Evaluation and Management of Patients with Acute Pancreatitis

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Acute Pancreatitis

- Case
- Background
- Diagnosis
- Evaluation
- Prognosis
- Treatment: Interstitial vs. Necrosis
- Take home messages
Case 1

- Forty year old female with 2 days of steady epigastric discomfort with radiation to her mid back.
- Vomiting x two, no F/C
- Has had rare, short lived attacks of intermittent pain in the RUQ for two months.
Case 1

• PMH: tubal ligation
• Meds: ibuprofen rarely, NKDA
• Social history:
  • Denies ETOH, tobacco, or drugs
  • No tattoos, transfusions
  • Lives with husband, 7 children (8-17yo)
Case 1

• Physical Exam

• Vitals:  T 98.7    BP 115/64    P 111
   RR 16    O₂ sat 97% on RA    BMI 30

• Gen:  obese female, moderate distress

• HEENT and neck:  Normal

• Cor:  RRR, no M/R/G

• Chest:  CTA and P bilaterally

• Abd:  Obese, soft, tender in epigastrium
   • No rebound, mild vol. guarding,
   • No HSM or masses, NI bowel sounds
**Case 1**

- Lab values

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase</td>
<td>1203</td>
</tr>
<tr>
<td>Lipase</td>
<td>1845</td>
</tr>
<tr>
<td>TBili</td>
<td>1.5</td>
</tr>
<tr>
<td>Alk phos</td>
<td>105</td>
</tr>
<tr>
<td>AST</td>
<td>202</td>
</tr>
<tr>
<td>ALT</td>
<td>182</td>
</tr>
<tr>
<td>U/A</td>
<td>nl</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>nl</td>
</tr>
<tr>
<td>Calcium</td>
<td>nl</td>
</tr>
</tbody>
</table>

- U/S: Stones in the gallbladder, 4mm bile duct

What is her diagnosis?
Diagnosis of Acute Pancreatitis

- Abdominal Pain
- Pancreatic Enzymes in Serum (3x normal)
- Inflammation on CT
Acute Pancreatitis

Background

- >220,000 hospital admissions in the United States each year
- Total cost $2.2 billion/yr
- Incidence increases with age
- 20% of cases may progress to severe acute pancreatitis
  - Mortality 20-30%
- Recurrence rate:
  - 50-60% in 1 year
Acute Pancreatitis

Etiologies of acute pancreatitis expanded

- Drug-induced
- ERCP
- Hyper TG, Ca
- Neoplastic
- Infectious
- Genetic
- Structural
- Toxic
- Traumatic
- Vascular
- Autoimmune
- IBD-related
# Drug Induced Pancreatitis

## Common
- azathioprine
- 6-mercaptopurine
- valproate
- pentamidine
- asparaginase
- didanosine DDI

## Uncommon
- ACE inhibitors
- acetaminophen
- 5-amino ASA
- furosemide
- sulfasalazine
- thiazides

## Rare
- carbamazepine
- corticosteroids
- estrogens
- minocycline
- nitrofurantoin
Ductal Anatomy

• Main pancreatic duct joins common bile duct and drains through major papilla into duodenum.

• 10%- main pancreatic duct drains through the minor papilla (pancreas divisum).
Evaluation for Acute Pancreatitis

- **History** - Alcohol, smoking, biliary dz, meds, trauma, surgery, family Hx, CTD, immunosuppression, occupation

- **Vitals, O₂ sat, Physical Exam**

- **Laboratory** - HCT, WBC, CRP, BUN/Cr, Lipase, LFTs, Triglyceride, Ca++
Conditions Associated with Hyperamylasemia and Hyperlipasemia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Amylase</th>
<th>Lipase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroditis, vomiting</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Tumors</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Biliary disease</td>
<td>yes</td>
<td>slight</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Renal failure</td>
<td>yes</td>
<td>slight</td>
</tr>
<tr>
<td>Intestinal obstruction, ulceration, ischemia</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Macroamylasemia</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Perforated viscus</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>
Parameters of hepatic injury with transient biliary tract obstruction

- Transient CBD Obstruction

Elevated >3x nl: 95% PPV for gallstone pancreatitis

Serum levels (U/L)

Hours

0 12 24 36
Back to our patient in the ER

She has gallstone pancreatitis…what now?

