

# **Biliary Infections: Cholecystitis**

## **Background**

### 1. Definitions

- Acute cholecystitis
  - Clinical syndrome of RUQ pain, fever and leukocytosis due to gallbladder inflammation
  - Usually caused by gallstones in cystic duct
- Acalculous cholecystitis
  - Associated with biliary stasis from burns, major surgery or sepsis
  - Gallbladder inflammation without gallstones
  - Usually in critically ill patients, carries high morbidity and mortality
- Ascending cholangitis
  - Bile duct bacterial infection caused by biliary flow obstruction
  - Usually due to choledocholithiasis (common duct stones)

## **Pathophysiology**

### 1. Pathology

- Acute cholecystitis
  - 95% of cases due to gallstones or biliary sludge obstructing cystic duct<sup>7,8,9</sup>
  - Prolonged obstruction, cholesterol-supersaturated bile and gallstone-induced trauma trigger acute gallbladder wall inflammatory response and edema mediated by PGE2 & 6-keto PGF1 alpha
  - Gallbladder dysmotility develops, distention and increased intraluminal pressure compromise blood flow to the mucosa
  - Bacterial contamination may develop as a late sequelae (E. coli most common)
- Acalculous cholecystitis
  - Stasis and obstruction in setting of stress, trauma, shock, TPN
  - Believed to be from direct ischemic compromise of gallbladder

### 2. Incidence, prevalence

- 10% of people in Western society
- 80% asymptomatic
- 1-3% of patients with symptomatic gallstones develop acute cholecystitis

### 3. Risk factors

- Gallstone risk factors
  - Obesity, rapid weight loss, childbearing, meds, postmenopausal estrogens, increasing age, hereditary
- Biliary colic
  - 30% of patients with biliary colic develop acute cholecystitis within 2 years
- Acalculous cholecystitis
  - Severe illness
  - Sepsis, major surgery, severe burns, multisystem organ failure, prolonged TPN, sickle cell disease, Salmonella infection
  - Elderly patients
  - Likely an ischemic process, similar risk factors as atherosclerosis

- Gender
  - <50 yo
    - 3x more common in women
  - >50 yo
    - Equal risk for both genders
- 4. Morbidity/mortality
  - Spontaneous resolution in 7-10 days if untreated in majority
  - Complications
    - Gallbladder gangrene (20% of untreated)
    - Perforation of gallbladder (2% of untreated)
      - Occurs after gangrene
      - Usually localized with pericholecystic abscess
      - Less commonly into peritoneum leading to generalized peritonitis
    - Cholecystoenteric fistula
      - Perforation of gallbladder into duodenum or jejunum
    - Gallstone ileus
      - Passage of gallstone through cholecystoenteric fistula leading to mechanical small bowel obstruction
    - Emphysematous cholecystitis
      - Secondary infection with gas-forming organisms like Clostridia perfringens, E. coli, staph, strep, klebsiella and pseudomonas
      - 30% cases are diabetics
      - Heralds the development of gangrene, perforation, and other complications

## **Diagnostics**

1. History/symptoms
  - RUQ/epigastric pain
    - Constant, severe, radiating to back/R shoulder, lasting > 3 hr
  - Fatty food ingestion >1 hr before onset of pain
  - Fever
  - Malaise
  - Anorexia
  - Nausea, vomiting
2. Physical exam
  - Febrile, tachycardia
  - Patients may lie motionless
    - Movement aggravates pain
  - Guarding
    - Voluntary and involuntary
  - Palpable gallbladder in 30-40%
  - Jaundice in 15%
  - + Murphy's sign
    - Severe RUQ pain with inspiration

### 3. Diagnostic tests

- Laboratory evaluation
  - Leukocytosis with left shift
  - If total bilirubin and alk phos elevated, possible cholangitis or gallstone in common bile duct (choledocholithiasis)
- Diagnostic imaging (SOR:B)
  - Ultrasound is first choice imaging modality
    - 81-100% sensitivity and 60-100% specificity in detecting acute cholecystitis
    - 84% sensitivity and 99% specificity in detecting gallstones >2 mm
    - Findings include distended gallbladder with pericholecystic fluid, gallbladder wall edema (>4 mm), presence of gallstones, positive sonographic Murphy's sign
  - HIDA scan
    - Gold standard
      - Does have problems with acalculous cholecystitis and cannot view pericholecystic structures
    - Indicated if ultrasound nondiagnostic
    - 97% sensitivity and 90% specificity in detecting cystic duct obstruction
    - Positive test shows absence of radiolabeled substance filling the gallbladder due to cystic duct obstruction, usually from edema of acute cholecystitis or obstructive stone
- Abdominal CT
  - Usually unnecessary given above modalities
  - More sensitive and specific than US
  - Findings include gallbladder wall edema, pericholecystic stranding and fluid, and high attenuation bile
  - Useful to rule out complications
    - Gallbladder perforation
    - Emphysematous cholecystitis
- Plain abdominal radiographs
  - Radiopaque gallstones in 10% of cases
  - