Relapsed Acute Pancreatitis as the Initial Presentation of Pancreatic Cancer in a Young Man: A Case Report

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In this report, we describe a 31-year-old man in whom acute pancreatitis was the initial feature of a subsequently diagnosed pancreatic adenocarcinoma with multiple metastases. He initially presented at our hospital with acute pancreatitis. Abdominal ultrasonography revealed a mildly dilated pancreatic duct and an enlarged pancreatic head. Although a follow-up abdominal ultrasonography revealed a progressively dilated pancreatic duct and a progressively enlarged pancreatic head, he refused further investigation and was lost to follow-up. Four months later, he returned to our hospital with relapsed acute pancreatitis. Obstructive jaundice was noted and drainage was performed. Because choledochoplasty with multiple balloon catheters was not fully effective, biliary tract bypass surgery was carried out. Intraoperative biopsy confirmed pancreatic adenocarcinoma with multiple metastases. The patient died of massive gastrointestinal bleeding a few weeks later. To our knowledge, this is the youngest case of pancreatic cancer with the uncommon initial presentation of acute pancreatitis reported in the literature. For a patient with acute pancreatitis, particularly recurrent episodes, but with no known risk factors for pancreatitis, a pancreatic neoplasm should be considered as a potential underlying cause, even in a young man.

Key Words: adenocarcinoma, pancreatic cancer, pancreatic neoplasms, pancreatitis (Kaohsiung J Med Sci 2010;26:448–55)

Pancreatic cancer is one of the most lethal human cancers and continues to be a major clinical problem, even in the 21st century [1]. It rarely develops in the first five decades of life [2,3]. Pancreatic cancer may initially present with dull epigastric pain radiating to the back, along with weight loss or jaundice; however, pancreatitis is not included in the list of common clinical manifestations. In this report, we describe a young man in whom relapsed acute pancreatitis was the initial feature of subsequently confirmed pancreatic cancer with multiple metastases. To our knowledge, this is the youngest case of pancreatic cancer with the uncommon initial feature of acute pancreatitis to be reported in the literature.

Case Presentation

A 31-year-old man without any remarkable family history of systemic disease or malignancy and without any remarkable past medical history, except for smoking 0.5 packs per day and alcohol consumption (on
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average, about 700 mL of beer, 3 times a week) for more
than 10 years, presented at the emergency department
of our hospital owing to intermittent abdominal pain
in the left upper quadrant over 2 days. He reported
having some sensation of acid regurgitation and hun-
ger pain for several days, but he denied experiencing
any nausea, vomiting or diarrhea. He was afebrile,
with normal vital signs, a soft abdomen without any
abdominal tenderness, and hyperactive bowel sounds.
Because his clinical presentation and plain abdominal
roentgenogram suggested stool impaction, he was
discharged with the prescription of some laxatives.

He returned to the emergency department 2 days
later with nausea and worsened abdominal pain in the
left upper quadrant and epigastric area. His abdomen
was still soft, but tender in the left upper quadrant.
Acute pancreatitis was diagnosed based on elevated
serum lipase level (970 IU/L; normal, 7–58 IU/L) and
computed tomography (CT) findings (Figure 1A). He
rejected admission owing to a rapid resolution of
abdominal pain soon after management performed
in the emergency department.

Six days later, he returned to the emergency depart-
ment because of severe abdominal pain with radiation
to the back after consumption of about 350 mL of beer.
His vital signs were normal and his abdomen was soft
with normoactive bowel sound. Laboratory tests re-
vealed a persistently elevated (although lower than
that 6 days earlier) serum lipase level of 411 IU/L. He
was admitted under the diagnosis of acute pancreatitis.
Abdominal ultrasonography performed during hos-
pitalization showed a mildly dilated pancreatic duct
and an enlarged pancreatic head. He was discharged
11 days later after successful conservative treatment.

At a follow-up visit at our outpatient department
5 days later, he reported experiencing mild abdomi-
nal pain after a heavy meal which subsided after a few
days. His serum lipase level at that time was 423 IU/L.
An elevated carbohydrate antigen 19-9 (CA19-9)
level (82.8 U/mL; normal, <37 U/mL) was also noted.
Follow-up abdominal ultrasonography about 1 month later revealed a progressively dilated pancreatic duct and an enlarged pancreatic head. He refused further CT investigation and was lost to follow-up.

