# Chapter 36
# Pancreatitis

Acute pancreatitis is a common disease that causes significant morbidity and mortality. Pancreatitis is the most common principle gastrointestinal discharge diagnosis in the United States [1]. More than 250,000 patients are admitted per year for pancreatitis and about 3,000 die from this disease per year in the US [1, 2]. Furthermore, the hospitalization rate for acute pancreatitis in the US is rising [2]. About 15 % of all patients with acute pancreatitis develop necrotizing pancreatitis. Mortality ranges from 3 % for patients with interstitial edematous pancreatitis to 15 % for patients who develop necrosis [3, 4]. In developed countries, obstruction of the common bile duct by stones (38 %) and alcohol abuse (36 %) are the most frequent causes of acute pancreatitis. Gallstone-induced pancreatitis is caused by duct obstruction of gallstone migration. Obstruction is localized in the bile duct, the pancreatic duct, or both. Other well established causes of acute pancreatitis include:

- Hypertriglyceridemia
- Post–ERCP
- Drug induced
- Autoimmune
- Genetic
- Abdominal trauma
- Postoperative
- Ischemia
- Infections
- Hypercalcemia and hyperparathyroidism
- Posterior penetrating ulcer
- Scorpion venom

Abdominal pain is the cardinal symptom. It occurs in about 95 % of cases. Typically it is generalized to the upper abdomen, but it may be more localized to the right upper quadrant, epigastric area, or, occasionally, left upper quadrant. The pain typically occurs acutely, without a prodrome, and rapidly reaches maximum intensity. It tends to be moderate to severe in intensity and tends to last for several days.

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The pain typically is boring and deep because of the retroperitoneal location of the pancreas. About 90 % of patients have nausea and vomiting, which can be severe and unremitting. The severity of the physical findings depends on the severity of the attack. Mild disease presents with only mild abdominal tenderness. Severe disease presents with severe abdominal tenderness and guarding, generally localized to the upper abdomen. Rebound tenderness is unusual.

## Diagnosis

- Leukocytosis is common because of a systemic inflammatory response.
- Mild hyperglycemia is common because of decreased insulin secretion and increased glucagon levels.
- The serum lipase level is the primary diagnostic marker for acute pancreatitis because of its high sensitivity and specificity. Serum lipase is more than 90 % sensitive for acute pancreatitis [5]. The serum lipase level rises early in pancreatitis and remains elevated for several days.
- Serum amylase concentrations exceeding three times the normal upper limit supports the diagnosis of acute pancreatitis. However, the serum amylase is within the normal range on admission in up to 20 % of the patients.
- In a meta-analysis, a serum ALT level higher than 150 IU/L had a positive predictive value of 95 % in diagnosing acute gallstone pancreatitis [6].
- Any patient who has unexplained, severe abdominal pain should undergo supine and upright chest and abdominal radiographs. Abdominal radiographs are performed mainly to exclude alternative abdominal diseases, such as gastrointestinal perforation.
- Abdominal ultrasonography is the primary imaging study for abdominal pain associated with jaundice and for excluding gallstones as the cause of acute pancreatitis. It has the advantages of low cost, ready availability, and easy portability for bedside application in very sick patients. It is ubiquitous in the evaluation of pancreatitis. When adequately visualized, an inflamed pancreas is recognized as hypoechoic and enlarged because of parenchymal edema. The pancreas is visualized inadequately in 30 % of cases.
- Patients who present with severe pancreatitis or who present initially with mild to moderate pancreatitis that does not improve after 5–7 days of supportive therapy should undergo abdominal CT imaging [7]. CT scan *with contrast* is the standard approach for the diagnosis and work-up of severe pancreatitis. Except in cases of initial diagnostic uncertainty, it is advisable to wait 5–7 days to obtain the initial scan. A contrast enhanced CT scan obtained within the first few days cannot be used to determine whether a patient has necrotizing or severe interstitial pancreatitis. Patients should receive both intravenous and oral contrast. Areas of necrosis with diminished or no enhancement upon contrast bolus are detected with an accuracy of 87 % (see

CT Grading system below). Renal insufficiency is a relative contraindication to the use of intravenous contrast agent.

- Magnetic resonance cholangiopancreatography (MRCP) has become a useful procedure for identifying retained common bile duct stones [7]. Selective use of MRCP can reduce the need for endoscopic retrograde cholangiopancreatography (ERCP) for patients with suspected gallstone pancreatitis.

