Diagnostic challenges of pancreatic carcinoma presenting as acute pancreatitis: A case series and literature review

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Abstract

Background: Pancreatic cancer can be challenging to diagnose, particularly when it presents with features resembling pancreatitis. Misdiagnosis can delay treatment and adversely affect patient outcomes. This case series highlights the diagnostic difficulties and clinical outcomes in patients initially diagnosed with pancreatitis, who were later found to have pancreatic malignancies such as pancreatic ductal adenocarcinoma (PDAC).

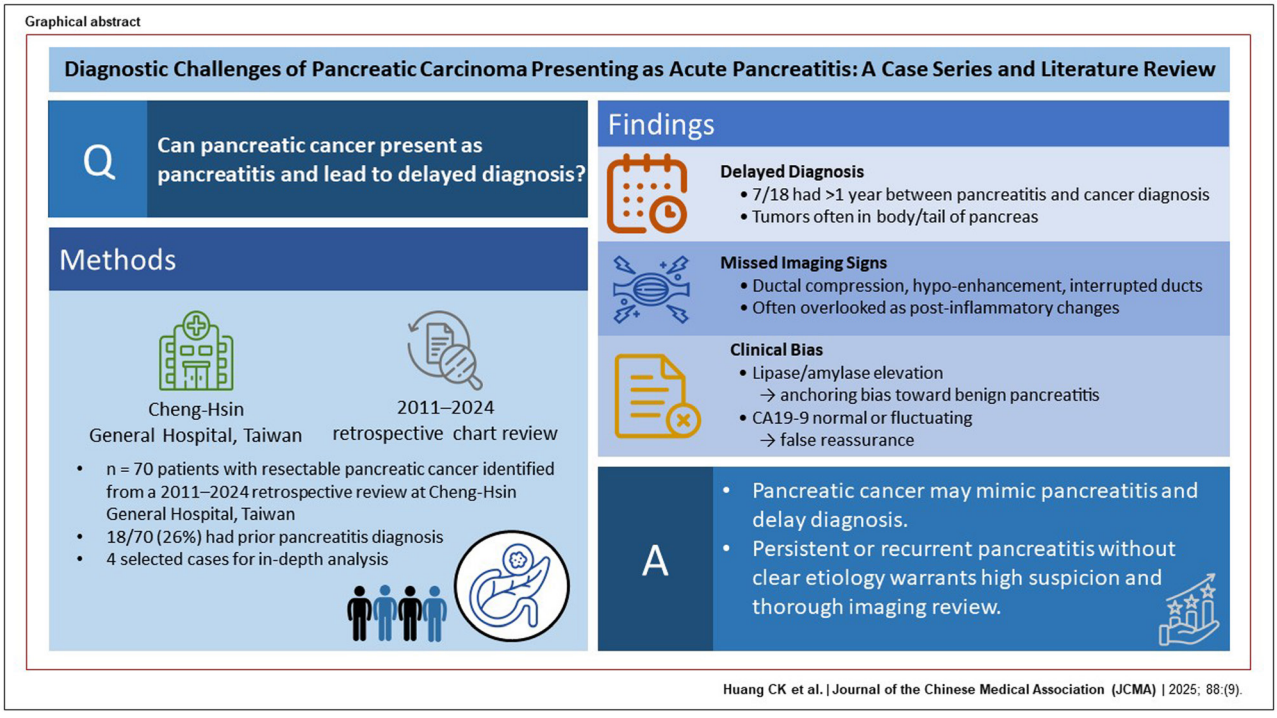
Methods: We reviewed the medical records of patients who underwent pancreatic-related procedures from 2011 to 2024 at a tertiary care hospital in Taiwan.

Results: The review identified 70 patients with resectable pancreatic malignancies, of whom 18 (26%) had a diagnosis of pancreatitis before their cancer was diagnosed. Four cases were selected for detailed presentation, highlighting the potential for missed or delayed pancreatic cancer diagnoses in patients with recurrent pancreatitis. Upon further investigation, we found that subtle signs of malignancy are often masked on initial imaging studies, leading to delays in definitive diagnosis and treatment.

Conclusion: This case series demonstrates the complexities in diagnosing pancreatic cancer, particularly when the presentation is that of pancreatitis. Our findings emphasize the need for careful review of imaging results and a high clinical suspicion of malignancy in patients with recurrent pancreatitis. Further research into more effective diagnostic tools and treatment strategies is warranted to enhance the early detection and management of pancreatic cancer in similar clinical scenarios.

Keywords: Diagnosis; Pancreatic cancer; Pancreatitis

Graphical abstract



Lay Summary: This study explores the challenges in diagnosing pancreatic cancer when it presents with symptoms similar to acute pancreatitis, a condition where the pancreas becomes inflamed. Pancreatic cancer is difficult to detect early, and its symptoms often overlap with those of acute pancreatitis, such as abdominal pain and elevated pancreatic enzymes. The study highlights four cases where patients were initially misdiagnosed with pancreatitis, leading to delays in diagnosing the underlying cancer. The cases demonstrate how imaging studies can be misleading due to the inflammation caused by pancreatitis, which can hide signs of cancer. The authors emphasize the importance of keeping a high level of suspicion for cancer in patients with unusual or recurrent episodes of pancreatitis, as timely diagnosis is crucial for better treatment outcomes. The study suggests that careful and repeated imaging, alongside thorough clinical evaluation, is necessary to avoid missing a cancer diagnosis.

