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Contemporary Treatment of Acute Pancreatitis

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Table of Contents

Introduction ............................................. 2
Case 1 .................................................. 2
Case 2 .................................................. 5
Case 3 .................................................. 8
Case 4 .................................................. 10
Summary Points ........................................ 11
References .............................................. 11

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Acute pancreatitis is an inflammatory disease of the pancreas that can progress into a systemic inflammatory state with resultant multi-organ dysfunction. It is estimated that most of the 250,000 individuals diagnosed with acute pancreatitis each year in the United States develop pancreatitis secondary to gallstones or alcohol intake. Most episodes of acute pancreatitis are mild and resolve with minimal specific interventions; however, approximately 2% to 5% of patients develop severe pancreatitis associated with pancreatic necrosis and may require operative intervention.¹ The precipitating factor induces acinar cell injury resulting from colocalization of zymogen granules and lysozymes. This localized inflammation in the pancreas can propagate systemically as pancreatic enzymes induce cytokine production in the pancreas and affected organs, such as the lungs, liver, and kidneys. Despite advancements in our understanding of the pathophysiology of acute pancreatitis, the mainstay of treatment remains nonoperative, except in patients with necrotizing pancreatitis. Multiple clinical trials utilizing anticytokine agents have failed to reduce mortality.²³ This monograph uses hypothetical cases to review the evaluation and management of acute pancreatitis.

CASE 1

PATIENT PRESENTATION

Patient 1 is a 42-year-old man who is admitted to the hospital with acute onset of abdominal pain, nausea, and vomiting. He has epigastric tenderness but no peritoneal signs. Admission laboratory test results are: hemoglobin, 16.2 mg/dL; leukocyte count, 18 × 10³/mm³; serum creatinine, 1.3 mg/dL; total bilirubin, 1.8 mg/dL; amylase, 432 U/L; lipase, 242 U/L; and alkaline phosphatase level, 260 U/L.

What is an appropriate diagnostic plan for this patient?

DISCUSSION

This patient’s clinical presentation is consistent with acute pancreatitis. Other abdominal conditions that mimic acute pancreatitis can be ruled out by history, physical examination, and laboratory data; however, imaging modalities should be used to confirm the diagnosis of acute pancreatitis.

Clinical Presentation

The cardinal clinical symptom of acute pancreatitis is constant epigastric pain of insidious onset, often radiating to the back. Other clinical findings include anorexia,
fever, nausea, vomiting, ileus, and abdominal distention (Table 1). The spectrum of clinical presentation depends on the severity of the disease process. Patients with severe necrotizing pancreatitis can present with jaundice, hypotension, and signs of retroperitoneal hemorrhage, producing blue discoloration of the flanks (Grey Turner sign), the umbilicus (Cullen sign), or the inguinal ligament (Fox sign). The differential diagnosis includes gastritis, peptic ulcer disease, acute cholecystitis, pyelonephritis, intestinal ischemia, intestinal obstruction, intestinal perforation, and hepatitis.

Laboratory Tests

No single laboratory test or physical finding is pathognomonic for pancreatitis. Hyperamylasemia in a patient with clinical signs and symptoms of acute pancreatitis is the usual means of confirming the diagnosis of acute pancreatitis.\textsuperscript{5} The degree of hyperamylasemia does not correlate with disease severity, perhaps because of the relatively rapid clearance of amylase from plasma (amylase half-life, 130 min). Clinical conditions associated with hyperamylasemia in nonpancreatic origin include the following: salivary gland injury, burns, head or multiple trauma, diabetic ketoacidosis, macroamylasemia, renal transplantation, renal dysfunction and hydronephrosis, pneumonia, pregnancy, fallopian tube pathology, afferent loop syndrome, acute appendicitis, dissecting aortic aneurysm, small bowel injury, perforated ulcer, small bowel obstruction, and mesenteric ischemia.