He returned to the emergency department 4 months later due to intermittent abdominal pain in the epigastric area and in the periumbilical area with radiating pain to his back. He reported that the intermittent abdominal pain started after a heavy meal with a large amount of beer before this visit. He denied having anorexia, postprandial pain or diarrhea. His serum lipase level was 567 IU/L at this time. Relapsed acute pancreatitis was diagnosed, based on the elevated serum lipase level and CT findings (Figure 1B). He was readmitted to our hospital for conservative treatment and was discharged 8 days later with good tolerance to a soft diet.

Five days later, he reported dull epigastric pain and diarrhea after a large meal. He also noticed that he was becoming icteric and passing dark urine, but without clay-colored stool. He did not have fever, chills or tenderness in the right upper quadrant of his abdomen. He was readmitted for further investigation and management. Laboratory examination showed elevated levels of total bilirubin (9.00 mg/dL; normal, 0.2–1.0 mg/dL), direct bilirubin (5.42 mg/dL; normal, 0–0.2 mg/dL), serum aspartate aminotransferase (347 U/L; normal, 10–35 U/L), serum alanine aminotransferase (668 U/L; normal, 10–40 U/L), serum alkaline phosphatase (321 U/L; normal, 32–92 U/L), serum γ-glutamyl transferase (171 U/L; normal, 7–64 U/L), serum lipase (326 IU/L), and serum amylase (299 U/L; normal, 63–123 U/L). Abdominal ultrasonography revealed dilatation of the common bile duct, common hepatic duct and gallbladder. Percutaneous transhepatic cholangiography was performed to relieve his jaundice. Percutaneous transhepatic cholangiography revealed complete obstruction of the distal common bile duct. Choledochoplasty with multiple balloon catheters was performed to dilate the distal common bile duct, but the follow-up cholangiography 1 week later showed narrowing of the previously dilated distal common bile duct. Two weeks later, extensively long (>3 cm) segmental stenosis of the distal common bile duct was noted during the sequential revision of the draining tube. Therefore, he was referred to our surgical department for pancreatic biopsy and for the possibility of biliary tract bypass surgery. Elevated serum levels of CA19-9 (1,822.3 U/mL) and carcinoembryonic antigen (12.0 ng/mL; normal, 0–5 ng/mL) were noted on the day before the operation. Multiple nodules on the omentum and liver surface were found during the operation. Excisional biopsy of the pancreatic head tumor and nodules on the omentum and liver was carried out. Choledochojejunostomy, Roux-en-Y anastomosis, gastrojejunostomy, and T-tube choledochoestomy were performed. Pathological examination of the surgical specimens (Figure 2) confirmed pancreatic adenocarcinoma with metastases to the liver and omentum. He was discharged 2 weeks after the operation.

Two days after discharge, he presented at the emergency department with hematemesis. Esophagogastroduodenoscopy showed suspected duodenal invasion of the pancreatic cancer with ulceration and hemorrhage. Endoscopic biopsy could not be performed at that time owing to the possibility of inducing further bleeding. He was admitted for further management with blood transfusion, proton pump inhibitors and sucralfate. He was discharged 19 days later with no evidence of hemorrhage. However, 3 weeks later, the hematemesis recurred. Emergency esophagogastroduodenoscopy failed to localize the source of bleeding due to the large amount of fresh blood that had accumulated in the prepyloric area and fundus. The patient died of massive bleeding the next day.

**DISCUSSION**

Pancreatic cancer is a devastating disease with poor prognosis, an overall 5-year survival rate of less than 1%, and a medium survival of approximately 5–6 months after tumor detection [4]. In Taiwan, it is the eighth leading cause of cancer-related deaths in men and the seventh in women [5]. It is now ranked fourth as the cause of death from cancer in the United States, Europe, and Japan, and is second only to colorectal cancer as a cause of digestive cancer-related death [2,6].

Many risk factors for pancreatic cancer have been identified, including old age, male sex, family history,
chronic pancreatitis, obesity, low physical activity, a “Western” dietary pattern (high intake of fat and/or meat, particularly smoked or processed meats), and cigarette smoking [1,3,6–9]. However, the only risk factors to be consistently reported are age and cigarette smoking [1,8]. Smoking was the only risk factor noted in our case. The risk for developing pancreatic cancer increases with age, with a mean age of onset in the seventh and eighth decades of life [9]. Pancreatic cancer rarely develops before the age of 50, but the incidence rises sharply thereafter [2,3]. Our patient was only 31 years old. About 5–10% of patients have a family history of pancreatic cancer and seem to present earlier than sporadic cases [3]. Certain syndromes with a specific germline may increase the risk of pancreatic cancer. For example, a recent study showed that the risk of pancreatic cancer was increased in families with germline DNA mismatch repair gene mutation, as compared with the general population [10]. Although no malignancy was noted in the family members of our patient, it is possible that genetic factors may have played a role in the carcinogenesis of this case at this young age.

