Chronic Pancreatitis with Synchronous and Metachronous Malignancy: Three Unusual Cases and a Literature Review

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HYPOTHESIS: Chronic pancreatitis is a risk factor for pancreatic cancer. The association between these 2 disease processes is not well known. We present 3 unusual cases of pancreatitis associated with pancreatic cancer and review the possible mechanisms that can cause pancreatitis to degenerate into pancreatic cancer.

DESIGN: A case series reviewing 3 unusual cases of chronic pancreatitis associated with pancreatic cancer. The patients' charts are reviewed, and a literature search is performed looking for chronic pancreatitis associated with pancreatic cancer.

SETTING: The cases were performed at a small community hospital in New York City, New York.

PARTICIPANTS: The surgeons involved are experienced pancreatic surgeons with a large referral group. The endoscopies were performed by gastroenterologists with years of experience in biliary and pancreatic disease.

RESULTS: The cases and the literature review support the hypothesis that there is an association between chronic pancreatitis and pancreatic cancer.

CONCLUSIONS: Three unusual case of chronic pancreatitis, 2 with synchronous and 1 with metachronous malignancies, are presented. The pathway of benign to malignant change is reviewed, and the constant awareness that pancreatitis is associated with malignancy must be kept in mind. (J Surg 64: 158-161. © 2007 by the Association of Program Directors in Surgery.)

KEY WORDS: pancreatitis, chronic, cancer, pancreas

COMPETENCY: Medical Knowledge

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INTRODUCTION

Cancer of the pancreas remains a lethal disease, with few long-term survivors. The presentation of pancreatic cancer is late stage and has remained unchanged over 4 decades. Jaundice, a mass, and weight loss characterize the presentation of lesions in the head of the pancreas and weight loss, severe pain, and a mass signal body and tail malignancies.

Chronic pancreatitis is a relatively uncommon disease. Its incidence is aproximately 8 to 10 per 100,000. Pancreatic insufficiency and pancreatic calcifications are complications of long-standing chronic pancreatitis. Chronic pancreatitis is associated with a 4-fold increase in the incidence of pancreatic cancer,[1] but it is unusual in the authors' experience to operate on patients with symptomatic pancreatitis who have or develop malignancies. Cancer of the pancreas may coexist, precede, or follow chronic pancreatitis. Three patients with chronic pancreatitis requiring reoperation, in 2 for pancreatitis and in 1 for pancreatic mass years after pancreatic surgery, are presented. In 2 it was totally unexpected.

The cases will be discussed and the literature reviewed, with the intent to increase awareness of the cancer–pancreatitis association, and an alert will be issued of this uncommon presentation.

CASE 1

A 60-year-old man with a 10-year history of chronic calcific pancreatitis, secondary to previous alcohol ingestion, was referred for surgical evaluation. Recurrent attacks of abdominal pain, pancreatic insufficiency, and insulin-dependent diabetes were present for 3 years. A computed tomography (CT) scan showed a dilated dorsal pancreatic duct with multiple calculi throughout the duct and parenchyma. Multiple endoscopic pancreatic stents were therapeutically placed in the pancreatic duct for 3 years preceding surgery. Pain relief and decreased frequency of attacks were initially noted after stenting. When

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the stents failed to give relief, surgical decompression was planned.

At surgery the pancreas was firm throughout without a dominant mass. The pancreatic duct was longitudinally incised and calculi removed. Within the pancreatic duct, which is ordinarily smooth, were 1-3-mm irregular fronds of tissue that, by biopsy, were invasive ductal carcinoma. Biopsy of the parenchyma showed poorly differentiated ductal carcinoma. A roux limb was placed to decompress the pancreatic duct. The patient recovered uneventfully, and the operative findings were reviewed and discussed. Total pancreatectomy was planned.

At subsequent surgery more extensive disease was found in the tail of the pancreas, after dividing the pancreas over the superior mesenteric vein. The previously noted thickened tail was in fact diffusely involved with cancer, invading the left kidney and spleen, both of which were removed with the distal pancreas. A coagulopathy developed, which was manifested by diffuse oozing. The left upper quadrant was packed to allow for stabilization of the patient. Forty-eight hours later, the packs were removed and the pancreaticojejunostomy completed to the proximal gland. The cancer was stage 4 (T4, N1, M0). The patient slowly deteriorated over the next 8 weeks and died on hospital day 61.