Fractionation of plasma isoenzyme levels can be used to differentiate pancreatic from salivary amylase. Amylase is cleared by the kidneys; therefore, renal dysfunction can result in hyperamylasemia. In such a patient, determination of the ratio of amylase to creatinine clearance is potentially useful. This fractional excretion of amylase (Fe\textsubscript{A}) can be calculated using the following formula:

\[
Fe\textsubscript{A} = \left( \frac{U\textsubscript{A} \times S\textsubscript{G}}{U\textsubscript{G} \times S\textsubscript{A}} \right) \times 10
\]

where S = serum and U = urine.

Clearance in excess of 4.5% to 6% is considered abnormal but is not specific for acute pancreatitis. However, clinical findings or abdominal computed tomography (CT) scans have made these laboratory tests unnecessary in most instances.

Although the specificity of serum lipase is high (> 95%), its sensitivity is lower (85%); therefore, serum lipase determinations have not been found to be more clinically useful than serum levels of amylase. Both tests cost about the same. Nevertheless, concomitant increases in serum amylase and lipase have a 90% to 95% sensitivity and specificity in detecting acute pancreatitis.\textsuperscript{5,6} Other enzymes and products of acinar cell injury—such as trypsin, chymotrypsin, elastase, and phospholipase—have not been shown to have any additional benefit to serum amylase levels. Other biochemical features of acute pancreatitis are listed in Table 2.

Diagnostic Imaging

Plain abdominal radiographs that demonstrate a sentinel loop, pancreatic calcifications, or an obscured psoas muscle margin are not specific for acute pancreatitis. Ultrasonography is a rapid, inexpensive, and noninvasive tool for evaluating patients with presumed mild

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**Table 1. Clinical Findings in Patients with Acute Pancreatitis**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>85–100</td>
</tr>
<tr>
<td>Anorexia</td>
<td>85</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>50–90</td>
</tr>
<tr>
<td>Ileus</td>
<td>50–80</td>
</tr>
<tr>
<td>Fever</td>
<td>10–80</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>5–20</td>
</tr>
</tbody>
</table>


**Table 2. Biochemical Profile of Patients with Acute Pancreatitis**

- Hemoconcentration
- Leukocytosis
- Azotemia and increased creatinine
- Hyperbilirubinemia
- Increased AST/ALT and γGT
- Increased alkaline phosphatase
- Hyperglycemia
- Hyperlipidemia/hypertriglyceridemia
- Hypercalcemia
- Hypomagnesemia
- Hypoxemia
- Acidosis/alkalosis
- Consumption coagulopathy

ALT = alanine aminotransferase; AST = aspartate aminotransferase; γGT = gamma glutamyltransferase.
pancreatitis by assessing for edema of the pancreas and by furnishing information on the status of the gallbladder and biliary ductal system. Ultrasonography is operator dependent and its utility is limited by dilated bowel loops as well as its inability to detect parenchymal necrosis. The most common use for ultrasound in the clinical setting of pancreatitis is to examine the biliary ductal system for the presence of dilated ducts or gallstones.

**Contrast-enhanced dynamic CT** has become the standard and most widely used test to evaluate patients with acute pancreatitis.\(^7\)–\(^9\) CT is more sensitive than ultrasonography for detecting parenchymal changes but less sensitive for detection of cholelithiasis and choledocholithiasis. Findings on CT indicative of pancreatitis include edema of the pancreas, peripancreatic fluid collections, as well as edema of the surrounding viscera and mesentery. Absence of enhancement of the pancreatic parenchyma by intravenous contrast signifies pancreatic necrosis. Extravisceral gas is pathognomonic of infection but is a rare finding. CT-based severity staging for acute pancreatitis is as follows: (A) normal, (B) pancreatic swelling, (C) peripancreatic fat abnormalities, (D) single fluid collection, and (E) multiple fluid collections.\(^8,10\)

Endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance imaging, and cholangiopancreatography serve little purpose, if any, as diagnostic modalities in acute uncomplicated pancreatitis. ERCP can provide useful anatomic information about patients with recurrent “idiopathic” or complicated pancreatitis; hence, it is indicated in these patients once the acute phase of the disease has resolved.