1. INTRODUCTION

Pancreatic cancer is an aggressive malignancy with a poor prognosis, often due to diagnosis when the disease is at an advanced stage.[1] Early symptoms are typically vague and nonspecific, leading to delays in detection. Diagnosis relies heavily on imaging studies such as contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP) to assess tumor size, location, and metastasis.[2,3] The global incidence of acute pancreatitis is increasing, and important risk factors include gallstones, chronic alcohol use, hypertriglyceridemia, certain medications, genetic variants, obesity, and smoking.[4–6] Acute pancreatitis generally presents with severe abdominal pain, nausea, and elevated pancreatic enzymes, while recurrent pain, weight loss, and steatorrhea are symptoms of chronic pancreatitis.[7]

The early detection of pancreatic cancer is particularly challenging when it presents with symptoms and imaging findings that mimic acute or chronic pancreatitis.[8,9] This overlap of symptoms makes it challenging to diagnose pancreatic cancer because the inflammatory features of pancreatitis can obscure underlying malignancies in imaging studies.[10] Consequently, this can lead to a delay in the diagnosis of the cancer and the timely initiation of appropriate treatment, potentially impacting patient outcomes.

In this report, we describe four cases of patients where pancreatic cancer was initially misdiagnosed as pancreatitis. The cases demonstrate the diagnostic challenges when pancreatic cancer mimics pancreatitis, and highlight the importance of maintaining a high index of suspicion for pancreatic malignancy in the cases of acute pancreatitis without a clear etiology.

2. METHODS

2.1. Patients

We reviewed the medical records of patients who underwent pancreatic-related procedures from 2011 to 2024 at Cheng-Hsin General Hospital, a tertiary care hospital in Taiwan.

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Patients with unresectable pancreatic masses and patients with pathological reports indicating non-pancreatic malignant tumors, such as duodenal cancer, common bile duct (CBD) cancer, or ampullary carcinoma, were excluded. Additional exclusion criteria were two different primary cancers, other cancers invading the pancreas, and patients with benign diseases such as autoimmune pancreatitis, chronic pancreatitis, pancreatic stones, pancreatic cysts, or intraductal papillary mucinous neoplasm (IPMN) without dysplasia. Lastly, cases where only biopsies were performed, or where peritoneal or mesenteric root metastasis was discovered intraoperatively, leading only to bypass surgery (palliative surgery), were also excluded.

After reviewing the medical records and applying the inclusion and exclusion criteria, 70 patients with resectable pancreatic malignancies were identified, and 18 (26%) of the patients had a diagnosis of pancreatitis before their cancer was diagnosed. The mean age of the 70 patients was 65 years, and 49% were male. The pancreatic head was the most commonly affected location (32 patients, 46%), and pancreatic ductal adenocarcinoma (PDAC) was the most frequent histological diagnosis (56 patients, 80%). Among patients with PDAC, none were diagnosed at American Joint Committee on Cancer (AJCC) stage 0; at diagnosis, 41.1% were at stage 1, 46.4% at stage 2, 10.7% at stage 3, and 1.8% at stage 4. Eighteen patients (26%) had a diagnosis of acute pancreatitis before their cancer was diagnosed, with seven patients diagnosed 1 year or more prior. (Of these seven patients, four had a tumor located in the pancreatic body, two in the pancreatic head, and one in the uncinate process.) Approximately half of the patients (37 patients, 53%) were treated with the Whipple procedure (Table 1).

Based on the judgment of the attending physicians and clinical relevance, we selected four cases for a detailed presentation. The four cases were chosen because they reflect notable diagnostic challenges and are considered representative of the potential for missed or delayed pancreatic cancer diagnosis in patients with recurrent pancreatitis.

3. RESULT

3.1. Case 1

A 57-year-old male presented to the emergency department (ED) of our institution on October 8, 2021, with the acute onset of abdominal pain and hyperglycemia (blood glucose: 406 mg/dL, glycated hemoglobin [HbA1c]: 15.2%). He had no history of alcohol use, hyperbilirubinemia, CBD stones/gallstones/obstructive jaundice, biliary tract disease, or previous biliary surgery. Admission laboratory tests revealed a markedly elevated lipase level (1382 U/L) and a mildly elevated CA19-9 level (84.6 U/mL). Clinically, he presented with classic symptoms of hyperglycemia, including dry mouth, polyphagia, and polyuria. Based on the constellation of symptoms and laboratory findings, he was diagnosed with new-onset type 2 diabetes mellitus—a known risk factor for pancreatitis—which subsequently led to a diagnosis of acute pancreatitis. The CT image revealed pancreatic swelling, fat stranding, and a dilated pancreatic duct, indicating inflammation. Subtle findings, such as main pancreatic duct compression and abnormal hypo-enhancement in the pancreatic body (Fig. 1A), were initially overlooked.

Despite receiving conservative treatment, the patient's lipase levels remained elevated for 1 month, and his blood glucose fluctuated between 200 and 300 mg/dL. During this period, CA19-9 levels returned to normal. Notably, he had experienced unexplained weight loss before the episode of acute pancreatitis, raising suspicion for underlying malignancy. Subsequently, on November 21, 2021, MRCP was performed, leading to a diagnosis of PDAC, initially staged as cT1N0M0. He subsequently underwent distal pancreatectomy, with a final

