Complications of Gallstones and Indications for ERCP

Matthew C. Rice, MD
7/23/2013
Lecture Outline

• Epidemiology of gallstone disease
• Physiology of gallstone formation and types of gallstones
• Complications related to gallstone disease
• Indications for ERCP
• Board review
Epidemiology

• 10% of all adults
• Predominantly women (67-75% of cases)
  – 5-20% incidence for women age 20-55
  – 25-30% incidence for women age >50
  – Men ½ the incidence of women
  – Difference between sexes decreases with age
• Native Americans and Hispanic ethnicity affected most; African American least
• Genetic factors
Epidemiology

• Higher incidence in those on a Western diet
• Other at risk groups
  – Pregnancy
  – Rapid weight loss (obesity surgery or calorie restriction
  – TPN use
  – Certain drugs (Estrogens, OCP’s, Octreotide, Ceftriaxone)
  – Obesity
  – Diabetes
  – Diseases of the ileum
  – Spinal cord injuries
Physiology
Basics

• Types of stones
  – Cholesterol (80%) and pigment (20%)
  – Sludge

• Five important factors for formation
  – Genetic factors (LITH genes)
  – Hepatic hypersecretion
  – Gallbladder hypomotility
  – Rapid phase transitions (nucleation and crystallization)
  – Intestinal factors
Stone Types

- **Cholesterol stones**
  - Cholesterol
  - Phospholipids
  - Bile salts

- **Pigment stones (excess unconjugated bilirubin)**
  - Black
    - Cross-linked polymer of Calcium Bilirubinate
    - Chronic hemolytic processes (β-thalassemia, hereditary spherocytosis, sickle cell disease, cirrhosis)
  - Brown
    - Monomeric Calcium Bilirubinate
    - Structural or functional stasis with biliary infections

- **Sludge**
  - Crystals and mucus
  - Precursors for cholesterol stones
  - Can cause same symptoms as stones and may resolve spontaneously
Hypersecretion & Hypomotility

• Excessive hepatic secretion of cholesterol
• Decreased bile salt or phospholipid secretion with normal cholesterol secretion
• Combination of the above
• Leads to supersaturation of cholesterol and precipitation of cholesterol monohydrate crystals
• Intestinal Factors
  – Increased intestinal absorption of cholesterol
  – Reduced intestinal absorption of bile salts
Nucleation & Crystallization

- Pro-nucleating agents
  - Mucin Gels
    - Pronucleating agent
    - Scaffolding for crystallization and stone growth
  - Other glycoproteins
- Anti-nucleating agents
- Defective acidification of the gallbladder
Complications of Gallstones
Stone intermittently obstructing cystic duct, causing intermittent biliary pain (20%) 

Asymptomatic stone (75%) 

Long-standing cholelithiasis, resulting in gallbladder carcinoma (<0.1%) 

Stone eroding through gallbladder into duodenum, resulting in cholecystoenteric fistula (prerequisite for gallstone ileus) and leading in some cases to Bouveret’s syndrome (gastric outlet obstruction) (<0.1%) 

Stone impacted in distal bile duct, causing jaundice, biliary-type pain, and risk of ascending cholangitis or acute biliary pancreatitis (5%) 

Stone impacted in cystic duct, causing acute cholecystitis (10%) 

Stone in the cystic duct compressing or fistulizing into the bile duct, causing Mirizzi’s syndrome (<0.1%)
Biliary Colic

- **Pathophysiology**
  - Intermittent obstruction of the cystic duct

- **Symptoms**
  - Severe episodic pain (epigastric and RUQ) which lasts hours, may radiate to shoulder
  - Post-prandial
  - Associated nausea & vomiting

- **Physical exam**
  - Mild to moderate RUQ/epigastric abdominal tenderness

- **Labs**
  - Usually normal

- **Imaging**
  - Gallstones seen in gallbladder
  - May be negative – can miss stones (GB contracted, obese patients)

- **Clinical course**
  - 70% will have recurrent symptoms within a 2 years period
  - 1-2% chance per year that patient will have gallstone complication requiring urgent surgical intervention

- **Treatment**
  - Laparoscopic cholecystectomy for patients with recurrent symptoms and signs of stones (may be considered in those with no stones seen)
  - No good medical therapeutic options
Acute Cholecystitis

• Pathophysiology
  – Impacted stone in the cystic duct causing continued obstruction leading to acute inflammation of the GB
  – Secondary bacterial infection in ~50%

• Symptoms
  – 75% preceded by biliary colic
  – Localized to RUQ with radiation to shoulder or back
  – May last hours to days
  – Associated with nausea/vomiting

• Physical exam
  – Fever (usually <102°F), Murphy’s sign, jaundice (20%), palpable GB (33%) (Courvoisier’s sign)

• Labs
  – Leukocytosis, T Bili 2-4, elevated AST/ALT/alk phos

• Imaging
  – U/S evidence of stone
  – Sonographic Murphy’s sign (90% PPV when gallstones present and in skilled hands)
  – HIDA scan

• Clinical course
  – 90% resolve spontaneously (Steinberg)
  – 5-10% mortality in elderly patients, associated with infection

• Treatment
  – Cholecystectomy (open or laparoscopic)
  – Cholecystostomy in severely ill patients or poor surgical candidates
  – Medical therapy (ursodiol – 20% success, but 50% recur)
Choledocholithiasis

- **Pathophysiology**
  - Intermittent obstruction of the bile duct

- **Symptoms**
  - May be asymptomatic, but when present are similar to biliary colic

- **Physical exam**
  - May be normal if obstruction is intermittent
  - Otherwise, similar to biliary colic

