunostomy, and side-to-side jejunojejunostomy) at three sites (Figure 4). The patient was then discharged uneventfully 19 days post-surgery. Subsequent pathological analysis revealed small intestinal mucosal tissues with adenocarcinoma. Unlike the normal intestinal mucosal tissues, the tumor cells tested positive for CK7 and negative for CK20 (Figures 5, 6, and 7). The morphology and immunostaining results were consistent with metastasis of pancreatic origin.

Figure 4: Anastamosis at Three Sites: An End-To-Side Pancreaticojejunostomy, End-To-Side Hepaticojejunostomy, and Side-To-Side Jejunojejunostomy

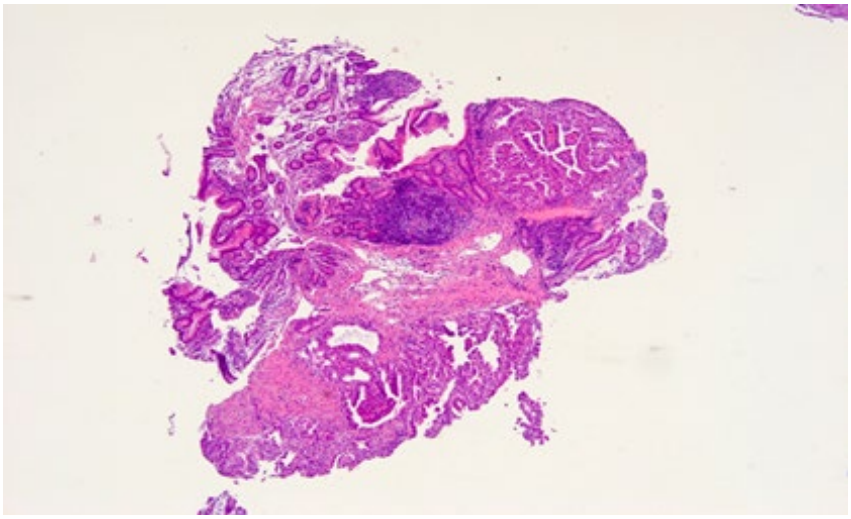

Figure 5: H&E Staining, 40×

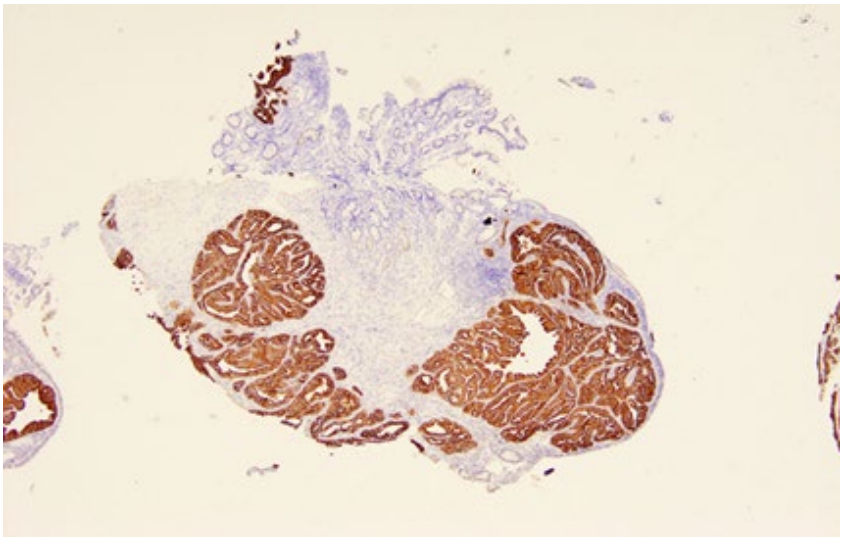

Figure 6: CK7 Immunostaining, 40×

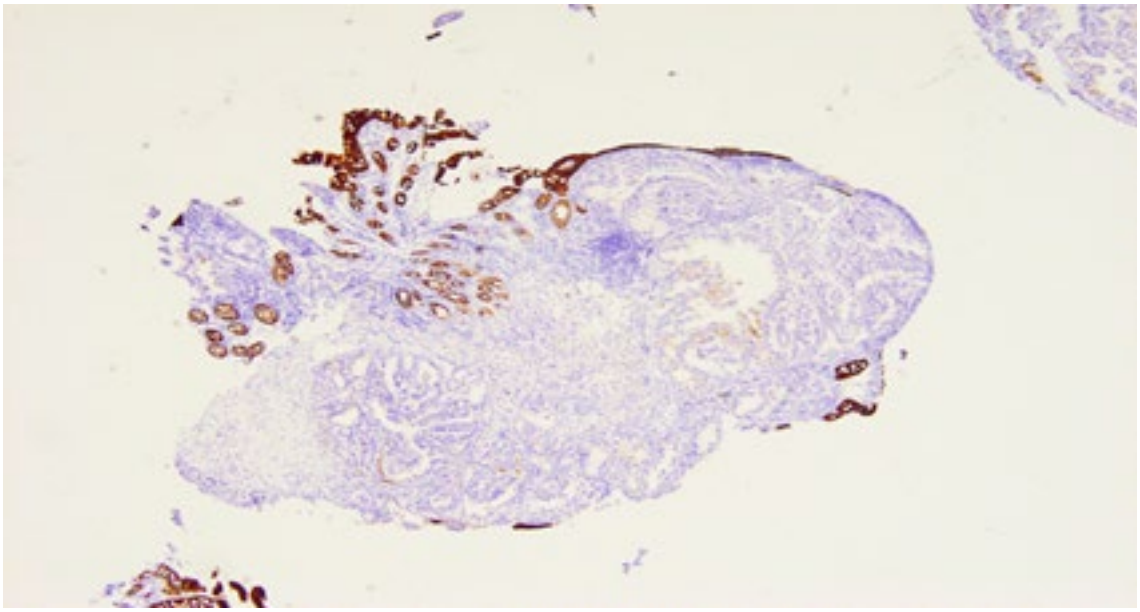

Figure 7: CK20 Immunostaining, 40×

3. Discussion

Pancreatic cancer is still relatively challenging to treat as it is often diagnosed at an advanced stage. In approximately 20% of resectable tumors, the recurrence rate of pancreatic cancer remains as high as 80% even after curative pancreaticoduodenectomy, with a 5-year survival rate of approximately 10%–40% [4]. The liver and local regional sites are the most common site of metastasis after curative resection, followed by the lung and peritoneum [5]. However, small-bowel metastasis is quite rare. To the best of our knowledge, only one case report, which was performed by Miyasaka et al. in 2018, documented small-bowel metastasis after pancreaticoduodenectomy [6]. In this case, the patient presented with fever and bowel obstruction at 2 years after the primary surgery, leading to the diagnosis of metastases in the transverse colon and jejunum. Due to this life-threatening condition, partial resection of these two sites was performed. The patient successfully recovered postoperatively and survived for 7 months but, ultimately, died due to metastasis in the mesenteric lymph nodes at 13 months after the index surgery.

