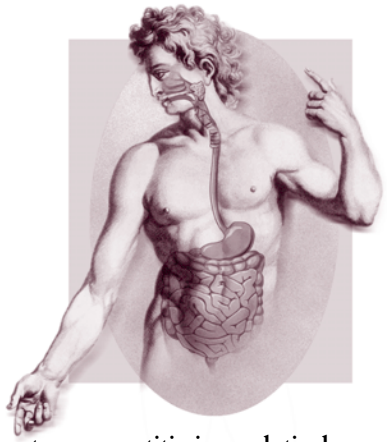

Acute pancreatitis

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Acute pancreatitis is a relatively common disease with an incidence of 30 per 100,000 persons per year. In the United States, more than 80% of the cases are related to biliary stones or alcohol use. It is a potentially fatal disease with an overall mortality of 5% to 10%. When first seen, patients have an acute abdomen. It is imperative that the diagnosis be established rapidly with a thorough history, physical examination, and appropriate laboratory and imaging studies. Prompt determination of patients who need referral for intensive care or consultation is crucial. There is no specific treatment for most patients with acute pancreatitis. Supportive care includes intravenous administration of fluids, parenterally administered analgesia, nutritional support, and prevention and treatment of complications.

(Key words: acute pancreatitis, biliary stones, pancreatic necrosis)

Acute pancreatitis is a relatively common disorder with an incidence of about 30 per 100,000 persons per year. Eighty percent of the cases are related to biliary stones or alcohol use. In 1925, Moynihan[1] described acute pancreatitis as,

> The most terrible of all calamities that occur in connection with the abdominal viscera. The suddenness of its onset, the illimitable agony which accompanies it, and the mortality attendant upon it render it the most formidable of catastrophes.

This article discusses the pathophysiology, differential diagnosis, and the most up-to-date treatment options.

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Classification

Acute pancreatitis is defined as an acute inflammatory process of the pancreas that usually resolves without any disruption of the normal morphology of the pancreas. In contrast, chronic pancreatitis is associated with structural changes and loss of exocrine and endocrine function.

The severity of the illness is variable, ranging from a brief self-limited illness to development of multiple-organ system failure, sepsis, and death.

Mild acute or interstitial pancreatitis is characterized by minimal or no organ dysfunction and an uncomplicated recovery. Severe necrotizing pancreatitis, in contrast, involves organ failure (shock, pulmonary insufficiency, renal failure, etc), and local complications, including infected necrosis, abscess, or pseudocyst formation.

Pancreatic necrosis can consist of either focal or diffuse areas of necrotic, nonviable pancreatic parenchyma. The distinction between necrotizing and interstitial pancreatitis can be made by a computed tomography (CT) scan with orally and intravenously administered contrast (dynamic contrast-enhanced CT).[2]

Causes of acute pancreatitis

Obstructive causes

Gallstones are the most common cause, accounting for about 30% to 45% of all cases. Also, about two thirds of the patients with idiopathic pancreatitis may actually have their disorder related to "microlithiasis," which is seen on the ultrasound as sludge within the gallbladder, or by examining bile obtained at endoscopic retrograde cholangiopancreatography (ERCP) for cholesterol and calcium bilirubinate crystals.[3] Gallstone pancreatitis is typically associated with significant abnormalities of liver chemistries, the levels of which return to normal within several days in the absence of persistent common bile duct obstruction. The presence of hyperbilirubinemia or an aspartate transaminase (AST or SGOT) level greater than three times normal is highly suggestive of gallstone pancreatitis. The most likely mechanism is ductal obstruction, the theory for which proposes that persistent obstruction of the pancreatic duct causes elevation in the pancreatic ductal pressure with ensuing pancreatitis.

Despite the increased risks for development of acute pancreatitis with gallstones, the incidence of the disease is too low to warrant prophylactic cholecystectomy in asymptomatic patients. The rate of development of symptoms or gallstone complications is estimated to be between 2% and 6% per year, based on the experience of one of the authors (M.J.K.).