## Risk Stratification

Most episodes of acute pancreatitis are mild and self-limiting, needing only brief hospitalization. However, 20 % of patients develop severe disease with local and extrapancreatic complications characterized by early development and persistence of hypovolemia and multiple organ dysfunction. Risk stratification plays a key role in the management of patients with acute pancreatitis. Although amylase and lipase remain the standard for diagnosis, they are poor predictors of severity. A number of scoring systems have been developed to assess the severity of pancreatitis. The Ranson Criteria was the first scoring system to be developed and remains commonly employed today [8]. More recently, the APACHE II Scoring System and the Imrie Score have been used to predict severity. The Balthazar computed tomography grading system is widely used in patients who have undergone CT scanning. Severe Acute Pancreatitis as defined by the Atlanta Symposium include a Ranson Score $\geq 3$, APACHE-II score $\geq 8$, organ failure and/or local complications (necrosis, abscess or pseudocyst) [9]. The Bedside Index of Severity in Acute Pancreatitis is a 5-factor scoring system that can be performed during the first 24 h of admission [10]. The Bedside Index of Severity in Acute Pancreatitis score >2 within 24 h is associated with a sevenfold increase in the risk of organ failure and a tenfold increase in the risk of mortality [11, 12].

(a) *Ranson's Criteria*

- At presentation
  - Age older than 55 years
  - Blood glucose level greater than 200 mg/dL
  - White blood cell count greater than 16,000/$mm^3$
  - Lactate dehydrogenase level greater than 350 IU/L
  - Alanine aminotransferase level greater than 250 IU/L
- 48 h after presentation
  - Hematocritd 10 % decrease
  - Serum calcium less than 8 mg/dL
  - Base deficit greater than 4 mEq/L
  - Blood urea nitrogen increase greater than 5 mg/dL
  - Fluid sequestration greater than 6 L
  - $PaO_2$ less than 60 mmHg

(b) *Glasgow (Imrie) Severity Scoring System*
- Age >55 years
- White cell count $>15 \times 10^9$/L
- $PaO_2 < 60$ mmHg Serum lactate dehydrogenase >600 units/L
- Serum aspartate aminotransferase >200 units/L*
- Serum albumin <3.2 g/dL
- Serum calcium <2 mmol/L (8 mg/dL)
- Serum glucose >10 mmol/L (180 mg/dL)
- Serum urea >16 mmol/L (44.8 mg/dL)

(c) *Balthazar CT Grading System*
- A: Normal
- B: Gland enlargement, small intrapancreatic fluid collections
- C: Peripancreatic inflammation, >30 % pancreatic necrosis
- D: Single extrahepatic fluid collection, 30–50 % pancreatic necrosis
- E: Extensive extrapancreatic fluid collections, >50 % pancreatic necrosis

(d) *The Bedside Index of Severity in Acute Pancreatitis* (one point each)
- Bun > 25 mg/dL
- Altered mental state
- Systemic inflammatory response syndrome (SIRS)
- Age ≥ 60 years
- Pleural effusion

(e) *The Revised Atlanta Classification recognizes 3° of severity* [13].
- Mild disease is defined as acute pancreatitis not associated with organ failure, local complications or systemic complications.
- Moderately severe acute pancreatitis is defined by the presence of transient organ failure, local complications or systemic complications. Transient organ failure is define by organ failure that is present for <48 h.
- Severe acute pancreatitis is defined by the presence of persistent organ failure (>48 h). Most patients with severe pancreatitis have pancreatic necrosis and a reported mortality of about 30 % [14].

## Complications

- Local complications
  - Interstitial pancreatitis involves acute collection of peripancreatic fluid formation
  - Pancreatic necrosis is the most severe local complication because it is frequently associated with pancreatic infection. Infection of pancreatic necrosis develops during the second or third week in 40–70 % of patients.
  - Pancreatic abscess consists of a circumscribed collection of pus that arises around a restricted area of pancreatic necrosis.

  - Pseudocyst is a collection of pancreatic fluid enclosed by a wall of granulation tissue that results from pancreatic duct leakage.
  - intraperitoneal hemorrhage
  - splenic vein thrombosis (causing left sided portal hypertension)
  - obstructive jaundice
- Renal dysfunction/failure
- Pulmonary complications
  - ARDS
  - Pleural effusion
  - Atelectasis
  - Pneumonia
- other
  - DIC/coagulopathy
  - upper GI bleeding
  - hypocalcemia
  - hyperglycemia
  - hypertriglyceridemia

## Management

Significant advancements in the management of patients with pancreatis have occurred in the last decade. These include three major area of focus:

- Less “aggressive” fluid resuscitation
- Early enteral nutrition
- A conservative and minimally invasive approach to necrotizing pancreatitis
- In mild forms of disease, besides the etiological treatment (mostly for gallstone-induced pancreatitis), therapy is supportive and includes fluid resuscitation, analgesia, oxygen administration, and antiemetics.
- Fluid resuscitation to correct fluid losses and maintain an adequate intravascular volume is an important component of the management of patients with severe pancreatitis (see Chap. 9). However, aggressive fluid therapy during the first days of hospitalization as recommended by most guidelines and reviews on this topic is not supported by clinical evidence. Aggressive fluid resuscitation based on non-physiologic end-points is associated with an increased risk of organ dysfunction. de-Madaria et al. demonstrated that administration of > 4.1 L of fluid (more than the third quartile) during the initial 24 h was significantly and independently associated with persistent organ failure, fluid collections, respiratory insufficiency, and renal insufficiency [15]. Fluid resuscitation should be guided by an assessment of the patient’s fluid responsiveness. Lactate Ringers solution (LR) is the fluid of choice; this fluid has been shown to have anti-inflammatory properties in patients with

pancreatitis [16]. An albumin infusion should be considered in patients with an albumin <3.0 g/dL.