- Where should she go: Floor bed or ICU?
- How will she do? (Prognosis)
- How should we treat her, and will it improve outcome?
  - Should be subject her to ERCP?
  - “Supportive care”: Pain meds, NPO, IVF
Acute Pancreatitis - Natural History

Organ failure
- SIRS
- Infection

Mild (Interstitial)
80-85%

Severe (Necrosis)
15-20%

Death
5%
Cytokine Production

Lungs

Liver

Microcirculation

Proinflammatory

ICAM-1

IL-1β

TNFα

PAF

INOS ICAM-1

• Leaky vessels
  → 3rd space fluid
• Hypoperfusion
• WBC activation
Assessment of Severity

- Ranson’s criteria
- APACHE-II
- BISAP (Bedside Index for Severity of Acute Pancreatitis)
- Balthazar CT criteria
**Acute Pancreatitis**

**Ranson’s Criteria of Severity**

<table>
<thead>
<tr>
<th>Admission</th>
<th>After 48 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age &gt; 55 years</td>
<td>• Hct decrease &gt; 10%</td>
</tr>
<tr>
<td>• WBC &gt; 16,000 mm³</td>
<td>• BUN increase &gt; 5 mg/dl</td>
</tr>
<tr>
<td>• Glucose &gt; 200 mg/dl</td>
<td>• Ca²⁺ &lt; 8 mg/dl</td>
</tr>
<tr>
<td>• LDH &gt; 350 IU/L</td>
<td>• PaO₂ &lt; 60 mm Hg</td>
</tr>
<tr>
<td>• AST &gt; 120 IU/L</td>
<td>• Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>• Negative fluid balance &gt; 6L</td>
</tr>
</tbody>
</table>

There’s an App for that: “Ranson Score Checklist”—Free!
BISAP Calculation

1. Urea nitrogen (BUN) > 25 mg/dl
2. Impaired mental status by evidence of disorientation
3. Age > 60 years
4. Pleural effusions
5. Presence of SIRS (Presence of ≥ 2 of the following):
   • Pulse > 90 beats/min
   • Respirations > 20 per min, or PaCO₂ < 32 mm Hg
   • Temperature > 100.4 °F or < 96.8 °F
   • WBC# > 12,000 or < 4,000/mm³
     or >10% Bands

There’s an App for that: “Med Calc” $1.99- Has BISAP, Ranson’s and 200 more
Comparison of scoring systems