Further, other case reports have documented about colon metastasis after primary resection of pancreatic cancer [7-9]. Most of these cases involved patients under regular surveillance, with an interval of 2–7 years from the initial surgery to recurrence. In all cases, the presenting symptom was abdominal pain, and CT scan revealed strictures or obstructions in various parts of the colon, including the cecum, ascending colon, and sigmoid colon. These findings suggest that bowel obstruction or narrowing causing symptoms can be an indication for surgical resection. In addition, Kim et al. emphasized the importance of utilizing tumor markers in the diagnosis of colon metastasis [7]. In their case, the patient exhibited slight elevations in tumor marker levels before any CT scan findings were apparent. After approximately 1 year, following the onset of symptoms, the patient's cancer antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) levels increased from 334.8 to 5133 U/mL and from 18.2 to 54.4 ng/mL, respectively. In the case of Inada et al., the patient had normal CEA levels. However, the patient's CA19-9 levels increased from normal levels to 1886.6. U/mL [8]. Moreover, according to a retrospective study on late recurrent pancreatic cancer in patients with long-term survival after pancreaticoduodenectomy, most patients with late recurrence were asymptomatic. Therefore, CT scans and CA19-9 surveillance should be continuously performed on all patients undergoing pancreaticoduodenectomy [4].