**CASE I CONTINUED**

Ultrasoundography in the case patient, who has a history of mild alcohol intake, demonstrates multiple small gallstones but no dilatation of the bile ducts.

- What is the most likely etiology of pancreatitis in this patient?

**DISCUSSION**

Many patients develop acute pancreatitis because of biliary tract stone disease or long-term ethanol abuse (Table 3). Alcohol intake increases pancreatic fluid, protein secretion, and the resistance of the ampulla. The subsequent proteinaceous precipitates and plugs induce pancreatic ductal hypertension and pancreatitis. With biliary tract stones, choledocholithiasis can be demonstrated in 20% of patients with pancreatitis; however, only 2% of patients present with an impacted stone in the ampulla. Nevertheless, gallstones are found in the stools of 90% of patients with acute pancreatitis.\(^1\) These are important considerations because therapeutic interventions, such as ERCP, are necessary to extract an impacted stone in only a few patients.

**Postprocedural Complications and Trauma**

Direct manipulation or retraction of the pancreas appears to be the most common cause of postprocedural pancreatitis (gastric resection, 1%; common bile duct exploration, 3%). Acute pancreatitis develops in about 5% of patients after ERCP as well as several other procedures remote from the pancreas.\(^11\) Hyperamylasemia is common after major trauma; however, the full clinical picture of pancreatitis occurs in less than 5% of patients who sustain major blunt abdominal trauma.\(^12\)

**Hyperlipidemia, Hyperparathyroidism, and Hypercalcemia**

Acinar cell injury is thought to result from the liberation of free fatty acids from circulating triglycerides by local action of lipases within pancreatic microcirculation. Hyperlipidemias may be the etiologic factor in patients with recurrent and previously “idiopathic” pancreatitis. Hyperthyroidism increases calcium, a known secretagogue that may cause pancreatitis because of calcium precipitation in the pancreatic duct; however, the exact mechanism is unknown.

**Table 3. Etiology of Acute Pancreatitis**

<table>
<thead>
<tr>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary tract stones</td>
</tr>
<tr>
<td>Alcohol abuse</td>
</tr>
<tr>
<td>Postprocedural (ERCP/postoperative)</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Hyperparathyroidism/hypercalcemia</td>
</tr>
<tr>
<td>Medications</td>
</tr>
<tr>
<td>Infections</td>
</tr>
<tr>
<td>Tumors</td>
</tr>
<tr>
<td>Pancreas divisum</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Penetrating duodenal ulcer</td>
</tr>
<tr>
<td>Parasites</td>
</tr>
<tr>
<td>Hereditary</td>
</tr>
<tr>
<td>Idiopathic</td>
</tr>
</tbody>
</table>

\(^{ERCP} = \) endoscopic retrograde cholangiopancreatography.
Infections and Medications

Bacterial, fungal, and viral infections sometimes cause pancreatitis. The recent epidemic of AIDS has uncovered many cases of pancreatitis, most commonly caused by cytomegalovirus infection and medications such as pentamidine. More than 85 drugs are suspected of causing acute pancreatitis, but a clear and defined association has been found with only a few,1 such as glucocorticoids, furosemide, thiazides, warfarin, cimetidine, quinidine, azathioprine, and clonidine. The mechanisms of drug-induced pancreatitis are largely elusive and likely involve different pathways.

Other Causes of Acute Pancreatitis

Other causes of acute pancreatitis include tumors, pancreas divisum, pregnancy, and idiopathic causes. Of patients with periampullary tumors, 1% to 3% present with acute pancreatitis because the pancreatic duct is obstructed. The association between pancreas divisum and acute pancreatitis, however, is not absolute because most individuals with pancreas divisum are asymptomatic and never develop pancreatitis. Acute pancreatitis also has been linked to pregnancy with an incidence of 0.01% to 0.1%, but it is unclear whether pregnancy is an independent risk factor. Finally, acute pancreatitis develops in the absence of ductal obstruction or any other identifiable cause in 10% of patients. Recent large clinical trials have shown that an etiology can be identified in most patients with idiopathic pancreatitis if thorough diagnostic testing is undertaken.1

CASE 1 FOLLOW-UP

The patient undergoes an uneventful laparoscopic cholecystectomy after resolution of acute pancreatitis. The patient is symptom-free after the procedure.