Table 1

Pancreatic cancer patient characteristics and their history of pancreatitis

Characteristics	All (n = 70)
Age, y	64.7 ± 11.2
Sex	
Male	34 (48.6)
Female	36 (51.4)
Year of pancreatic cancer diagnosis	
2012-2015	21 (30.0)
2016-2020	17 (24.3)
2021-2024	32 (45.7)
History of pancreatitis before diagnosis of pancreatic cancer	
No	52 (74.3)
Yes	18 (25.7)
The time interval between pancreatitis diagnosis and pancreatic cancer diagnosis among patients with a history of pancreatitis[a]	
<1 y	11 (61.1)
1 y or more	7 (38.9)
AJCC stage of PDAC (n = 56)	
0	0 (0.0)
1	23 (41.1)
2	26 (46.4)
3	6 (10.7)
4	1 (1.8)
Tumor location in pancreas	
Tail	17 (24.3)
Body	11 (15.7)
Head	32 (45.7)
Tail-body	5 (7.1)
Head-body	3 (4.3)
Uncinate process	2 (2.9)
Histology	
PDAC	56 (80.0)
IPMN with dysplasia	5 (7.1)
MCT	2 (2.9)
Neuroendocrine tumor	3 (4.3)
SPN	2 (2.9)
Mucinous adenocarcinoma	1 (1.4)
Undifferentiated	1 (1.4)
Surgery	
Whipple operation (including variations)	37 (52.9)
Distal pancreatectomy + splenectomy[b]	32 (45.7)
Total pancreatectomy	1 (1.4)

Continuous variables are presented as mean ± SD; categorical variables are presented as number (percentage).

AJCC = American Joint Committee on Cancer; IPMN = intraductal papillary mucinous neoplasm; MCT = mucinous cystic tumor; PDAC = pancreatic ductal adenocarcinoma; SPN = solid pseudopapillary neoplasm.

[a]Patients who had a history of pancreatitis were included.

[b]Partial visceral resection if invasion was suspected.

pathological staging of stage IIB, pT1cN1M0. The resected specimen is shown in Fig. 1B. Postoperatively, he experienced serious complications including a pancreatic leak and duodenal perforation, requiring embolization and further surgeries. Although chemotherapy initially managed the disease, it progressed within a year.

3.2. Case 2

A 60-year-old female presented with acute epigastric pain on February 5, 2019. She had no history of alcohol use, biliary tract disease, or metabolic abnormalities. She was diagnosed with acute pancreatitis, which was treated conservatively. On March 3, 2019, she underwent a cholecystectomy based on a diagnosis of chronic cholecystitis to rule out the possibility of biliary pancreatitis. She subsequently continued to experience multiple episodes of acute pancreatitis through December 4, 2019, all of which were managed conservatively. Suspicion of an abnormal biliopancreatic junction led to an endoscopic papillotomy and pancreatic stent placement on December 11, 2019. Subsequent interventions included endoscopic retrograde cholangiopancreatography (ERCP) with stent placement on July 14, 2020, and a second ERCP with stent replacement after stent dropout on July 8, 2020. Although a stent was placed, the patient continued to experience recurrent episodes of pancreatitis. Notably, the patient experienced over 20 documented episodes of acute pancreatitis within 2 years. Her amylase and lipase levels both exceeded 1000 U/L during onset, while her triglyceride and cholesterol levels remained within the normal range throughout the course. Notably, CA19-9 was not tested during the 1.5-year period following her initial presentation.

MRI on October 23, 2020, showed generalized dilatation of the pancreatic duct on T2WI, but no abnormal mass was visualized. MRI on June 21, 2021, revealed a dilated pancreatic duct with stenosis in the middle section, which was interpreted as post-pancreatitis fibrosis (Fig. 2A). Due to persistent symptoms, an MRCP was performed on October 25, 2021, which revealed a pancreatic tail lesion. She underwent a distal pancreatectomy and splenectomy on November 16, 2021 (Fig. 2B), and pathological examination confirmed a 3 × 3 × 2.5 cm well-differentiated ductal adenocarcinoma in the pancreatic tail, with no metastasis in the 21 lymph nodes examined. Postoperatively, the patient received adjuvant chemotherapy. Despite treatment, positron emission tomography (PET)/CT on December 20, 2023, confirmed tumor recurrence at the original surgical site and in the left upper abdomen.

3.3. Case 3

An 81-year-old male, with no documented history of excessive alcohol use or biliary disease, presented with acute abdominal pain on July 26, 2019. Initial CT imaging revealed swelling of the pancreatic body and tail, blurring of adjacent fat planes, and fluid retention in the left anterior pararenal space. These findings, along with elevated lipase and amylase levels, led to the diagnosis of acute pancreatitis. After treatment and discharge, he experienced repeated acute pancreatitis episodes requiring admissions on September 16, September 29, October 26, and November 20, 2019. During these episodes, his lipase and amylase levels exceeded 1000 U/L. However, his CA19-9 levels had been monitored every 6 months and consistently remained within the normal range.

An MRCP performed on September 17, 2019, showed an interrupted pancreatic duct suggestive of an occupying lesion, although this finding was not reported at the time. Additionally, T1-weighted images from the same study demonstrated hypoenhancement in the pancreatic body, which was also overlooked (Fig. 3). A follow-up MRCP on February 27, 2020, again showed an interrupted pancreatic duct, but this finding was similarly not emphasized. MRI on August 25, 2020, revealed marked dilation of the distal pancreatic duct and a 0.8 × 1.0 × 0.8 cm hypointense nodule in the pancreatic neck. Subsequent distal pancreatectomy confirmed a 1.5 × 1.0 × 0.8 cm moderately differentiated adenocarcinoma with sarcomatoid changes and perineural invasion.