In most cases, pancreatic cancer recurrence is treated with chemotherapy. However, recent reports on successful re-surgeries indicate that surgical intervention can be possibly beneficial for these patients. Moletta et al. performed a literature review. Results showed that the overall survival rate of patients with recurrent pancreatic cancer who underwent surgical treatment was 26% after a median follow-up of 64.5 months [4]. The disease-free interval after resection of recurrent lesions was 14.2 months. Patients with recurrent pancreatic cancer who underwent surgery had a significantly higher median 26-month overall survival (range: 6–11 months after recurrence diagnosis) than those who did not undergo resection. The postoperative mortality and morbidity rates were 1.8% and 28.1%, both of which are considered acceptable. Serafini et al. conducted a more recent meta-analysis that supported these findings [10]. They compared six large retrospective studies. Results showed that the median overall survival benefit was 28.7 months and that the median survival benefit was 15.2 months after re-resection. These results indicate that surgery should be considered as a possible treatment option for recurrent pancreatic cancer.

Patients with disseminated distant metastasis are not eligible for surgery. However, surgical resection should be considered in cases of limited (oligometastatic) recurrence if complete tumor excision is feasible. Nienhüser et al. conducted a literature review to identify which patients can benefit from surgery [11]. Several prognostic benefits were found in patients who survived after reresection for local recurrence or isolated metastatic recurrence. The most important factors included successful complete resection, an interval of >9–10 months from the initial resection to the development of recurrence, and effective chemotherapy prior to the second surgery. The other factors were age under 65 years, tumor measuring <2 cm, positive lymph node status, and a BMI of >20 kg/m2. These results are consistent with those of the previous literature. Based on a 2020 multicenter database study, multivariate analysis revealed that a time to recurrence from resection of <1 year and peritoneal recurrence were significant independent predictors of poor overall survival in patients with recurrent pancreatic cancer [12]. In addition, lymph vessel invasion was an independent risk factor of long-term survival [4]. Nevertheless, only the current National Comprehensive Cancer Network guidelines recommend the use of alternative treatment strategies for patients with recurrent pancreatic cancer who have undergone surgery [13]. In particular, there are other options for re-surgery, with particular emphasis on the potential benefits of pulmonary metastasectomy in cases of lung metastasis. However, further data should be collected to support this approach.

4. Conclusion

To the best of our knowledge, only a few isolated case studies have reported about pancreatic cancer recurrence in the small intestine after primary resection for pancreatic cancer. In addition to imaging techniques, tumor markers such as CEA and CA19-9 can be useful predictors of recurrence. Surgery is commonly used for the emergency management of symptomatic bowel obstructions. However, with consideration of its potential benefits in overall survival and acceptable postoperative mortality and morbidity rates, it may also be a viable elective option for specific patients, such as those with limited recurrence. Younger patients who have undergone a successful resection of recurrent pancreatic cancer have a longer interval before recurrence, and patients who have received chemotherapy before re-resection are more likely to have better prognoses.

Herein, we present a 56-year-old female patient who was relatively young and diagnosed with IPMN-associated pancreatic cancer without lymph node metastasis. She underwent pancreaticoduodenectomy in 2019. After approximately 5 years, in 2024, recurrence was detected, indicating a relatively long interval from the initial resection to the development of recurrence. The patient had regular follow-ups postoperatively, without recurrence findings on CT scans and with normal CEA and CA19-9 levels. Recurrence was incidentally identified on positron emission tomography-CT scan. After a successful re-surgery, to date, the patient has remained complication-free under regular outpatient department follow-ups. This case represents a successful re-resection of recurrent pancreatic cancer in the small intestine after pancreaticoduodenectomy. Therefore, in selected cases, surgical intervention is a feasible option and may provide substantial benefits.

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