Table 4. Ranson’s Criteria for Predicting the Severity of Acute Pancreatitis

<table>
<thead>
<tr>
<th>Time</th>
<th>Nonbiliary Pancreatitis</th>
<th>Biliary Pancreatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>&gt; 55</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>Leukocytes (× 10³/mm³)</td>
<td>&gt; 16</td>
<td>&gt; 18</td>
</tr>
<tr>
<td>Blood glucose (mg/dL)</td>
<td>&gt; 200</td>
<td>&gt; 220</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>&gt; 350</td>
<td>&gt; 400</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>&gt; 250</td>
<td>&gt; 250</td>
</tr>
<tr>
<td>Within 48 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit decrease (points)</td>
<td>&gt; 10</td>
<td>&gt; 10</td>
</tr>
<tr>
<td>BUN increase (mg/dL)</td>
<td>&gt; 5</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Serum calcium (mg/dL)</td>
<td>&lt; 8</td>
<td>&lt; 8</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>&lt; 60</td>
<td>&lt; 60</td>
</tr>
<tr>
<td>Base deficit (mEq/L)</td>
<td>&gt; 4</td>
<td>&gt; 5</td>
</tr>
<tr>
<td>Fluid requirement (L)</td>
<td>&gt; 6</td>
<td>&gt; 4</td>
</tr>
</tbody>
</table>

AST = aspartate aminotransferase; BUN = blood urea nitrogen; LDH = lactic dehydrogenase; PaO₂ = arterial oxygen partial pressure.

*Three or more Ranson criteria within 48 hours of onset of acute pancreatitis suggest severe acute pancreatitis.

**Is this patient a candidate for intensive care unit (ICU) admission?**

DISCUSSION

Ranson’s Criteria

Because of the propensity for acute pancreatitis to progress into multisystem organ failure, a mechanism to predict its severity and to allocate treatment resources is essential. Ranson’s criteria take into consideration 11 clinical findings over a 48-hour period (Table 4). Three or more Ranson’s criteria within 48 hours of onset of acute pancreatitis suggest severe acute pancreatitis. Patients with 1 or 2 criteria have a predicted mortality of 1%, which increases to 10% for 3 criteria and to 50% for patients with 7 or more criteria. The major limitations of Ranson’s criteria are that complete assessment requires data that may not be available until 48 hours after admission and that these criteria cannot be calculated serially at later times during hospitalization. This particular patient meets one criterion; therefore, she is at a reduced risk for developing complicated pancreatitis and does not require triage to the ICU.
Glasgow Score

This scoring system is more popular in Europe. It utilizes 8 clinical criteria similar to the Ranson’s criteria.

Acute Physiology Score and Chronic Health Evaluation (APACHE II)

The APACHE II scoring system is a severity-of-illness index that overcomes the limitations of Ranson’s criteria but is cumbersome to calculate. It utilizes 12 physiologic and laboratory parameters available at admission, as well as age and preexisting comorbid conditions (Table 5). The APACHE II score can be calculated on a daily basis, thus providing a mechanism to serially evaluate the disease process. An APACHE II score higher than 8 denotes severe acute pancreatitis.13

Multi-Organ Dysfunction Score (MODS)

More recently, many investigators have employed this end-organ injury–based scoring system to predict the severity of acute pancreatitis. A MODS of 2 or more seems to predict early mortality.14