3.4. Case 4

A 55-year-old male presented in January 2004 with abdominal pain, and CT showed pancreatic swelling and retroperitoneal fluid, consistent with acute pancreatitis. Over the following years, he experienced multiple episodes of pancreatitis, with imaging studies over time suggesting a more complex pancreatic pathology. In August 2008, the patient sought medical attention

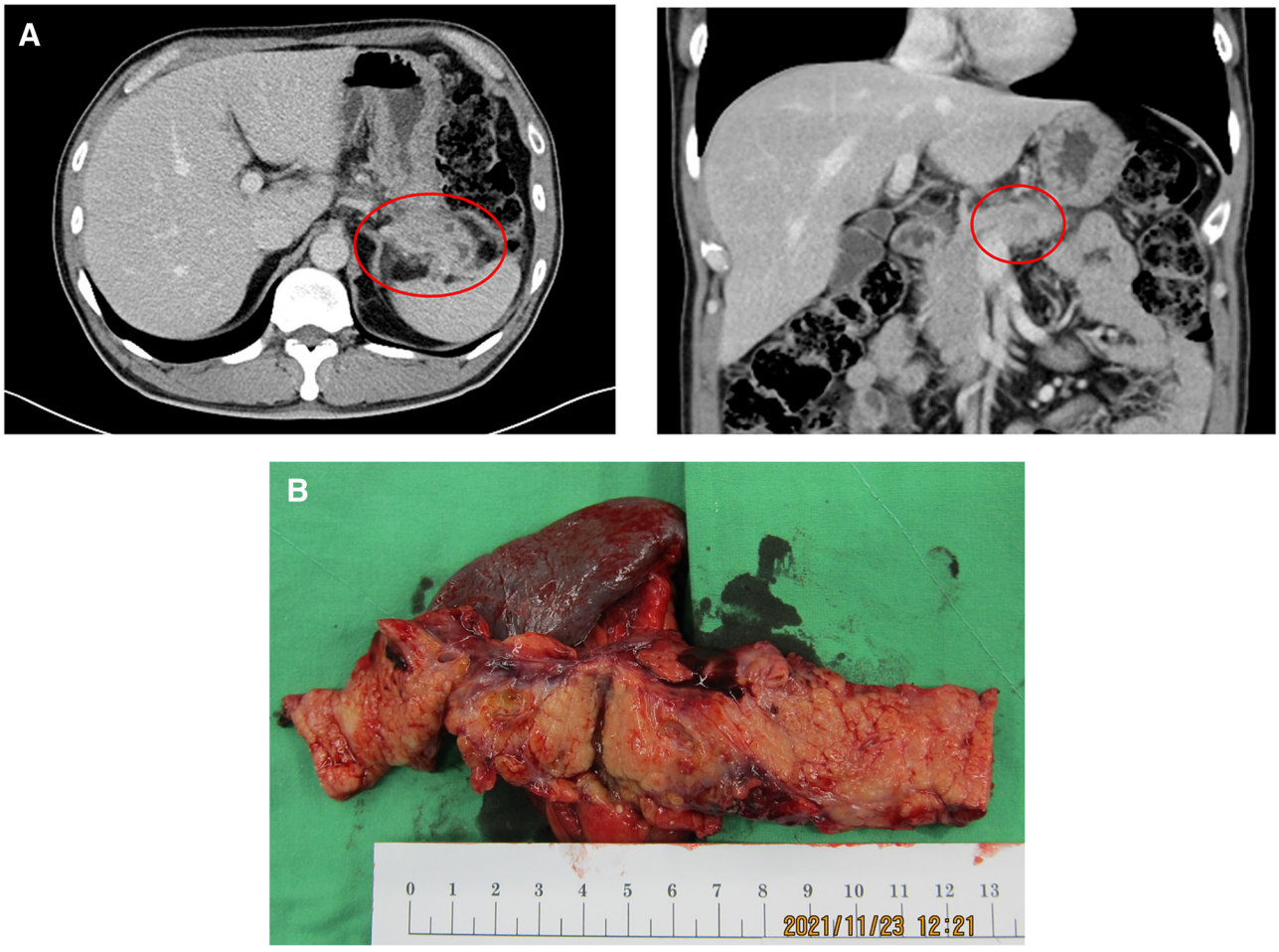

Fig. 1 Initial imaging and distal pancreatectomy specimen from Case 1. A, Initial CT on October 8, 2021, revealed diffuse infiltrations in the left pararenal area, mesenteric root, and peripancreatic regions. Additionally, dilated pancreatic ducts with branching were observed in the pancreatic tail region (left). Acute pancreatitis was suspected based on these findings. The compression of the pancreatic duct and hypo-enhancement were overlooked (right). The red circles indicate the region of abnormal hypo-enhancement and associated ductal changes. B, The pancreas was partially bisected into anterior and posterior halves, with the tumor measured 1 × 0.6 cm. CT = computed tomography .

due to abdominal pain. At that time, his lipase level was 287 U/L and his amylase level was 186 IU/L. A CT scan showed pancreatic duct dilation with a small cyst-like lesion in the pancreas, and he was still diagnosed with pancreatitis and received conservative treatments. A CT in February 2013 showed marked ductal tortuosity and a 4.0 × 3.2 × 4.8 cm cyst-like mass. The differential diagnosis included cystic lesions or neoplasms with intraductal mucinous production.

A CT scan on November 1, 2014, revealed a lobulated cystic lesion in the pancreatic body, measuring 2.7 × 2.4 × 2.6 cm, with internal septations and a dilated duct (1.44 cm). The image findings were interpreted as a pancreatic cystic neoplasm, possibly an IPMN with possible invasion into the stomach wall (Fig. 4). It was only at that point that the patient was referred to the surgical department. The patient underwent a distal pancreatectomy with splenectomy and wedge resection of the stomach wall. Pathological examination confirmed a 4 × 3 × 2.9 cm IPMN without invasion, classified as pTisN0M0. Surgical margins were clear, with no lymphovascular or perineural invasion.

