Acute pancreatitis is not an uncommon disease, with high morbidity and mortality. It is an acute inflammatory process of the pancreas, with variable involvement of other regional tissues or other organ systems (1). A definite diagnosis is often elusive. Elevation of serum levels of pancreatic enzymes > 3-5 times of normal values (>10 SD) and USG or CT abdomen offer a high degree of diagnostic specificity and sensitivity (>80-90%). Recent concepts in etiopathogenesis, diagnosis and management are being reviewed in this article.

**Pathology & pathogenesis**

The pathologic spectrum of acute pancreatitis includes acute oedematous pancreatitis, necrotizing pancreatitis, haemorrhagic pancreatitis, pseudocyst pancreas, pancreatic abscess and pancreatic ascites. The pathogenesis of acute pancreatitis is not clear but considerable recent advances have been made in the elucidation of its pathogenesis. Autoactivation of trypsinogen, role of clotting cascade, cytokines, immunocytes and PGI2 have enabled us to understand the mechanism of autodigestion. This theory of autodigestion of pancreas explains many of the pathogenic and clinical manifestations of acute pancreatitis (2) (Fig 1).

Various other pathogenetic hypotheses leading to autodigestion are – common channel hypothesis, reflux of duodenal contents, altered pancreatic duct permeability (due to ethanol, drugs, histamine, calcium), premature activation of zymogens and embolic occlusion of small pancreatic vessels (3-5).

**Clinical features**

Abdominal pain is the major symptom. Pain may vary from mild and tolerable discomfort to severe, constant & incapacitating distress in the epigastrium and periumbilical region radiating to the back. Low grade fever, tachycardia, hypotension, jaundice and pulmonary findings may occur in 10-20 percent. Bluish discoloration (Cullen’s sign) and green, brown discoloration of the flanks (Turner’s sign) may be seen (6).

**Laboratory diagnosis**

Estimation of pancreatic enzymes viz., serum amylase and lipase >3-5 times the normal and urinary amylase have sensitivity and specificity of >90-92% (7). Non-
specific markers of acute pancreatitis like C-reactive protein (CRP), tumour necrosis factor (TNF), β₂ microglobulin, complement levels, interleukin-6 (IL-6), procalcitonin and urinary trypsinogen activation peptide (UrTAP) are useful indicators (8). Measurement of isoaamylase-P increases the diagnostic specificity. Another new rapid test for diagnosing acute pancreatitis is urinary trypsinogen-2 strip test (9).

**Radiology**

Radiological investigations include plain x-ray abdomen which may show sentinel loop, colon cut-off sign, mass shadow (pseudocyst) and duodenal distention. Ultrasound abdomen can show diffusely enlarged hypoechoic areas, peripancreatic fluid collection and pseudocyst. CT abdomen (unenhanced and contrast enhanced) further adds to diagnostic value. ERCP is another important investigation for diagnosing pancreatitis (10).

**Aetiology**

Causes of acute pancreatitis are variable. They are gallstones, and other causes of mechanical ampullary obstruction, hypertriglyceridemia, drugs, ERCP. Alcohol is known to be a major cause of pancreatitis, toxic effects of alcohol are at the cellular and microvascular levels. A high concentration of ethanol reduces gastrointestinal and pancreatic blood flow. Gastrointestinal haemorrhage and pancreatitis are initiated by microvascular disturbances of gastrointestinal mucosa and pancreas. Vasoactive agents, such as endothelins, nitricoxide and oxidative stress does have a pathogenetic role in ethanol induced pancreatitis. Ten percent of chronic alcoholics develop acute pancreatitis (11, 12).

**Drugs**

The drugs which are incriminated to cause acute pancreatitis include antimicrobials (metronidazole, stibogluconate, sulfonamides and tetracyclines); diuretics (frusemide, thiazides); sulphasalazine; 5ASA; Immunosuppressive drugs (L-asparaginase, azathioprine); anti-inflammatory (salicylates); and calcium and drugs used in AIDS treatment (didanosine, pentamidine).