*Am J Gastroenterol* 2010; 105:435–441

- Good at predicting mild disease
- Not as good predicting necrosis

<table>
<thead>
<tr>
<th>%</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BISAP</td>
<td>37.5 (24.2–53.0)</td>
<td>92.4 (86.9–95.7)</td>
<td>57.7 (38.9–74.5)</td>
<td>84.3 (77.8–89.1)</td>
</tr>
<tr>
<td>Ranson’s</td>
<td>84.2 (69.6–92.6)</td>
<td>89.8 (83.6–93.8)</td>
<td>69.6 (55.2–80.9)</td>
<td>95.3 (90.2–97.9)</td>
</tr>
<tr>
<td>APACHE-II</td>
<td>70.3 (54.2–82.5)</td>
<td>71.9 (64.0–78.7)</td>
<td>40.0 (29.0–52.1)</td>
<td>90.1 (83.1–94.4)</td>
</tr>
<tr>
<td>CTSI</td>
<td>85.7 (70.6–93.7)</td>
<td>71.0 (61.5–79.0)</td>
<td>50.8 (34.4–63.2)</td>
<td>93.4 (85.5–97.2)</td>
</tr>
<tr>
<td><strong>P Nec</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BISAP</td>
<td>33.3 (20.2–49.7)</td>
<td>90.6 (84.8–94.3)</td>
<td>46.2 (28.8–64.5)</td>
<td>84.9 (78.5–89.6)</td>
</tr>
<tr>
<td>Ranson’s</td>
<td>77.4 (60.2–88.6)</td>
<td>88.4 (82.0–92.7)</td>
<td>52.2 (38.1–65.9)</td>
<td>94.6 (89.2–97.3)</td>
</tr>
<tr>
<td>APACHE-II</td>
<td>63.3 (45.5–78.1)</td>
<td>68.5 (60.6–75.5)</td>
<td>29.2 (19.6–41.2)</td>
<td>90.1 (83.1–94.4)</td>
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<tr>
<td>CTSI</td>
<td>97.2 (85.8–99.5)</td>
<td>75.8 (66.5–83.1)</td>
<td>59.3 (46.6–70.9)</td>
<td>98.7 (92.9–99.8)</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BISAP</td>
<td>57.1 (25.0–84.2)</td>
<td>87.6 (82.0–91.7)</td>
<td>15.4 (6.2–33.5)</td>
<td>98.1 (94.6–99.4)</td>
</tr>
<tr>
<td>Ranson’s</td>
<td>100 (64.6–100)</td>
<td>76.8 (69.8–82.5)</td>
<td>15.2 (7.6–23.2)</td>
<td>100 (97.1–100)</td>
</tr>
<tr>
<td>APACHE-II</td>
<td>100 (64.6–100)</td>
<td>65.7 (58.2–72.4)</td>
<td>10.8 (5.3–20.6)</td>
<td>100 (96.7–100)</td>
</tr>
<tr>
<td>CTSI</td>
<td>100 (56.6–100)</td>
<td>58.5 (49.9–66.6)</td>
<td>8.5 (3.7–18.4)</td>
<td>100 (95.2–100)</td>
</tr>
</tbody>
</table>
Early Indicators of Severity

- Hemoconcentration (Hct >44%)*
- Oliguria, increased BUN (25)
- Age >55 yrs
- Tachypnea, hypoxemia
- Tachycardia, hypotension
- Presence of Organ failure
- Obesity (BMI >30)
Indications for Computed Tomography (CT) in Acute Pancreatitis

- Diagnosis in question
- Prognosis (necrosis)
- Detect complications
Interstitial Pancreatitis
- mild/ moderate
Acute Pancreatitis: Necrosis

Progression

Day 1

Day 3
Can we prevent necrosis and improve prognosis?

YES! (maybe)

HOW?

IV FLUID(LR)
Vigorous IV Hydration and Prevention of Severity/Necrosis

- Correction of early organ failure reduces mortality (Gut 2004;53:1340)
- Rising Hct in 1st 24 hrs predicts necrosis
- **Theory:** IV fluids reverses impaired pancreatic microcirculation from SIRS and volume depletion
- Animal studies and retrospective analyses support concept

*Review, Clin Gastro Hep 2008;6:1070*
Aggressive Hydration with Lactated Ringer’s (LR) Reduces SIRS and CRP at 24hrs

Wu et. al. CGH, Aug 2011, 9:710–717

Randomized MCT: 40 Pts received LR vs. Saline(NS)
Initial bolus:1400 ml in 30 min, average of 4400 ml over 24 hrs
Treatment –Mild and Moderate (Interstitial) Pancreatitis

- Aggressive IV Fluid!!!
  - LR: 20ml/kg bolus (1400 ml for 70 kg man)
  - Repeat bolus if needed, then 200-300ml/h
  - Careful in CHF, ESRD, use NS for hyperCa
- Hold drug if drug-related, treat TG, Ca++
- Analgesia, NPO, and Monitor:
  - Vital signs, O₂ sat, Urine output (50 cc/hr)
  - CBC, BUN/Cr @ 8-12 hr, w/ LFTs if gallstone case
Treatment – Mild and Moderate (Interstitial) Pancreatitis

When should we refeed our patient?


- Patient is hungry
- Pain and tenderness resolve, (+) bowel sounds
- Lipase <3x normal (“Near normal”)

Moraes JM et al, J Clin Gastro 2010; 44(7):517

- RCT 210 pts
- OK to start with full diet, not clear liquids
- Reduced length of stay by 1.5 days
Back to our patient in the ER

Our patient has gallstone pancreatitis..