4. DISCUSSION

This case series illustrates the diagnostic challenges of pancreatic cancer, particularly when it mimics pancreatitis. The review of 13 years of our medical records revealed that a substantial proportion of patients who were diagnosed with and surgically treated for pancreatic cancer had prior diagnoses of pancreatitis. Among these patients, 7 (39%) experienced a long interval from initial symptom onset to diagnosis of cancer, with pancreatitis being diagnosed more than 1 year before ultimately receiving a diagnosis of pancreatic malignancy. Among these seven patients, four had tumors found in the pancreatic body. This suggests the importance of diligently reviewing imaging for indirect signs of tumors in cases of recurrent pancreatitis in the pancreatic body. Furthermore, our analysis of four initially misdiagnosed cases revealed that subtle but critical imaging signs of malignancy were overlooked or masked by the overall impression of pancreatitis, leading to delays in accurate diagnosis and treatment. Additionally, elevated serum levels of biochemical markers such as lipase also led clinicians to a diagnosis of pancreatitis, potentially overlooking the presence of underlying pancreatic cancer. In summary, pancreatic cancer and pancreatitis can coexist or mimic each other, complicating the diagnostic process. In clinical practice, this overlap can cause anchoring bias, where clinicians become fixed on an initial diagnosis of pancreatitis, particularly in the presence of enzyme elevation, and may fail to pursue further investigations unless symptoms persist. Together, these findings emphasize the critical importance of thorough diagnostic

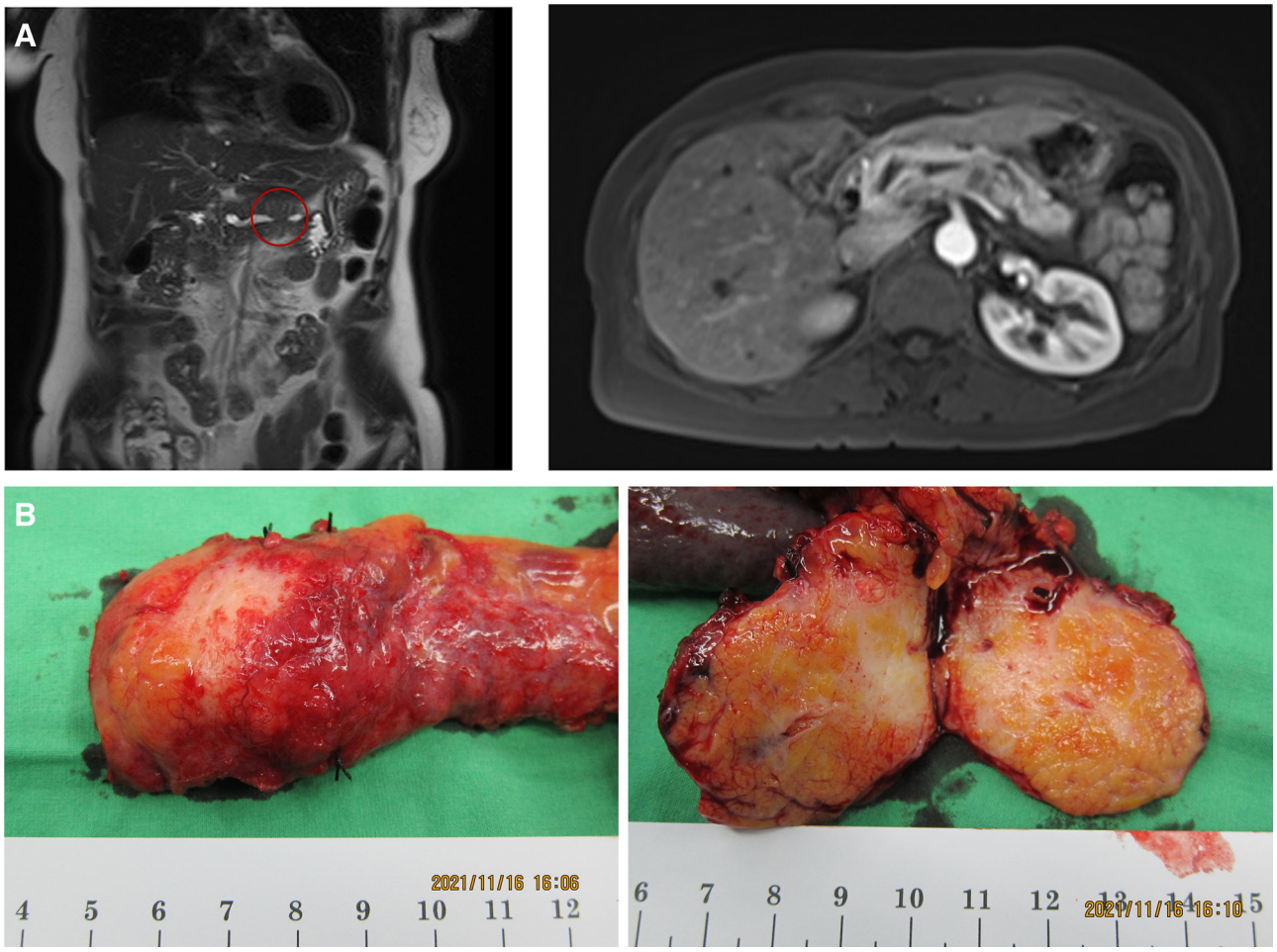

Fig. 2 MR images and surgical specimen from Case 2. A, An MR T2WI image obtained on June 21, 2021, showed dilatation of the pancreatic duct with stenosis in the middle section (left). T1WI MR indicated relative delayed intensity in the body of the pancreas, interpreted as previous pancreatitis with associated fibrosis (right). The red circle highlights the region of ductal stenosis and subtle signal changes later confirmed as tumor. B, The tumor (3×3 × 2.5 cm) invaded the peripancreatic soft tissues and extended to the free serosal surface.