**Infections**

Various viruses like Mumps, Coxsackie, HBV, CMV, Varicella, Herpes simplex; bacteria like Mycoplasma, Leptospira, Salmonella and Legionella; fungi (Aspergilliosis); and parasitic infections (Toxoplasmosis, Cryptosporidium, Ascarisis) have been invariably associated with pancreatitis (14).

In over 30% cases of acute pancreatitis in younger age <35 years there is no obvious cause. Recent discovery of genes of cationic trypsinogen (PRSSI), pancreatic secretory trypsin inhibitor (PSTI or SPINKI) and cystic fibrosis transmembrane conductance regulator (CFTR) and sphincter of oddi dysfunction in hereditary (idiopathic recurrent pancreatitis) further adds to our understanding of this entity (15-16).

**Management of acute pancreatitis**

Advances in our knowledge of pathogenesis of the disease and together with newer techniques of timely diagnosis and management of severe cases in intensive care unit helped in decreasing the morbidity and mortality of acute pancreatitis.

Mild acute pancreatitis is clinically a self limiting disease that accounts for the majority (70-80%) of acute pancreatitis cases, patient generally need only a short hospitalization of 3-7 days with medical supportive therapy, and do not suffer organ failure or local complications (17).

Severe acute pancreatitis (20-30%) is frequently a progressive disease and can progress to multiple organ failure, which is difficult to treat outside an intensive care unit (ICU) and contributes to a very high mortality (70-90%). Very often, a multi-disciplinary approach is required in the management of such patients (17).

**Assessment of severity**

It is done by various scoring systems as described below :-

a) Ranson's criteria (17)

b) Glasgow scoring (18)
c) APACHE-II (19)
d) Balthazar's scoring system based on CT scan findings (20).

**Assessment of severity's scoring systems**

**Ranson's criteria :**

At admission : Age >55 years  
Leucocytosis > 16000/mm³  
Hyperglycaemia >200 mg/dL  
S. LDH>400 IU/L  
AST >250 IU/L

Initial 48 hours : Fall in HCT >10%  
Fluid deficit >4000 ml  
Hypocalcemia <8 mg/dL  
Hypoxemia PaO₂ <60 mmHg
↑ In BUN to >5 mg/dL after IV fluid
Hypoalbuminemia <3.2 g/dL

Score >6 indicates severe acute pancreatitis

**Glasgow system to predict severity of acute pancreatitis:**

Poor prognostic factors in patients with acute pancreatitis.

- White blood cell count > 15,000 /L
- Serum glucose concentration > 180 g/dL (10 mmol/L) with no history of diabetes
- Blood urea nitrogen > 45 mg/dL (16 mmol/L) with no response to fluids
- PO\textsubscript{2} < 60 mmHg
- Serum calcium concentration < 8 mg/dL (2 mmol/L)
- Serum albumin concentration < 3.2 g/dL (32 g/L)
- Lactate dehydrogenase > 600 U/L
- Aspartate aminotransferase > 200 U/L

The presence of three or more of these criteria within the first 48 hours is indicative of severe pancreatitis.

**APACHE-II**

1. **Physiologic points:**
   - Temperature
   - MAP (Mean Arterial Pressure)
   - Heart rate
   - Respiratory rate
   - Oxygenation (PaO\textsubscript{2})
   - Arterial pH
   - Serum sodium
   - Serum potassium
   - Hematocrit
   - White cell count
   - Glasgow coma score

2. **Age points**

3. **Chronic health points:**
   - Liver
   - Cardiovascular
   - Respiratory
   - Renal
   - Immunocompromised

1+2+3 = Total Score

Score >8 indicate severe pancreatitis

**Obesity (BMI>29):** Obesity is a prognostic factor favouring the development of systemic and local complications in pancreatitis (21).