- Respiratory, cardiovascular, and renal function must be closely monitored.
- Morphine traditionally has been disfavored for acute pancreatitis because it increases the sphincter of Oddi pressure. Meperidine, 50–100 mg every 4–6 h, has been the traditional opiate regimen of choice because it does not raise the sphincter pressure. Caution should be used with this agent as it active metabolite normeperidine accumulates with renal dysfunction and can cause seizures. Fentanyl is a useful alternative in this situation.
- Nasogastric tube aspiration traditionally was used to prevent pancreatic stimulation induced by gastric distention and acid secretion. Multiple clinical trials, however, have demonstrated no benefit from nasogastric aspiration (see feeding below) [17].
- Prophylactic antibiotics have previously been recommended to reduce the risk of pancreatic infection [18]. However, meta-analyses have failed to demonstrate a benefit from prophylactic antibiotics [19–21]. Guidelines issued by the American College of Gastroenterology do not recommend antibiotic prophylaxis to prevent pancreatic infection [22, 23]. In most patients, infection of pancreatic or extrapancreatic necrosis does not occur until week 3 or 4. Antimicrobial agents with favorable pancreatic tissue penetration such as carbapenems and quinolones are recommended at this time [24].
- Peritoneal lavage to remove toxic necrotic compounds is no longer recommended for severe pancreatitis. In a meta-analysis of eight RCTs involving a total of 333 patients, peritoneal lavage did not reduce morbidity or mortality [25].
- Adrenal insufficiency (CIRCI) has been reported to occur in up to 35 % of patients with severe pancreatitis [26]. A cosyntropin stimulation test and treatment with hydrocortisones is recommended in those patients with adrenal insufficiency (see Chap. 39).
- Most patients with gallstone-induced pancreatitis present with mild disease and quickly recover after early resuscitation. ERCP is indicated for clearance of bile duct stones in patients with severe pancreatitis, in those with cholangitis, in those who are poor candidates for cholecystectomy, in those who are postcholecystectomy, and in those with strong evidence of persistent biliary obstruction [22].
- Probiotics should be avoided in patients with pancreatitis [27]. The role of prebiotic fiber supplementation is controversial [28].
- Patients with acute pancreatitis have traditionally been treated with "bowel rest"; this included NG suction and NPO. Patients with mild pancreatitis were started on oral feeds once the pain had subsided while patients with severe pancreatitis were treated with parenteral nutrition until the disease process resolved. There is, however, no scientific data to support this approach to the management of patients with acute pancreatitis. "Bowel" rest is a meaningless term and it is impossible to rest the bowel (see Chap. 32). Trying to rest the bowel by not feeding is akin to inducing asystole to rest the heart. Both experimental and clinical data strongly support the concept that enteral nutri-

tion started within 24 h of admission to hospital reduces complications (primarily pancreatic infection), length of hospital stay and mortality in patients with acute pancreatitis [29, 30]. Enteral nutrition should begin within 24 h after admission and following the initial period of volume resuscitation and control of nausea and pain. Patients with mild pancreatitis can take a low fatty diet by mouth while patients with severe pancreatitis should receive enteral tube feeds. Clinical trials suggest that both gastric and jejunal tube feeding are well tolerated in patients with severe pancreatitis. However, post-pyloric feeding is generally recommended. While there is limited data as to the optimal type of tube feed, a semi-elemental formula with structured lipids is recommended (see Chap. 32). An elemental formula may be appropriate in patients with very severe pancreatitis or in those demonstrating gastro-intestinal intolerance. Parenteral nutrition is associated with increased complications and mortality and should be avoided in patients with acute pancreatitis.

- There has been a shift away from urgent surgical debridement of infected necrosis toward more conservative, less invasive approaches. This approach is recommended by the most recent international consensus for the management of necrotizing pancreatitis [31]. In a multicenter, randomized, controlled trial from the Netherlands, a step-up approach to management of infected necrosis was compared with open necrosectomy [32]. The step up approach involved placement of percutaneous drainage catheters in addition to treatment with antibiotics. Among patients whose clinical condition failed to improve within 72 h, minimally invasive debridement was performed via a retroperitoneal approach. The step up approach reduced major complications or death by 29 % compared with traditional open necrosectomy. Van Santvoort et al collected data from 639 patients with necrotizing pancreatitis treated at 21 Dutch hospitals [4]. Treatment was conservative in 62 % of patients; the mortality in these patients was 7 % as compared to 38 % in those treated by an invasive approach. Furthermore, patients with longer times between admission and intervention had a lower mortality. Fine needle aspiration culture of pancreatic or extrapancreatic necrosis to diagnose “infected necrosis” does not lead to a significant change in management and is therefore not routinely recommended [24].

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