Biochemical Assays

The central role of cytokines in the pathogenesis of pancreatitis has been well established. With the possible exception of interleukin 6 (IL-6) and IL-8, many biochemical markers of acute pancreatitis and inflammation have not been proven to be superior to the clinical scoring systems in predicting the severity of pancreatitis.15 Despite their predictive value, clinical use of IL-6 and IL-8 levels has been hindered by the lack of a rapid assay. The utility of trypsinogen-activating peptide and C-reactive protein as predictors of severity has been shown in small studies and warrants further investigation.16

FURTHER CLINICAL MANIFESTATIONS IN PATIENT 2

Within hours of admission to the ward, the case patient develops tachycardia, tachypnea, oliguria, and hypotension. Laboratory data are as follows: total bilirubin, 6.3 mg/dL; leukocyte count, 29 \times 10^{3}/\text{mm}^{3}; blood urea nitrogen, 32 mg/dL; and arterial oxygen partial pressure (PaO2), 61 mm Hg on room air. Her APACHE II score is 10.

• What treatment plan should this patient receive after initial stabilization in the ICU?

Discussion

Although Ranson’s criteria predicted a mild pancreatitis, this patient’s clinical condition took a different course. Her clinical course reflects the pathophysiology of systemic super inflammation during severe pancreatitis, and her clinical manifestations are a result of circulating inflammatory cytokines (Figure 1). The fundamental pathophysiologic event of acute pancreatitis is injury to acinar cells, after which inflammatory cytokines (IL-1, IL-6, IL-8, and tumor necrosis factor) are produced by leukocytes that invade the pancreas. After a latent period, cytokines are produced to a larger extent in the lungs and the liver by macrophages and neutrophils that are activated by circulating pancreatic enzymes.17-19

In these patients, aggressive fluid and electrolyte resuscitation should be undertaken to correct and prevent further hypovolemia and prerenal azotemia. Supplemental oxygen should be administered and mechanical ventilation should be carried out in the event of respiratory insufficiency. Invasive monitoring (pulmonary artery catheter, arterial line) should be undertaken as clinical circumstances dictate.

Currently, the mainstay of treatment of acute pancreatitis is supportive (Figure 2). The term “bowel rest” is misleading and is not based on a current understanding of pancreatitis. In acute pancreatitis, the pancreas is in a state of hyperinflammation and autodigestion, and further stimulation by food may be clinically insignificant. Most experts advocate resumption of oral intake as soon as it can be tolerated. However, patients should be given nothing by mouth until ileus resolves. Routine nasogastric tube use should be reserved for patients with severe pancreatitis or for those demonstrating signs of gastric outlet obstruction.

Table 5. Physiologic Variables for APACHE II Severity of Disease Classification*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td></td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td></td>
</tr>
<tr>
<td>Respirations</td>
<td></td>
</tr>
<tr>
<td>PaO2</td>
<td></td>
</tr>
<tr>
<td>Arterial pH</td>
<td></td>
</tr>
<tr>
<td>Serum Na+</td>
<td></td>
</tr>
<tr>
<td>Serum K+</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine</td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td></td>
</tr>
<tr>
<td>Leukocyte count</td>
<td></td>
</tr>
<tr>
<td>Glasgow coma score</td>
<td></td>
</tr>
</tbody>
</table>

*The APACHE II score is derived by adding points calculated by assessing these variables to points based on age and chronic health characteristics. A score of > 8 denotes severe acute pancreatitis.

APACHE = acute physiology score and chronic health evaluation.
Pain control is an important aspect of treatment and should be carried out diligently; narcotics usually are needed. The theoretical disadvantage of morphine-induced spasm of the sphincter of Oddi has not been shown to be of any clinical significance. Prophylaxis for deep venous thrombosis is required as well. Most surgeons also institute acid suppression.