Other forms of obstruction include ampullary or pancreatic tumors, pancreas divisum, choledochocele, duodenal diverticula, and sphincter of Oddi dysfunction. Pancreas divisum is a developmental anomaly caused by a failure of fusion of the ventral pancreatic duct with the dorsal duct, resulting in the majority of the gland being drained through the duct of Santorini. This anomaly affects up to 6% of the general population. Among those affected in whom pancreatitis actually develops, there is stenosis of the minor papilla.

Toxins and drugs

Alcohol is the most common toxin and the second leading cause of pancreatitis, accounting for about 30% to 35% of all the cases. Alcohol-induced pancreatitis may be related to direct toxic effects of alcohol or obstruction of the small pancreatic ductules by proteinaceous plugs.

Drugs associated with the highest incidence are azathioprine and mercaptopurine (incidence 3% to 5%) and didanosine (incidence up to 20% to 25%).

Trauma

Blunt trauma to the abdomen may cause contusion, laceration, or complete transection of the gland when the pancreas is compressed against the spine.

Iatrogenic causes

Pancreatitis is probably induced by ERCP in about 1% to 5% of the cases. In most cases, ERCP-induced pancreatitis is mild. Its incidence is increased with the volume and pressure of the injected contrast material, number of injections, ampullary trauma by multiple attempts at cannulation, and overfilling of the pancreatic ducts.[4] Also, ERCP-induced pancreatitis occurs more frequently with manometry of the sphincter of Oddi.

Acute pancreatitis can occur postoperatively with thoracic (such as coronary artery bypass grafting) and abdominal surgery. Risk factors include perioperative hypotension, renal insufficiency, and perioperative infusion of calcium chloride.

Infectious causes

Viral (mumps; coxsackievirus; cytomegalovirus; hepatitis A, B, and C; etc), bacterial (mycobacterium, legionella, mycoplasma), and parasitic (*Ascaris*, *Opisthorchis*) infections have been associated with acute pancreatitis.

Metabolic causes

Hypertriglyceridemia is a cause of acute pancreatitis in up to 4% of cases, occurring in patients with poorly controlled diabetes or those with familial hypertriglyceridemias. In most patients, triglyceride levels are in excess of 1000 mg/dL. Hyperparathyroidism and hypercalcemia account for less that 1% of all cases.

Miscellaneous causes

Posterior penetrating peptic ulcer can cause acute pancreatitis. Hereditary pancreatitis rarely presents as acute pancreatitis.

Clinical presentation

Patients have epigastric pain that is continuous and boring, with radiation to the back in about 50% of the cases. The pain is made worse by the supine position, reaches its peak intensity in about 30 to 60 minutes after onset, and can last for several hours to days. Patients frequently have nausea and vomiting. Abdominal distension is common. Patients may have ecchymosis in one or both flanks (Grey Turner's sign) or in the periumbilical region (Cullen's sign). The ecchymosis is due to the extravasation of the pancreatic exudate to these regions. With third spacing of fluids, patients may have hypotension and other signs of shock. They may also have a low-grade fever, with a temperature of 37.7°C to 38.3°C.

Laboratory diagnosis

The serum amylase level is elevated in acute pancreatitis; it rises rapidly and is also cleared rapidly (about 5 to 10 days). Normally, about 40% of the amylase is of pancreatic origin (P isoamylase), and 60% is of salivary origin (S isoamylase). S isoamylase is also produced by the fallopian tubes, ovaries, and in some form of lung cancer, and this reduces the specificity of amylase. It is also increased with common bile duct obstruction, mesenteric ischemia, intestinal perforation (increased absorption from the bowel into the systemic circulation) and with parotitis, ruptured ectopic pregnancy (increased production of salivary amylase), and with renal failure (reduced renal clearance). The measurement of the P isoamylase is cumbersome and not widely available. When cutoff values just above the normal range are used, it has a sensitivity of greater than 90% and specificity of less than 70%. If the cutoff is increased to three times the upper limit of normal, the specificity is nearly 100%, but the sensitivity drops to less than 60%.