The initial presentations of pancreatic cancer vary according to tumor location [1–3]. Abdominal pain, weight loss, jaundice and the development of diabetes mellitus have been reported as the initial presentations for pancreatic cancer [1–3]. Abdominal pain is often felt as a dull ache in the upper abdomen and may radiate to the back, and often improve on leaning forward [3]. Uncommonly, such pain may be severe and transient, along with associated hyperamylasemia,
indicating acute pancreatitis caused by substantial ductal obstruction by tumor [1,3,11,12]. Our case initially presented with this uncommon manifestation. At the first admission, abdominal ultrasonography and CT showed a mildly dilated pancreatic duct and an enlarged pancreatic head. These findings were considered to be caused by tissue swelling as a result of the inflammatory process, but no definitive pancreatic tumor could be found.

An elevated serum CA19-9 level and progressive dilatation of the pancreatic duct with an enlarged pancreatic head noted on ultrasonography after the episode of pancreatitis subsided might suggest superimposed pancreatic cancer. Follow-up CT performed after resolution of acute pancreatitis would be useful to evaluate the possibility of superimposed cancer or to locate the suspected lesion for biopsy. Unfortunately, this patient did not accept our suggestion and was lost to follow-up. As in the first CT scan, the second and third CT scans were also performed during episodes of pancreatitis. The findings of these scans could still be explained by the process of pancreatitis but could be used to diagnose superimposed cancer.

Magnetic resonance imaging is becoming more widely used for acute pancreatitis. A recent study showed no differences in the ability to detect acute pancreatitis between diffusion-weighted imaging, an increasingly used sequence of magnetic resonance imaging, and CT imaging [13]. However, diffusion-weighted imaging can detect acute pancreatitis more clearly than CT without using enhancing material and can detect pancreatic cancer as a cause of acute pancreatitis [13]. Meanwhile, magnetic resonance cholangiopancreatography can detect choledocholithiasis and pancreas divisum as a cause of acute pancreatitis and can offer an alternative to endoscopic retrograde cholangiopancreatography, at least for diagnosis [13,14].

Although CA19-9 is frequently elevated in patients with various benign pancreaticobiliary disorders, it is still useful for diagnosis of pancreatic cancer [2,15–18]. Since its first description in 1979, studies have suggested that a serum concentration > 37 U/mL represents the most accurate cutoff value for discriminating pancreatic cancer from benign pancreatic disease, with a sensitivity of up to 90% and a specificity approaching 98% [9,16–19]. In practice, a very high CA19-9 level (e.g. > 1,000 U/mL) along with a clinical presentation consistent with pancreatic cancer is essentially diagnostic for malignancy and is often associated with surgically unresectable disease [2,9,19]. The preoperative serum CA19-9 level in our patient was 1,561.5 U/mL, which was compatible with his unresectable disease.

For patients presenting with liver nodules and an obvious pancreatic mass, liver biopsy offers an appropriate alternative method for diagnosis, and the diagnosis of pancreatic cancer with liver metastasis is acceptable when the liver biopsy reveals adenocarcinoma [1]. A recent study showed that ultrasound-guided percutaneous pancreatic biopsy, as compared with metastatic liver tumor biopsy, is an effective and safe modality for confirming the pathologic diagnosis in patients with unresectable pancreatic cancer [20]. In clinical practice, however, a CT-guided biopsy of pancreatic tumor is more widely performed because air interference limits the utility of ultrasound-guided biopsy. Endoscopic ultrasound-guided fine-needle aspiration has recently emerged as a diagnostic adjunct for pancreatic lesions [21]. In a large, well-controlled study, endoscopic ultrasound-guided fine-needle aspiration with aspiration cytology was an accurate test for detecting pancreatic adenocarcinoma [22]. Some experts have also advocated biliary biopsy via transhepatic tracts when performed during percutaneous biliary drainage [23]. In our patient, because bypass surgery was warranted for the extensively long segmental stenosis of the common bile duct, preoperative image-guided biopsy was not arranged. Furthermore, image-guided biopsy was difficult to perform in this patient because it was not easy to differentiate between tumor tissue and inflammatory tissue on images. Therefore, we arranged an intraoperative biopsy for our patient.