The use of prophylactic antibiotics has become a hotly debated issue. A meta-analysis demonstrated that prophylactic antibiotics reduce morbidity and mortality of severe acute pancreatitis. However, a recent placebo-controlled, double-blind study of ciprofloxacin/metronidazole did not detect any difference in the risk of developing infected pancreatic necrosis with the use of prophylactic antibiotics versus placebo. Moreover, the benefit of prophylactic antibiotics in acute mild pancreatitis is not well established. Imipenem is the antibiotic of choice because it has superior concentration in the pancreatic parenchyma (including the necrotic pancreatic tissue) and has a broad spectrum of activity. Empiric antifungal therapy with fluconazole is recommended because fungal infections in severe pancreatitis can potentially result in significant morbidity. Use of the sandostatin analogue in managing acute pancreatitis has been controversial because of a lack of demonstrable benefit. Newer generation antibiotics with similar penetration in the pancreas have not been evaluated clinically, but they may find a role in the future.

Nutritional support should be instituted promptly after hemodynamic stability has been established. Initially, parenteral administration is the most practical route for nutritional support because of many considerations, including fluid and electrolyte shifts as well as ileus. Parenteral nutrition should be switched to enteral nutrition as soon as the latter can be tolerated. The normal increase in pancreatic secretions in response to intravenous lipid infusions has not been shown to worsen the course of pancreatitis. Once the ileus has resolved, feedings can be given orally or through a jejunal feeding tube.

At least 4 clinical trials have demonstrated that endoscopic sphincterotomy can effectively relieve biliary obstruction and reduce morbidity of biliary sepsis during pancreatitis, but its effects on the overall mortality are not as clear. To achieve these outcomes, ERCP should be carried out in the first 24 hours after onset of severe pancreatitis to assess whether biliary obstruction is present; endoscopic sphincterotomy can be performed during the ERCP. This patient’s laboratory data strongly suggest biliary obstruction, and she is within the initial 24- to 48-hour window; therefore, she is a candidate for ERCP. The risk of routine early ERCP (especially in mild pancreatitis) outweighs its benefits. Patient 2 undergoes ERCP, and small stones are recovered from the bile duct.

Treatment of hyperlipidemia should prevent recurrences in most cases. Cholecystectomy for cholelithiasis should be carried out for all patients with gallstone pancreatitis as well as for all patients with recurrent or idiopathic pancreatitis. Most surgeons recommend cholecystectomy during the same hospitalization as soon as the pancreatitis has resolved and the patient is nearing discharge. Abstinence from alcohol reduces the recurrences of alcoholic pancreatitis.

FURTHER PRESENTATION OF PATIENT 2

One week later, a CT scan is performed because of continued fever (Figure 3A). The radiologist offers to drain the easily accessible fluid collection or “pseudocyst” in the lesser sac.

Figure 1. The role of inflammatory mediators in acute pancreatitis. Immunocompetent cells produce tumor necrosis factor (TNF), interleukins (ILs), nitric oxide (NO), and platelet activation factor (PAF) in response to stimulation by pancreatic enzymes. Cytokines induce the clinical picture associated with the systemic inflammatory response syndrome (SIRS).
• What is the role of nonoperative drainage of pancreatic fluid collections?

**Discussion**

This patient developed acute pancreatic fluid collections (Figure 3A) that are commonly but erroneously called phlegmon (small fluid component) or pseudocysts (predominant fluid component). These peripancreatic fluid collections can regress spontaneously (Figure 3B) or may persist to form a pseudocyst. This patient has no evidence of infected pancreatic necrosis or pancreatic abscess and therefore drainage is not indicated at this time.

**CASE 2 FOLLOW-UP**

The surgeon does not drain the acute peripancreatic fluid collection. The patient recovers from respiratory failure after 6 days of endotracheal intubation. Aggressive fluid resuscitation prevents her from progressing into renal failure. She receives antibiotics, and her fever resolves in 4 days. She is transferred to the surgical ward after 8 days in the ICU.