The amylase-to-creatinine-clearance ratio (ACR) is useful for the diagnosis of macroamylasemia, in which the amylase level is elevated as it is bound to macromolecules, which impair its renal clearance. In these instances, the ACR is low (<1%). Lipase is as sensitive and more specific than amylase. The level of serum lipase rises early and stays elevated longer than the level of amylase. Unlike amylase, lipase is not elevated in patients with salivary disease, gynecologic conditions, or macroamylasemia. It is elevated, however, in patients with intestinal ischemia and perforation as a result of increased absorption of the luminal lipase into the systemic circulation.

Obstructive causes of pancreatitis are associated with elevated levels of serum AST, alanine transaminase (ALT or SGPT), alkaline phosphatase, and bilirubin. An ALT level greater than 150 IU/L has a specificity of about 96% for gallstone pancreatitis.[5]

Imaging

Chest and abdominal radiographs are useful to exclude perforation. Chest radiographs may show pleural effusion, atelectasis, pneumonia, congestive heart failure, or adult respiratory distress syndrome. Abdominal radiographs may reveal dilated loop of duodenum (sentinel loop) or spasm of the colon with dilation of the loop proximal to it (colon cutoff sign). Pancreatic calcification may be seen in radiographs of patients with alcoholic pancreatitis, and calcified gallstones may be seen in radiographs of patients with biliary pancreatitis.

Ultrasound is a relatively sensitive test when the pancreas can be visualized. It is limited by obesity and bowel gas in about 30% to 40% of cases. It is very useful for evaluating the biliary tract for gallstones or ductal dilation. Computed tomography scans show no abnormality in about 15% to 30% of patients with mild pancreatitis. In most severe cases, dynamic

contrast-enhanced CT may show the presence of pancreatic necrosis.

Endoscopic retrograde cholangiopancreatography is useful for evaluation of recurrent pancreatitis, especially for diagnosis of microlithiasis, pancreas divisum, sphincter of Oddi dysfunction, or pancreatic or ampullary carcinoma.

Evaluation of severity

Numerous tools have been developed to assess the severity of pancreatitis as early as possible to maximize therapy and to minimize or prevent organ dysfunction and local complications. Ranson's criteria (*Figure*) are the most commonly used. The first five variables are measured at the time of admission and the next five during the first 48 hours. Measurement of fluid sequestration necessitates accurate measurement of fluid intake and output and has to be measured at the end of the 48 hours. The combination of more severe CT grades (C, D, and E) and greater than three Ranson's criteria predict higher risk of pancreatic infection and mortality.

Treatment

Medical treatment is primarily supportive, with close attention to fluid resuscitation with crystalloids. As much as 5 L to 6 L of fluid per day is essential to reduce hypotension and the associated hypoperfusion of the pancreas, with worsening ischemia and necrosis of the gland, and to prevent prerenal azotemia.

Despite some continued controversy, it appears that urgent endoscopic sphincterotomy is beneficial for gallstone-induced bile duct obstruction in patients with severe acute pancreatitis.[6]

Abdominal pain is generally well relieved with meperidine hydrochloride (Demerol), though with increased severity of pain, morphine may be required. Although morphine may increase the tone of the sphincter of Oddi, there is no evidence that its use intensifies the disease process. Patients are kept on orders of nothing by mouth to rest the pancreas.

Nasogastric suction is reserved for patients with intractable nausea/vomiting due to gastric or intestinal ileus. Prophylactic antibiotic therapy with agents that achieve good concentration in the pancreas (such as ciprofloxacin, ofloxacin, imipenem) may be beneficial for patients with severe necrotizing pancreatitis.