Immunohistochemistry is often useful to reach a diagnosis of a malignancy. Cytokeratin (CK) 7 and CK20 expression was present in 96% and 63% of cases of pancreatic adenocarcinoma, respectively [24]. CK20 is an excellent marker for metastatic pancreatic cancer [25] and overexpression of CK20 indicates a subtype of pancreatic adenocarcinoma with decreased overall survival [24,26]. Therefore, metastatic adenocarcinoma of the liver positive for both CK20 and CK7, as in our case, indicates that the primary tumor was localized in the pancreaticobiliary system [27].

In addition to traditional treatment with bypass surgery, biliary stricture may also be treated by stenting. Percutaneous metallic biliary stenting was shown to provide good palliation for malignant jaundice [28].
However, owing to a lack of data on long-term patency, the use of metallic endobiliary stents for the treatment of benign biliary strictures remains controversial [29,30]. Some experts have even suggested that metallic endobiliary stents should not be used for benign strictures in patients with a predicted life expectancy >2 years [29]. Furthermore, lesions such as strictures due to chronic pancreatitis are more difficult to treat, and endoscopic therapy with gradual dilation and insertion of multiple plastic stents is reserved for patients who are not candidates for surgery [31]. In our case, no definitive evidence was available to determine whether the stricture of the common bile duct was caused by a benign disorder or by a malignancy. Therefore, placement of a biliary stent was not indicated owing to his young age and the diagnostic uncertainty.

Invasive pancreatic cancer as a cause of massive gastrointestinal hemorrhage is exceedingly rare [32–35]. Mechanisms responsible for massive gastrointestinal hemorrhage caused by a pancreatic tumor may include gastric variceal hemorrhage secondary to splenic vein occlusion [36–39], a fistula from the blood vessel to the duodenum (wirsungorrhage), direct tumor hemorrhage via the pancreatic duct (hemosuccus), or hemorrhage from the tumor invading into the gastrointestinal tract [32–35]. In a review of 859 endoscopies in patients with upper gastrointestinal hemorrhage, only three patients had a pancreatic tumor invading the duodenum [40]. Furthermore, patients with massive gastrointestinal hemorrhage from invasive pancreatic cancer usually present with hematochezia or tarry stool, rarely with hematemesis, as in our patient [32,34].

Despite the recent advances in early diagnosis and surgical treatment, the prognosis of patients with pancreatic cancer has not improved substantially. Surgical resection is the only potentially curative treatment. Unfortunately, due to the late presentation of the disease and the early dissemination of tumor cells, only 15–20% of patients are candidates for pancreatectomy, and the prognosis of pancreatic cancer is even discouraging in those with potentially resectable disease [2]. To date, the 5-year survival rate for adenocarcinoma of the pancreas is less than 5%, and most patients die within the first 2 years [9]. Therefore, further studies are needed to identify high risk individuals, to develop strategies for early detection, and to optimize treatments.

In conclusion, we report a young man with advanced pancreatic cancer and multiple metastases who initially presented with relapsing acute pancreatitis, an uncommon initial presentation for pancreatic cancer. Although young cases of pancreatic cancer have been reported before [41,42], to our knowledge, this is the youngest case of pancreatic cancer presenting initially with relapsing acute pancreatitis. For a patient with acute pancreatitis, particularly one who has recurrent bouts and who has no known risk factors for relapsing pancreatitis, a pancreatic neoplasm should be considered as a potential underlying cause, even in a young man.

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REFERENCES


一年輕男性的胰臟癌以
反覆性急性胰臟炎表現：一病例報告

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我們報告一個 31 歲男性以急性胰臟炎為其胰臟癌的初始表現。病人起初是因急性
胰臟炎來本院求診，腹部超音波發現胰臟頭部稍腫大及胰管稍擴大，且在追蹤下
更加明顯。然而病人拒絕進一步詳檢且不再回診。四個月後，病人再次因急性胰臟炎
來本院求診。不久，因阻塞性黃疸的現象而接受引流管置放。由於氣球擴張術效果不
佳，病人接受膽道繞道手術。術中所做的切片檢查證實是胰臟腺癌併多處轉移。病人
於術後數週後因大量胃腸出血而過世。由文獻搜尋，這是我們所知最年輕以此一初
始表現的個案。急性胰臟炎的病人，特別是有反覆性發作且沒有其他危險因子，即
使是年輕男性，仍然需要考慮胰臟腫瘤的可能性。

關鍵詞：胰臟腫瘤，胰臟癌，腺癌，胰臟炎
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