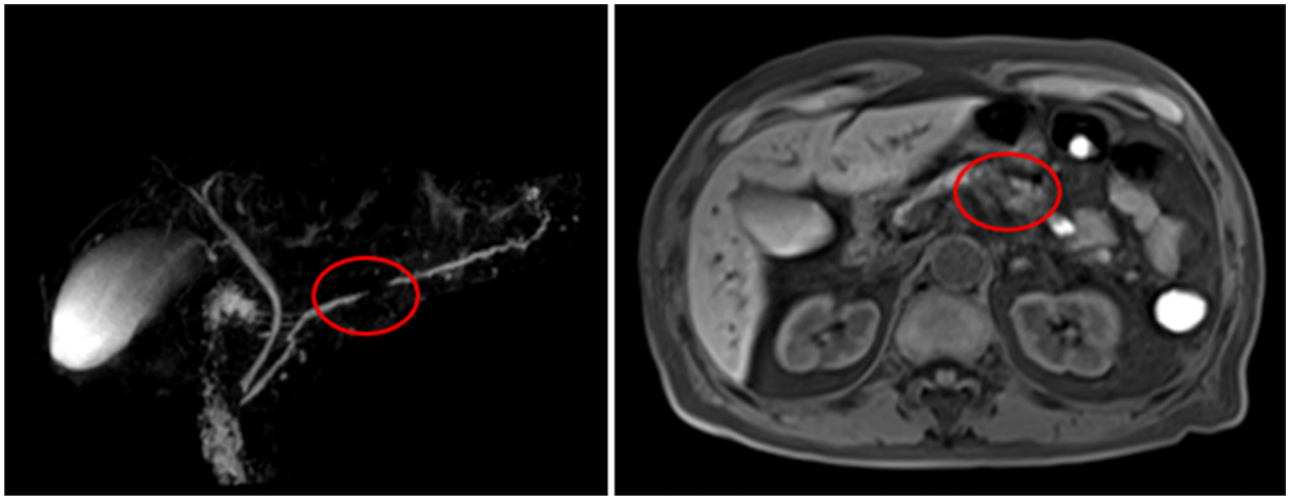

Fig. 3 MRCP performed on September 17, 2019, showed an interrupted pancreatic duct (left), suggesting a possible lesion. This was not pointed out in the original report. T1WI MR revealed hypo-enhancement (right), which was also overlooked. The red circles highlight the region of ductal interruption and abnormal hypo-enhancement. MRCP = magnetic resonance cholangiopancreatography.

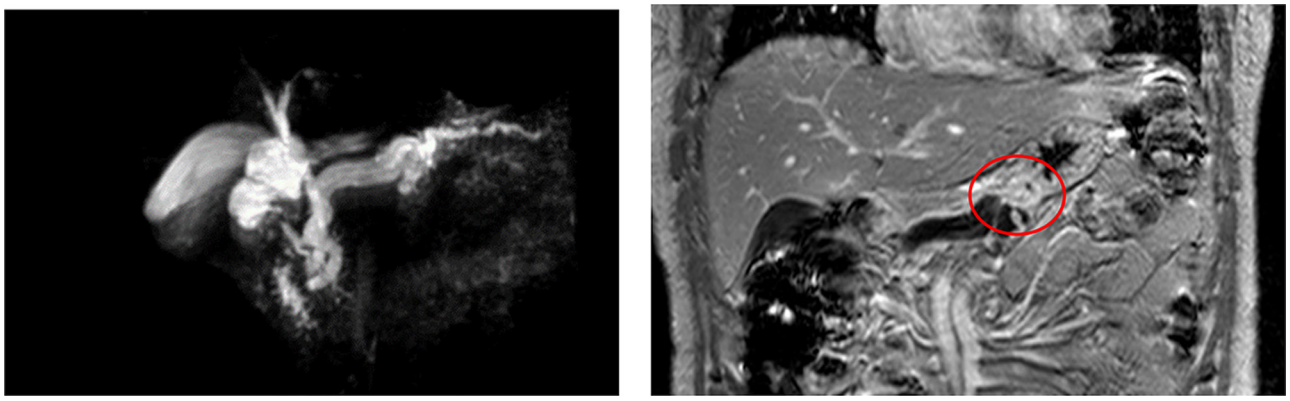

Fig. 4 MRCP performed on November 6, 2014, revealed a lobulated cystic lesion in the pancreatic body with internal multi-septations and an associated dilated pancreatic duct (left), indicating a pancreatic cystic neoplasm. As the right and left biliary ducts descend, there is a segment showing marked contrast enhancement, corresponding to the duodenum on imaging. Additionally, a hyperintense mass with possible invasion into the stomach wall was shown (right). The red circle highlights the hyperintense mass suggestive of tumor invasion. MRCP = magnetic resonance cholangiopancreatography.

evaluation in cases of recurrent or acute pancreatitis without a clear etiology to avoid misdiagnosis and ensure timely detection of underlying pancreatic malignancies.

