Section 13

LECTURE

Acute and Chronic Pancreatitis
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Acute Pancreatitis

1) Etiology

- Alcohol
- Gallstones
- "Idiopathic" (2/3rds from biliary sludge or crystals)
- Drugs
- Post-ERCP
- Hypertriglyceridemia
- Hypercalcemia
- Post-operative
- Trauma
- Cancer or other obstructions of the pancreatic duct
- Other

2) Putative mechanism of intracellular injury

- Blocked secretion
- Fusion of lysosomes and zymogens
- Enzyme activation
- Intracellular injury

3) Local effects: can explain kidney, pulmonary, and intestinal damage

- Inflammation
- Third space fluid accumulation
- Peri-pancreatic and retroperitoneal fat necrosis
- Pancreatic necrosis

4) Systemic effects: can explain shock, adult respiratory distress syndrome (ARDS), diffuse intravascular coagulation (DIC), death

- Activation of kallikrein leads to bradykinin generation, capillary permeability and vasodilatation
- Activation of complement leads to increased WBC chemotaxis, release of WBC elastase, phospholipase A2 and leukotrienes
- Activation of thrombin leads to DIC
- Activation of phospholipase A2 damages cell membranes and lung surfactant
- Activation of elastase leads to blood vessel damage
- Activation of chymotrypsin leads to capillary permeability
- Release of lipase leads to local and/or distal fat necrosis
- Overload of endogenous protease inactivation pathways
5) Clinical Features

- Abdominal pain
  Common, virtually all patients
  Classically, epigastric with radiation to back, but can be RUQ, LOQ or diffuse
  Long duration (days)
  Some relief by bending forward

- Nausea and vomiting

- Physical examination
  Abdominal tenderness +/- guarding, distention, and rebound
  Fever
  Tachycardia
  Grey-Turner or Cullen sign, rare

6) Laboratory

- Serum amylase
  May be normal
  No prognostic significance
  Not specific; elevated in many other GI and non-GI diseases
  Rapid rise and quickly cleared
  Pancreatic isoamylase is more specific than total serum amylase

- Urinary amylase
  Normally, 3% of filtered serum amylase is excreted
  During acute pancreatitis, more is excreted
  No advantage over serum measurement in diagnosis except to exclude macroamylasemia

- Serum lipase
  May be normal
  No prognostic significance
  Not specific; elevated in many other GI and non-GI diseases
  Elevations last longer than serum amylase

- Other serum or urine markers
  Phospholipase A, trypsin, carboxylester lipase, carboxypeptidase A, colipase, urinary and serum trypsinogen-2, pancreatitis associated protein, trypsinogen activation peptide
None of these, either alone or in combination, has a clinical advantage over measurement of serum amylase and lipase

- Ranson's criteria for prognosis of acute pancreatitis

At admission

- Age > 55 years
- WBC > 16,000
- Glucose > 200 mg/dl
- LDH > 350 IU/L
- AST > 250 IU/L

During first 48 hours of hospitalization

- Hct decrease > 10%
- BUN increase of > 5 mg/dl
- Ca++ < 8 mg/dl
- PaO2 < 60 mm/Hg
- Base deficit > 4 meq/L
- Fluid sequestration > 6L

7) Radiology

- Abdominal plain film (KUB): Sentinel loop or colon cut-off sign, exclude obstruction or perforation

- Chest film: 30% will be abnormal with pleural effusion, infiltrate, atelectasis, or adult respiratory distress syndrome (ARDS)

- Abdominal ultrasonography: best method to detect gallbladder stones

- Abdominal CT scan: most important radiologic test for diagnosis, complications, and prognosis

  Interstitial pancreatitis:

  - Uniform enhancement after contrast
  - Represents 75% of all cases of pancreatitis
  - Infection and morality rate

  Hemorrhagic or necrotizing:

  - Non-homogenous uptake of contrast
  - Represents 25% of all cases of pancreatitis
  - Infection rate high (30-50%)
  - Mortality high (10-30%)

Grading scale for severity:

  A: normal
B: focal or diffuse pancreatic enlargement w/o peripancreatic inflammation
C: peripancreatic inflammation
D: single fluid collection
E: > 1 fluid collection or gas in pancreas or retroperitoneum