**CASE 3**

**PATIENT PRESENTATION**

Patient 3 is a 52-year-old woman who is admitted to the ICU with severe acute pancreatitis and acute respiratory distress syndrome (ARDS). Despite aggressive supportive treatment, she develops hypotension, tachycardia, and increased serum creatinine. An abdominal CT scan is performed (Figure 4). The results of laboratory tests are: alkaline phosphatase level, 320 U/L; leukocyte count, $20 \times 10^9$ mm$^3$; glucose, 310 mg/dL; LDH, 380 U/L; and AST, 300 U/L. Her APACHE II score is 12.

**SEVERE PANCREATITIS WITH PANCREATIC NECROSIS**

Approximately 2% to 5% of patients develop severe acute pancreatitis associated with pancreatic necrosis and may require operative intervention. The CT scan in Figure 4 shows necrotizing pancreatitis because the body and tail of the pancreas are not enhanced after an intravenous contrast bolus (> 30% of the parenchyma).
As with mild forms of pancreatitis, the mainstay of initial treatment in severe necrotizing pancreatitis is supportive, as outlined in the algorithm (Figure 2). The role of operative treatment in patients with necrotizing pancreatitis continues to evolve. However, the consensus is that operative treatment is indicated in patients who develop infected necrosis or who continue to deteriorate despite maximal nonoperative treatment whether or not they have infected necrosis.24,25 In patients who are suspected of having infected necrosis, sampling the necrotic areas in the lesser sac via CT-directed fine needle aspiration can confirm the diagnosis. Findings of extravisceral air on CT would indicate the need for operative débridement in the appropriate clinical setting because extraluminal gas is indicative of infected necrosis or peripancreatic abscess. Regarding this patient, a necrosectomy should be entertained if she does not respond to aggressive resuscitative measures within the next 24 to 48 hours.

The rationale for operative treatment is to remove the necrotic peripancreatic and pancreatic tissue that acts as a reservoir for infection and sepsis. Surgical techniques for managing ongoing necrosis in the lesser sac after the initial necrosectomy include wide drainage (closed packing), high volume closed lavage, or open packing.24 A more aggressive approach of repeated planned necrosectomy every 48 hours involves closing the abdominal wall with a zipper; this approach has resulted in a low rate of recurrent abdominal abscesses and incisional hernias25 (Figure 5).

Mortality of operative treatment of necrotizing pancreatitis ranges from 7% (closed packing)25 to 22% (planned necrosectomy),26 which is more favorable than
the uniformly fatal outcome of untreated infected pancreatic necrosis. It has become clear that in the appropriate clinical setting (stable patient, mild symptoms) postponing necrosectomy may carry a more favorable outcome; however, waiting longer than 28 days is of no additional benefit. Long-term outcomes after necrosectomy are characterized by pancreatic endocrine and/or exocrine insufficiency in 50% of the patients.

Percutaneous catheter aspiration or drainage achieves little in the evacuation of the thick necrotic material and augments the risk of infection; therefore, this method is not recommended. Endoscopic transgastric drainage of pancreatic necrosis and pseudocysts is an exciting new approach for patients in whom the necrotizing process is limited to the lesser sac and who are considered high risk for operative treatment. Pancreatic resection and peritoneal lavage have no proven role in the treatment of necrotizing pancreatitis.

CASE 3 FOLLOW-UP

The patient is managed nonoperatively and recovers after 30 days in the ICU.

CASE 4

PATIENT PRESENTATION

Patient 4 is a 24-year-old woman who has returned for a routine visit 6 weeks after developing an episode of mild pancreatitis. She has minimal epigastric discomfort and is tolerating regular food. She has an abdominal CT scan done by another physician the previous week that demonstrates a 5-cm pseudocyst in the lesser sac.

- What is the rationale for operative treatment of pseudocysts?

DISCUSSION

Less than 10% of all patients with acute pancreatitis develop pseudocysts, which are more common with alcoholic than biliary pancreatitis. Acute peripancreatic fluid collections that are found within a few weeks from the onset of pancreatitis should not be mistaken for or treated as if they were pseudocysts. Pseudocysts of the pancreas most commonly occur as a result of pancreatitis and disruption of the pancreatic duct. The extravasated pancreatic fluid is walled off by a dense inflammatory reaction. Thus, the lining of a pseudocyst, which takes weeks to form, is nonepithelial granulation tissue and is made from the surrounding viscera. Symptoms arise from compression of adjacent organs, causing abdominal pain, nausea, vomiting, or jaundice.