The clinical diagnosis of pancreatic cancer is inherently challenging due to overlapping symptoms with other conditions, particularly pancreatitis. Both PDAC and pancreatitis present with nonspecific symptoms such as abdominal pain, weight loss, nausea, and vomiting, making it difficult to differentiate between the two based on symptoms alone.[2,11] Additionally, tumor markers like CA19-9[12] are frequently elevated in both conditions and thus have limited value in distinguishing between them. Further, CA19-9 levels may initially appear no significant elevation in the presence of active pancreatitis, as demonstrated in Cases 1 and 3, which could lead to false reassurance and contribute to diagnostic delay. Interestingly, a study by Teng et al[13] suggests that markedly elevated CA19-9 levels during acute pancreatitis may signal an underlying malignancy, warranting further investigation.

Chronic pancreatitis and PDAC commonly have overlapping features on imaging studies, thus complicating the diagnosis, especially when the findings are ductal dilation. Chronic pancreatitis is a known risk factor for pancreatic cancer,[14] and can mimic PDAC on imaging studies due to inflammatory changes, increasing the risk of misdiagnosis.[15] Case 1 highlights a diagnostic challenge where early signs of malignancy—such as main pancreatic duct compression and abnormal hypo-enhancement—were subtle and initially overlooked in the setting of new-onset diabetes and acute pancreatitis. The mildly elevated CA19-9 level normalized following conservative treatment, further reducing suspicion. It was only after persistent symptoms and significant weight loss that further imaging revealed PDAC. The case emphasizes the importance of a thorough review of imaging studies, including pancreatic cancer in the differential diagnosis in patients with persistent symptoms or without a clear etiology despite standard pancreatitis treatment.

In Case 2, the diagnostic challenge stemmed from recurrent episodes of pancreatitis in a patient without traditional risk factors such as alcohol use or metabolic abnormalities. Imaging showed pancreatic ductal dilatation, but the absence of a clear mass and coexisting inflammation led to repeated attribution of symptoms to post-inflammatory changes rather than malignancy. Also, as a result of this clinical impression, CA19-9 was not assessed during the 1.5 years following the initial diagnosis, which may have contributed to the delayed detection of an underlying malignancy. This case highlights that, in patients with recurrent pancreatitis without a history of excessive alcohol consumption, clinicians should not only rule out metabolic abnormalities, biliary stones, pancreatic vascular disease, and congenital anomalies, but also maintain a high index of suspicion for pancreatic cancer as a potential underlying cause. Nevertheless, it should also be noted that chronic inflammation and fibrotic responses in pancreatitis may contribute to PDAC development. Macrophage-driven fibrosis, which typically supports tissue repair during pancreatitis, may also contribute to the progression of PDAC by creating a tumor-supportive microenvironment.[16]

Case 3 demonstrates how subtle imaging abnormalities—such as pancreatic duct interruption and hypo-enhancement on T1WI—were missed on multiple studies. Despite repeated hospitalizations for pancreatitis and progressive weight loss, the absence of a visible mass led to a missed opportunity for early intervention. The diagnosis was made only after serial imaging revealed a small nodule. This case underscores how recurrent acute pancreatitis within a short interval, particularly when unexplained, should prompt a detailed review of prior imaging and further evaluation, even in the absence of overt mass lesions.

Case 4 highlights a different diagnostic scenario involving pancreatic cystic neoplasm. The patient was followed in the Department of Gastroenterology, where he was diagnosed with chronic pancreatitis. Imaging revealed abnormal pancreatic duct morphology and elevated amylase and lipase levels, while CA19-9 remained within the normal range. The clinical impression at the time attributed these findings to pancreatitis. However, the patient experienced recurrent episodes for nearly a decade, during which evolving imaging features were consistently interpreted as chronic inflammatory changes. In retrospect, had a pancreatic cystic neoplasm been considered earlier, the diagnostic approach and follow-up strategy might have been significantly different. The eventual suspicion of invasion into the stomach prompted surgical referral. However, pathology revealed an IPMN without invasion. This case illustrates how reliance on clinical impression—rather than a systematic approach using cyst fluid analysis or endoscopic ultrasonography (EUS)-guided biopsy—can delay accurate diagnosis of cystic pancreatic tumors.

Based on our clinical experience, abdominal CT is commonly performed during the initial evaluation of patients presenting with abdominal pain; however, it is often conducted without a dedicated pancreatic protocol. When initial imaging reveals blurred pancreatic margins or focal/diffuse enlargement with heterogeneous enhancement—accompanied by elevated amylase or lipase levels—acute pancreatitis

is typically diagnosed. Subsequent imaging findings, such as ductal dilatation or strictures, are frequently interpreted as post-inflammatory changes, further reinforcing the initial impression. While laboratory evaluations, including triglyceride and cholesterol levels as well as alcohol history, are routinely assessed to determine the underlying etiology, advanced imaging modalities such as MRCP or contrast-enhanced CT are less commonly utilized early in the diagnostic process. Moreover, certain cases of PDAC may present as iso-attenuating lesions on CT or MRI, making early detection challenging. A further limitation in our clinical setting is the limited access to experienced EUS specialists, which restricts the timely use of EUS-guided fine-needle aspiration or biopsy for definitive diagnosis of suspicious pancreatic lesions.

As previously noted, the association between tumor development and prior episodes of pancreatitis can contribute to diagnostic challenges in several ways. First, overlapping imaging features—such as fibrosis and inflammation from recurrent pancreatitis—can mask the presence of an underlying malignancy. Second, tumor-associated pancreatitis, resulting from pancreatic duct obstruction by a tumor, can induce a desmoplastic reaction with fibrous tissue proliferation, producing poorly defined lesions that closely resemble inflammatory changes. Additionally, both CT and MRI have limited sensitivity and specificity for detecting pancreatic cancer, and diagnostic accuracy may be further compromised by cognitive biases. One such bias is inattentional blindness—a phenomenon in which radiologists may overlook critical abnormalities due to the distracting presence of concurrent conditions.