8) **Treatment**

- Reverse underlying precipitating cause
  
  Early ERCP in patients with acute severe gallstone pancreatitis
  
  Correction of hypertriglyceridemia or hypercalcemia
  
  Discontinuation of causative drugs

- Initial treatment is identical regardless of the cause of pancreatitis

  Supportive care

  Nasogastric tube
  NPO
  IV fluids
  Analgesics
  Nutritional support

- Antibiotics

  Older studies showed no benefit

  Recent, better designed studies show benefit in patients with severe necrotizing pancreatitis who received cefuroxime, imipenem, or a combination of ceftazidime, amikacin, and metronidazole

  CT guided aspiration or surgical drainage of pancreatic fluid collections

- Experimental agents

  Possible benefit

  Somatostatin or octreotide
  Gabexate mesilate, a protease inhibitor

  No benefit

  Histamine-2 antagonists
  Anticholinergic medications
  Glucagon
Peritoneal lavage

9) Gallstone versus alcoholic pancreatitis

- Important therapeutic implications: Gallstone pancreatitis has a very high recurrence rate without definitive treatment (25% have an additional episode within 6 weeks).

- Factors favoring gallstone pancreatitis

  ALT > 150 IU/L
  Female gender
  Age > 50 years
  Amylase > 4000
  Alkaline phosphatase > 300 IU/L

- All patients with their first attack of acute pancreatitis need abdominal ultrasonography to look for gallstones in the gallbladder.

- Patients with gallstone pancreatitis should have a cholecystectomy after recovery and before discharge from the hospital.

10) Complications

- Hypocalemia from loss of ionized calcium within areas of fat necrosis by binding to fatty acids.

- Pseudocyst

  Encapsulated, non-epithelial lined collection of fluid arising from pancreatic inflammation

  Can cause pain, obstruction, become infected, or rupture

  Common in up to 40% of patients with pancreatitis

  Most resolve spontaneously

  Treat if complications occur or if pseudocyst persists > 6 weeks
Chronic Pancreatitis

1) Clinical Features

2) Abdominal pain

- Common, but not invariable (20-45% have no pain).
- Usually epigastric, radiating to back.
- Variable pattern
  - Episodic lasting < 10 days with pain free intervals of months
  - Almost continuous with exacerbations which may require hospitalization

3) Pancreatic Insufficiency

- Enzymes
  - Steatorrhea > protein malabsorption.
  - Must lose >90% of pancreatic function.

- Hormones
  - Glucose intolerance common.
  - Diabetes, a late complication.
    - loss of insulin & glucagon,
    - low insulin requirements
    - no down regulation of insulin receptors
    - no insulin antibodies.
    - diabetic complications can occur.

4. Complications

- Pseudocyst
- Bile duct obstruction
- Duodenal obstruction
- Pancreatic ascites
- Splenic vein thrombosis
- Pseudoaneurysms
- Pancreatic cancer (25-fold increased risk)

5. Diagnosis is difficult

- Acute on chronic disease
- Laboratory and radiographic findings can be normal.

Laboratory
Amylase & lipase usually normal because fibrosis reduces concentration of these enzymes.

Elevated liver enzymes suggest bile duct stricture or pancreatic cancer.

Fat in stool (oil droplets) by Sudan stain.

**Imaging**

KUB: calcification

CT: calcification, ductal distortion, fluid collections, and enlargement of gland

ERCP: beading of the duct which may correlate to functional changes; normal ducts no decreased function; mild to moderate duct changes associated with pancreatic insufficiency in 50% of patients.

Endoscopic ultrasound (EUS): stones, visible side branches, ysts, lobularity, irregular main duct

Magnetic resonance cholangiopancreatography (MRCP): lacks sensitivity and specificity of ERCP or EUS.

- **Pancreatic function tests**

  **Secretin stimulation test**

  Intravenous secretin stimulates pancreatic bicarbonate secretion
  Collect duodenal fluid after IV secretin administration
  Peak [HCO₃] <80 meq/L suggests chronic pancreatitis
  15% of patients with normal ERCP have abnormal secretin test
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  **Bentiromide test**

  Bentiromide administered orally
  Cleaved by chymotrypsin releasing p-aminobenzoic acid (PABA)
  Measure urinary excretion of PABA
  Equally sensitive and specific as secretin test
References:

Acute pancreatitis


**Chronic pancreatitis**