CASE 2

A 71-year-old man who was a former heavy drinker, with an 8-year history of chronic, calcific pancreatitis presented in follow-up with worsening attacks of abdominal pain, increasing in intensity and frequency. In September 2000 he underwent a splenectomy, distal pancreatectomy, and pancreaticojejunostomy. Pathology revealed chonic, fibrosing pancreatitis. Postoperatively there was relief of pain for 3 years, after which the abdominal pain returned. He also was treated with endoscopic stents placed in the pancreatic duct and changed as needed. The stents provided some relief, allowing the patient to be functional without pain medications. A CT scan showed a perfused pancreas with dilation of the dorsal duct with calcifications within the duct and parenchyma. No mass was observed.

Because of increasing symptoms and suspicion that the dorsal duct was obstructed, a pancreaticojejunostomy with removal of the calculi was planned. At surgery the pancreas was rock hard. It was also noted to be irregular with direct involvement of the posterior wall of the stomach and duodenum. Upon opening the dorsal pancreatic duct, abnormal fronds of tissue were noted. Biopsies of the parenchyma and duct tissue revealed adenocarcinoma with invasion of the posterior wall of the stomach. Because of extensive regional spread, the pancreaticojejunostomy was reestablished and the patient was closed. The cancer was stage 4 (T4, Nx, M0).

CASE 3

A 68-year-old woman, who originally presented in 1990 with chronic pancreatitis limited to the body and tail of the gland. The etiology of her pancreatitis was unknown. Her symptoms were of disabling abdominal pain. She had a stricture in the distal part of her pancreatic duct on ERCP, and no mass was seen on CT. She underwent a distal pancreatectomy. Pathology showed chronic, sclerosing pancreatitis. She remained symptom free and was followed with annual physical examination and routine blood work (SMA 7, LFTs, amylase and lipase). In March 2003 she developed abdominal pain and a moderate amount of weight loss. A CT scan revealed a mass in the head of the pancreas. She underwent a total pancreatectomy. Pathology showed moderately differentiated ductal adenocarcinoma. It was a stage 1 cancer (T2, N0, M0). She is presently alive and well after receiving chemotherapy for 2 years.

DISCUSSION

Cancer of the head, body, and tail of the pancreas has defied inexhaustible attempts to cure it, diagnose it earlier, or downstage it without success. Despite more widespread use of axial imaging by CT or magnetic resonance imaging, more curable pancreatic neoplasms have not been diagnosed, save anecdotal, incidental experiences.

Chronic pancreatitis is characterized by irreversible destruction of pancreatic acinar and ductal cells. These cells are replaced by fibrous tissue and deposition of extracellular matrix.[2] Chronic pancreatitis is a spectrum of a disease that ranges from mild, with occasional attacks; to moderate, with frequent attacks and more irreversible glandular changes; to severe, with disabling sequelae, such as intractable pain, diabetes, and pancreatic insufficiency.[1] Today, earlier diagnosis of chronic pancreatitis by awareness, endoscopy and CT and nonoperative intervention for mild symptoms may delay the decline in secretory function and exocrine and endocrine malfunction.[3]

Although chronic pancreatitis is well known, its prevelence is 8 to 10 cases per 100,000 population. Long-term consumption of alcohol accounts for 75% of patients. Primary duct obstruction as a cause of chronic pancreatitis is present in only 5% of patients.[4] Idiopathic pancreatitis and autoimmune pancreatitis are less common but are prevalent at tertiary centers. The cause of chronic pancreatitis is important only in preventing ongoing glandular insult by removing an exogenous toxin.[1]

Complications of chronic pancreatitis are secondary to parenchymal fibrosis and deposition of inspissated proteinaceous material in the pancreatic duct. Pancreatic tissue samples from patients undergoing pancreatic resection for chronic pancreatitis demonstrate an increased tissue level of connective tissue growth factor (CTGF) and transforming growth factor-beta (TGF-beta). The overexpression of CTGF and TGF-beta suggests that these proteins may contribute to the enhanced extracellular matrix synthesis, leading to fibrin and collagen deposition in chronic pancreatitis.[2] The complications that develop as a result of pancreatic fibrosis are (1) bile duct obstruction, (2) duodenal obstruction, (3) gastric and splenic varicies, (4) obstruction of the pancreatic duct, (5) pancreatic ascites, and (6) pancreatic pseudocyst.[1]