- **Labs**
  - Elevated bilirubin (2-5, rarely over 12) and alk phos
  - Spike may indicated passed stone

- **Imaging**
  - U/S liver, ERCP, MRCP, EUS, or percutaneous cholangiography
  - See stones or dilation of the bile ducts

- **Clinical course**
  - Not well known – can develop into cholangitis and acute pancreatitis

- **Treatment**
  - Based on suspicion of the presence of a stone
  - ERCP with sphincterotomy has 90% success rate
  - Eventual cholecystectomy
Cholangitis

- **Pathophysiology**
  - Stone in bile duct causing bile stasis, bacterial superinfection and early bacteremia

- **Symptoms**
  - Charcot’s triad (pain, jaundice, fever) in 70%
  - Pain may be mild and transient
  - Signs related to sepsis (confusion, lethargy, etc)

- **Physical exam**
  - Fever (95%); RUQ tenderness (90%); jaundice (80%); peritoneal signs (15%); hypotension and mental confusion (15%)

- **Labs**
  - Leukocytosis (80%), so some may actually have normal WBC
  - Bilirubin >2 (80%), elevated alk phos
  - Positive blood cultures (may even be 2 organisms in 50% of patients)

- **Imaging**
  - ERCP or PTC

- **Clinical course**
  - High mortality if unrecognized

- **Treatment**
  - ERCP or percutaneous cholangiogram with drainage (subsequent cholecystectomy)
  - Antibiotics
Rare Complications

• Emphysematous Cholecystitis
• Cholecystoenteric fistula
  – Can lead to gallstone ileus, gastric outlet obstruction (Bouveret’s syndrome), or small bowel obstruction
• Mirizzi’s syndrome
• Porcelain gallbladder
• Gallbladder cancer
Indications for ERCP
# Table 2. A proposed strategy to assign risk of choledocholithiasis in patients with symptomatic cholelithiasis based on clinical predictors

<table>
<thead>
<tr>
<th>Predictors of choledocholithiasis\textsuperscript{13,14,29,31,32}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very strong</td>
</tr>
<tr>
<td>CBD stone on transabdominal US</td>
</tr>
<tr>
<td>Clinical ascending cholangitis</td>
</tr>
<tr>
<td>Bilirubin &gt; 4 mg/dL</td>
</tr>
<tr>
<td>Strong</td>
</tr>
<tr>
<td>Dilated CBD on US (&gt; 6 mm with gallbladder in situ)</td>
</tr>
<tr>
<td>Bilirubin level 1.8-4 mg/dL</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Abnormal liver biochemical test other than bilirubin</td>
</tr>
<tr>
<td>Age older than 55 y</td>
</tr>
<tr>
<td>Clinical gallstone pancreatitis</td>
</tr>
</tbody>
</table>

Assigning a likelihood of choledocholithiasis based on clinical predictors\textsuperscript{12,14,28,29,31,32}

- Presence of any very strong predictor: **High**
- Presence of both strong predictors: **High**
- No predictors present: **Low**
- All other patients: **Intermediate**

CBD, Common bile duct.
• Diagnosis and treatment based on level of clinical suspicion

• ERCP before surgery (15%) – High risk
  – Any one very strong indicator
  – Both strong indicators

• MRCP or EUS before surgery (85%) intermediate or low risk
  – All others not listed above
Symptomatic Patient with Cholelithiasis

Likelihood of CBD Stone Based on Clinical Predictors (Table 2)

- Low
  - Laparoscopic Cholecystectomy
  - No Cholangiography
- Intermediate
  - OR*
    - Negative
      - Laparoscopic IOC or Laparoscopic Ultrasound
      - Laparoscopic Cholecystectomy
    - Positive
      - OR*
        - Laparoscopic Common Bile Duct Exploration
        - Post-operative ERCP
- High
  - Pre-operative ERCP
    - If Positive, or If Unavailable
* Depending on costs and local expertise
Board Review

65-year-old man admitted with a large MI and has been in the ICU for 2 weeks. He develops a fever and leukocytosis. Empiric antibiotics are started. CXR and blood cultures are negative. Physical exam reveals mild tenderness in the RUQ. Labs reveal Tbilii 1.8, WBC 14.5, AST 77, ALT 95. U/S shows a distended gallbladder with wall thickening and pericholecystic fluid without stones.

What do you recommend?
A. ERCP with GB stent
B. EUS FNA of GB contents
C. Percutaneous cholecystostomy
D. Urgent cholecystectomy
E. Continue antibiotics and supportive care
21-year-old woman with one year of episodic, epigastric and RUQ pain on a daily basis. Pain may relate to meals, but not associated with stress. No change in bowels, nausea/vomiting, or bloating. Physical exam reveals epigastric tenderness. Labs are normal. EGD with gastritis. Symptoms not improved with PPI. U/S and CT abdomen are normal. HIDA scan shows delayed emptying with EF of 15%.

What do you advise the patient?
A. Cholecystectomy will resolve symptoms
B. Cholecystectomy can be done but may not resolve symptoms
C. Abnormal gallbladder emptying occurs in 50% of asymptomatic patients
D. Treatment trial of ursodiol
58-year-old woman with 8 hours of biliary pain. She is morbidly obese with HTN, hyperlipidemia, NIDDM, TAH 20 years ago. Meds are lisinopril, simvastatin, and metformin. HR 112, Temp 98.5°F, mild epigastric tenderness. Labs with normal CBC, ALT 230, Alk phos 98, and bilirubin 4.5. U/S shows heterogenous liver and 10 mm CBD, GB is contracted and no stones seen.

What is the most likely diagnosis?

A. NASH
B. Pancreatic neoplasm
C. Bile duct stone
D. Cholecystitis
E. Bile duct stricture