The ready availability of imaging modalities has helped elucidate the natural history of pseudocysts. Recently, it became apparent that not all pseudocysts require operative treatment because many resolve spontaneously. The treatment of pseudocysts has evolved over the years from recommending operative drainage in all pseudocysts larger than 6 cm to a more selective approach. Two reports demonstrate that selective nonoperative management of pseudocysts is successful in 50% to 60% of asymptomatic patients irrespective of pseudocyst size. Patients who are treated expectantly should be monitored closely for the development of complications (10%) that require prompt intervention. Rupture of a pseudocyst may be accompanied by intra-abdominal hemorrhage and sepsis. Bleeding into a pseudocyst can result in severe abdominal pain and shock; emergency angiographic control of the bleeding vessel has become widely accepted. Pancreatic ascites and pleural effusion from a disrupted pancreatic duct can be treated with hyperalimentation, aspiration of ascites or pleural effusions, and transpapillary stenting of the pancreatic duct.

In this particular patient, management of the pseudocyst should take into consideration the clinical presentation (symptomatic versus asymptomatic, presence of complications) and resolution of pancreatitis. Patient 4 may require no further treatment than a
cholecystectomy, especially because she is asymptomatic, and her pseudocyst may resolve without further intervention. The presence of symptoms and the “maturing” period of 6 weeks should be the principal factors in determining whether a pseudocyst should be drained.

Infected pseudocysts should be drained externally because they contain debris and necrotic material that will not be adequately drained by small caliber percutaneous drains. Enteric internal drainage of sterile pseudocysts can be achieved by anastomosing the pseudocyst wall to the stomach, jejunum, or duodenum. New endoscopic approaches have yielded encouraging results, but their long-term outcome is not known. Laparoscopic drainage is an appealing alternative, especially when a biopsy of the pseudocyst wall is desired in patients with a “less than typical” history of acute pancreatitis. Recent evidence shows that percutaneous drainage of pseudocysts is acceptable in patients with normal pancreatic duct anatomy and results in satisfactory outcomes and resolution of pancreatic fluid collections.31

**CASE 4 FOLLOW-UP**

A CT scan is repeated 3 weeks later, and it shows almost complete resolution of the pseudocyst. Subsequently, the patient undergoes laparoscopic cholecystectomy and recovers without incident. It is essential that the pseudocyst resolve before the cholecystectomy; open cholecystectomy may be indicated when laparoscopy cannot be done.

**SUMMARY POINTS**

- The spectrum of clinical presentations of acute pancreatitis depends on the severity of disease process.
- No single laboratory test or physical finding is pathognomonic for pancreatitis. The cardinal clinical symptom of acute pancreatitis is constant epigastric pain of insidious onset, often radiating to the back. Other clinical findings include anorexia, fever, nausea, vomiting, ileus, and abdominal distention.
- Contrast-enhanced dynamic CT has become the standard test used to evaluate patients with acute pancreatitis. However, ultrasonography is useful in mild cases to assess for gallstones.
- Currently, the mainstay of treatment of acute pancreatitis remains supportive.
- Approximately 2% to 5% of patients develop severe pancreatitis that is associated with pancreatic necrosis and is responsible for 90% of the mortality from acute pancreatitis.
- The rationale for operative treatment is removal of the necrotic peripancreatic and pancreatic tissue that acts as a reservoir for infection and sepsis.
- Acute peripancreatic fluid collections found within a few weeks from the onset of pancreatitis tend to resolve spontaneously. Acute fluid collections should not be mistaken for or treated as if they were pseudocysts.
- Nonoperative management of pseudocysts is successful in 50% to 60% of asymptomatic patients irrespective of pseudocyst size.

**REFERENCES**