The gold standard for confirming the diagnosis is ultimately pathological examination. Transcutaneous image-guided tests based on existing imaging technology are prone to false negative results (pancreatitis), and patients are also reluctant to accept the torture of multiple percutaneous sampling. This actually reflects the importance of accurate sampling of target lesions. Therefore, EUS-guided fine-needle aspiration (EUS-FNA)[17] is expected to be a powerful tool for improving the accuracy of pancreatic cancer diagnosis in the future. Additionally, advanced diagnostics such as liquid biopsy or emerging technologies like 68Ga-Trivehexin PET may also be considered to aid in the earlier detection of malignancies.[18] In case 4, there was a 10-year interval between the initial pancreatitis diagnosis and the diagnosis of IPMN, raising the question of whether surgery is necessary for a definitive diagnosis or if earlier insights could be gained through EUS-FNA with cyst fluid carcinoembryonic antigen (CEA) and molecular analysis.

Current knowledge suggests that the extent of surgical resection for pancreatic cystic neoplasms (PCNs) is guided by malignancy risk, highlighting the importance of an accurate diagnosis, which relies on imaging studies, cyst fluid analysis, and molecular markers.[19] Furthermore, following IPMN resection, regular surveillance, including MRI or CT scans, EUS, and tumor marker monitoring, is crucial to detect any recurrence.[20]

A study by Kang et al[21] assessed the impact of missed or misinterpreted imaging examinations on the diagnostic interval and survival of 257 patients with PDAC. One-fourth of the patients had imaging findings that were misinterpreted or the malignancy was not identified.[21] As reported in an earlier study, an initial misdiagnosis of PDAC impacts the timing and stage of the disease at diagnosis. Patients who were misdiagnosed experienced a median time from symptom onset to diagnosis of 4.2 months, compared to 1.4 months for those correctly diagnosed ($p < 0.001$). This delay often results in a higher rate of advanced-stage disease at diagnosis, with 61% of misdiagnosed patients being diagnosed at stages III-IV, compared to 44% of correctly diagnosed patients, reflecting a 1.4-times higher risk of advanced-stage disease at the time of diagnosis.[22]

A retrospective study by Kang et al[23] found that 59% of misdiagnosed cases of PDAC were diagnosed as pancreatitis, where underlying masses or secondary signs were overlooked due to inflammatory changes. The most commonly missed sign was vascular encasement which was overlooked in 90% of the cases, emphasizing the need for careful evaluation of the peripancreatic vasculature in imaging studies. Several factors contribute to these challenges in identifying pancreatic cancer. Tumors smaller than 2 cm often lack clear contours and exhibit iso-attenuation on CT scans, making them difficult to distinguish from surrounding tissues. Concurrent conditions like pancreatitis can obscure or mimic PDAC, further complicating diagnosis. Technical errors such as suboptimal contrast dosing can hinder the detection of subtle malignancies, and cognitive biases can result in critical signs being overlooked. Key indicators of PDAC, including the double duct sign, loss of normal fat, changes to peripancreatic vessels, lumen deformity, and vascular encasement, are frequently missed.

A study by Parker et al[24] reported that specific MRI features, such as main duct dilatation, focal duct stricture with distal dilatation, duct irregularity, side branch dilation, parenchymal atrophy, and focal signal abnormalities, were significantly more common in patients who later developed pancreatic cancer compared to controls.[24] These findings suggest that these MRI features are associated with a higher risk of pancreatic cancer and may indicate potential missed lesions. In a retrospective review by Hoogenboom et al[25] of 595 PDAC cases diagnosed from 2010 to 2016, two radiologists blinded to the diagnoses evaluated pre-diagnostic imaging. When radiologists retrospectively reviewed imaging 1 month to 3 years before PDAC diagnosis, pancreatic masses were identifiable in 50% to 70% of cases—even though these masses were missed or not reported originally, suggesting a substantial proportion of possible misdiagnosis. The authors emphasized that early indicators of PDAC, such as pancreatic duct dilation, duct interruption, and focal atrophy, are frequently overlooked.[25] Together, these studies reinforce the importance of detailed imaging review, particularly in cases where initial findings are equivocal.

Additionally, although not specifically described in our cases, the clinical and radiological presentation of PDAC may also be similar to that of inflammatory pancreatic masses, such as those seen in autoimmune pancreatitis (AIP) and mass-forming chronic pancreatitis (MFCP). Pancreatic masses in which the diagnosis is uncertain require a multidisciplinary approach by highly experienced specialists, including radiologists, gastroenterologists, surgeons, and pathologists.[26] A review of nine studies involving 775 patients identified four significant MRI features that can help differentiate AIP from PDAC: multiple main pancreatic duct (MPD) strictures, absence of upstream marked MPD dilatation, peripancreatic rim, and the duct penetration sign. The absence of MPD dilatation had the highest sensitivity (87%), while the low-density halo or peripancreatic rim had the highest specificity (100%). The findings emphasize the importance of a meticulous, collaborative approach to evaluating pancreatic masses.[27]

In conclusion, this case series and literature review highlight that while heightened vigilance and awareness of potential missed diagnoses of pancreatic cancer are critical, they are often insufficient. The presence of pancreatitis may delay the diagnosis of an underlying malignancy, thereby affecting the timeliness of treatment. When faced with recurrent clinical courses of pancreatitis without a clear etiology, clinicians should consider the possibility of malignancy, as imaging findings of cancer may be obscured by inflammation or other features. This calls for meticulous imaging reviews and maintaining a strong clinical suspicion in cases of recurrent pancreatitis.

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