• Should we subject her to urgent ERCP?
  • 85% of patients will pass the stone
# Gallstone Pancreatitis: Trials of Urgent ERCP

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>↓ Morbidity</th>
<th>↓ Mortality</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoptolemos</td>
<td>121</td>
<td>Yes</td>
<td>No</td>
<td>Benefit only in predicted severe disease</td>
</tr>
<tr>
<td>Fan</td>
<td>195</td>
<td>Yes</td>
<td>No</td>
<td>Reduced biliary sepsis</td>
</tr>
<tr>
<td>Folsch</td>
<td>238</td>
<td>No</td>
<td>No</td>
<td>Excluded jaundiced pts</td>
</tr>
</tbody>
</table>
Urgent ERCP in Gallstone Pancreatitis

- Clinically evident cholangitis
- Jaundice: Bili of 5
- Evidence of ongoing obstruction: Significantly increased LFTs in 8-12 hrs
- (?)Severe disease early in elderly
- Note: Data from Expert centers
Detect Choledocholithiasis Less Invasively

MRCP

EUS

Useful for moderate evidence for stone obstruction
- if expertise exists
Case 2

- History -

- A 46 year-old, previously healthy male truck driver presents to the ER with epigastric and LUQ pain radiating into the back.
- This pain awoke him from sleep about 24 hours ago and has progressively worsened since then.
- He has been nauseated and vomited several times.
- He is now complaining of slight difficulty breathing.
Case 2
-Past History-

- Fractured ankle in past
- Meds: none
- Allergies none
- SH: Heavy alcohol, no tobacco use; no IVDA
- ROS: non-contributory
Case 2
-Physical Exam-

- Obese male in marked distress; Confused
- Vital signs: BP-86/50  P-160  RR-36  T-102.0 Weight 260 lbs  BMI 30, O₂ sat 92% on 40% FIO₂
- Dry mucous membranes
- CV- Tachycardic, no murmur
- Lungs- decreased BS with dullness both bases, (+) crackles
- Abd-obese, markedly distended, absent bowel sounds  Tender in the epigastrium and LUQ; no rebound
Case 3

-Labs-

- ABG: 7.28 / 68 / 54 / 27 / 92% on 40%
- HC03 13  BUN 51  Cr 1.4  glucose 251  Ca 8.1  T. protein 6.3  albumin 2.8
- Alk phos 130  TB 1.4  DB 0.3  AST 82  ALT 45
- amylase 7,462  lipase 4,688
- WBC 24.5 (17 bands)  Hct 50, plt 337
- PT 16  INR 1.3  PT
- C-reactive protein( CRP): 163
- Triglyceride: 1436 (high)
Case 2

- CXR: RLL infiltrate; bilateral effusions
- Abdomen X-ray: dilated loops of small bowel
- CT in ER: Peripancreatic fluid collection w/ necrosis
Early Indicators of Severity

- Hemoconcentration (Hct >44%)*
- Oliguria, increased BUN (25)
- Age >55 yrs
- Tachypnea, hypoxemia
- Tachycardia, hypotension
- Presence of Organ failure
- Obesity (BMI 30)

Banks, Freeman, ACG Practice, AJG 2006, 101:2379
• Where should our patient go: Floor bed or ICU?
• What is his prognosis?
  • Apache II score = 19 ---- 25% mortality
  • BISAP score = 4 ---- >15% mortality
  • Ranson score: = 3 ---- 15% mortality
• How should we treat him?
Prophylactic Antibiotics Not Recommended

• Better recent double-blind trials showed no benefit
  • Placebo-controlled, double-blind trial.
  • Randomized, double-blind, placebo-controlled study.