**Balthazar’s scoring system for severity of acute pancreatitis**

<table>
<thead>
<tr>
<th>CT grade of acute pancreatitis</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A = Normal</td>
<td>0</td>
</tr>
<tr>
<td>B = Pancreatic enlargement</td>
<td>1</td>
</tr>
<tr>
<td>C = Peripancreatic inflammation</td>
<td>2</td>
</tr>
<tr>
<td>D = Peripancreatic fluid collection (one)</td>
<td>3</td>
</tr>
<tr>
<td>E = Two or more peripancreatic fluid collections</td>
<td>4</td>
</tr>
</tbody>
</table>

**Necrosis grade**

| A = No necrosis               | 0     |
| B = Necrosis of 1/3 of pancreas | 2   |
| C = Necrosis of 1/2 of pancreas | 4   |
| D = Necrosis of more than 1/2 of pancreas | 6 |

**Appropriate measurements and bedside care in severe acute pancreatitis**

- Vital signs : atleast hourly
- CVP : atleast hourly
- PAP : if indicated
- ABG : every 12 hours
- Intake / output charting every 8 hours
- Catheterisation
- NG tube with suction (maintain intragastric pH at 7, antacids every 2 hours)
- Humidified oxygen at 2 lt. per min
- Pain management
- Record weight daily
- ECG, daily
- Blood tests (haemogram & biochemistry) once or twice daily
- Liver function tests every 2 to 4 days

**Nasogastric aspiration**

Nasogastric tube is indicated only if there is persistent nausea or vomiting, or ileus. For mild cases, oral feeding may be started when symptoms subside or usually within 3-7 days. For severe acute pancreatitis, oral feeding may be considered after 3 weeks if not contraindicated (22).

**Fluid therapy**

Fluid input is modulated according to haemodynamic stability and fluid balance. Electrolyte imbalance should be corrected to reduce the complications.

**Analgesic medication**

NSAIDS, mepridine or fentanyl are used for pain control. Morphine is contraindicated as it increases the contractility and tone of sphincter of oddi & also increases serum amylase (23).
Total parenteral nutrition / artificial nutrition

Where it is feasible and when enteral nutrition is contraindicated, use of amino acid infusion about 1-1.5 g/kg/day and the use of intravenous lipids, unless contraindicated by elevated triglyceride levels, in several cases especially in sepsis cases has helped to decrease morbidity and mortality.

Recent studies on intensive care patients with trauma and sepsis showed that enteral feeding was associated with a reduction in the acute phase response and the severity of septic complications compared to total parenteral nutrition (24, 25).

Antibiotics

Cefuroxime (1.5 g tds), ciprofloxacin (200 mg bd), imipenam (500 mg tds) in combination with drugs effective against anaerobes like metronidazole (500 mg tds) for 2 weeks are used via intravenous route for control of infection. Recently prophylactic use of anti-fungal drugs has been recommended (26, 27).

Somatostatin/octreotide

These are useful and effective in acute pancreatitis and in preventing complications following ERCP (28). Somatostatin and its 8 amino acid analogue, octreotide, share similar cytoprotective effects on the pancreas. They inhibit basal and stimulated pancreatic secretion, stimulate reticuloendothelial system activity and modulate the cytokine cascade. However, they have different onset of action and exert different effects on sphincters of oddi motility. Somatostatin relaxes the sphincter of oddi whereas octreotide increases its contractility (29).

Inhibition of MAPKs (Mitogen-activated protein kinases)

In a recent study, it was concluded that simultaneous inhibition of TNF-α products (by pentoxifylline) and xanthine oxidase activity (by oxypurinol) greatly reduced local and systemic inflammatory response in acute pancreatitis and decreased mortality rate. These act by inhibiting MAPKs (30).

Surgical treatment

Early surgery is indicated only for infected pancreatic necrosis and pancreatic abscess. Emergency surgery is indicated when there is haemoperitoneum or intestinal ischaemia (31, 32).

Endoscopic treatment for gallstone pancreatitis

Based on various studies, it is recommended that an emergent ERCP should be performed in patients with acute pancreatitis and suspected or proven gallstone aetiology when criteria for severity are met and / or there is co-existent cholangitis, jaundice, dilated CBD or when there is clinical deterioration in patients with initial mild prognostic signs (33, 34).

“In acute pancreatitis”, the goal is an early detection and early treatment of systemic complications because this is probably the most important policy to reduce mortality.

References