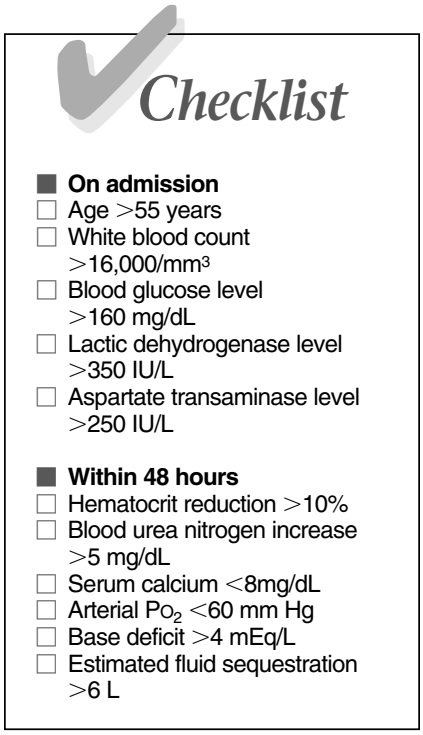

Figure. *Ranson's criteria for non–gallstone pancreatitis.*

Oxygen saturation should be closely monitored to observe for hypoxemia. Patients should receive transfusions as necessary to keep the hemoglobin level at greater than 10 g/dL. In patients with severe pancreatitis, a variety of cardiac complications may develop, including myocardial infarction, congestive heart failure, and shock, which must be treated appropriately.

Patients may be fed when their abdominal pain and ileus resolve. Patients, at least in theory, benefit from a diet high in carbohydrates, which do not stimulate the pancreas as much as proteins or fats. Patients with hypertriglyceridemias need to make the necessary changes in their diet. In most severe forms of pancreatitis, total parenteral nutrition (TPN) may be needed for 4 to 6 weeks. Triglyceride levels should be closely monitored during TPN.

Complications

Pancreatic necrosis

Pancreatic necrosis occurs in approximately 20% of the cases and should be suspected when it is predicted that the patient has severe pancreatitis. It may be appropriate to use prophylactic antibiotics as discussed earlier. Infected necrosis should be suspected if there is persisting systemic toxicity, including a high white blood cell count, fever, and organ failure after 7 to 10 days. The diagnosis is made by percutaneous aspiration. Most of the infections are caused by gram-negative rods, staphylococci and, occasionally, *Candida* spp. Aggressive surgical debridement and antibiotic therapy (initially based on the Gram stain results and later as guided by cultures) are required.

Pancreatic pseudocyst

The fluid collections seen in and around the pancreas initially are termed *acute fluid collections.* Most of these fluid collections resolve. If the fluid collection persists after 4 to 6 weeks, a fibrous capsule called a *pseudocyst* develops. Asymptomatic pseudocysts should be managed expectantly. If they become symptomatic with pain, obstruction of the common bile duct or the bowel, or if they become infected (in which case they are considered to be an abscess), they should be drained. The drainage can be achieved endoscopically, surgically, or radiographically, depending on their location and the availability of the physicians with the required skill.[7,8]

Pancreatic abscess

Pancreatic abscesses occur about 4 to 6 weeks after the initial episode and are heralded by pain, fever, and chills. They can be drained either surgically or radiographically.

Fistulas

Pancreatic fistulas are caused by disruption of the main pancreatic duct and should be suspected in patients in whom massive ascites or pleural effusions develop. Treatment usually involves hyperalimentation, drainage of fluid collection if

symptomatic, and the use of agents to suppress pancreatic secretion (such as octreotide acetate).

Comment

Acute pancreatitis may range from a mild to a life-threatening condition. Rapid diagnosis is important. In patients with signs of severe disease at onset or clinical deterioration after hospital admission, consultation with a gastroenterologist and possibly a surgeon would be recommended. Even with aggressive supportive care, acute pancreatitis has an overall mortality of 5% to 10%, with a 30% to 35% mortality in patients in whom complications develop.

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