• Meta-analysis of seven randomized controlled trials: No benefit of antibiotics on infected necrosis or mortality
# Treatment – Severe/Necrotic Pancreatitis

<table>
<thead>
<tr>
<th>ICU monitoring</th>
<th>Other treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Aggressive fluid and electrolyte replacement</td>
<td>• Acid suppression</td>
</tr>
<tr>
<td>• Intubation, ventilatory support if needed</td>
<td>• DO NOT give Prophylactic Antibiotics</td>
</tr>
<tr>
<td>• Monitoring</td>
<td>• Early enteric feedings (NJ)</td>
</tr>
<tr>
<td>Vital signs</td>
<td>• Family, patient counseling</td>
</tr>
<tr>
<td>Urine output, CVP line</td>
<td>• Consider transfer to Tertiary center</td>
</tr>
<tr>
<td>$O_2$ saturation</td>
<td></td>
</tr>
<tr>
<td>Labs: TG, lactate, routine</td>
<td></td>
</tr>
</tbody>
</table>
Enteral Feeding Preferred over TPN in Severe Acute Pancreatitis

By Meta-analysis:

• Trend to lower mortality
• Fewer infectious complications
  – (Preserves gut mucosal barrier)
• Safe in necrotic pancreatitis, most achieve goal rate
• Nasojejunal tubes preferred:
  – Lower aspiration risk
  – Avoids pancreatic stimulation
  – Elemental formula most common

Arch Surg 2008 143(11):1111-1117
Evolution of pancreatic necrosis into a pseudocyst

Organized Pancreatitis Necrosis

Day 1  Day 7  Day 28
Case 2
Further course - Day 7

- Tolerating NJ feedings at goal rate
- Still intubated, on ventilator, Renal function is ok
- Develops fever of 102.5°
- No obvious source in urine, lines, lungs, etc.
- What could be the cause of the fever?
- Answer:
  - Consider Infected necrosis
    - Repeat CT with aspiration of fluid/necrotic tissue
    - Send for Gm stain, culture
Infected pancreatic necrosis
Acute Pancreatitis

The incidence of pancreatic infections increases with time.

Timing of Pancreatic Infections

<table>
<thead>
<tr>
<th>Timing</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 7 days</td>
<td>20</td>
</tr>
<tr>
<td>7-14 days</td>
<td>40</td>
</tr>
<tr>
<td>14-21 days</td>
<td>60</td>
</tr>
<tr>
<td>&gt; 21 days</td>
<td>100</td>
</tr>
</tbody>
</table>

Adapted from H. Beger et al., Gastroenterology 1986; 91:433
Pancreatic Necrosis: Treatment Strategies

Sterile
- Supportive therapy
- Waiting for maturation
- No debridement

Infected
- Antibiotics
- Urgent surgical debridement (minimally invasive is optimal)
- Endo/IR at specialized centers

Pancreatic necrosis-treatment strategies are modified by infection.
Pancreatitis management

Aggressive IVF (Ringer’s)

**Severe**
- ICU: Foley, CVP
- Monitor Hct, BUN, O₂

- Contrast CT (72hrs)
- Prominent necrosis
- Enteral feeding -NJ tube

- Fever, Infection
- Organ failure

- Repeat CT, aspiration

- No Necrosis

- Improvement

- Suspicion of pancreatic infection

- Suspection of pancreatic infection

**Mild to moderate**

- No early indicators of severity

- IVF, Supportive
- If gallstone: ERCP for ongoing obstruction

- Transfer?

**Infected**
- Debride/Drain

**Sterile**
- Supportive Care, wait
Take Home Messages

• 80% of acute pancreatitis is due to alcohol and gallstones (look for AST/ALT peak)
• Urgent ERCP only for evidence of ongoing biliary obstruction, if expertise exists
• Hct >44, high BUN, other early signs of severity require ICU care
• Aggressive IV fluid resuscitation may limit severity, necrosis!
• Mild(interstitial) pancreatitis is benign: supportive care only
Take Home Messages

• For Severe/Necrotic Pancreatitis:
  • Early enteral feedings (NJ) are beneficial and limit infection.
  • Prophylactic Antibiotics are NOT recommended, but use for:
    • Suspicion of infection after CT aspiration
    • Crashing patients
  • Infected necrosis must be drained
Thank you!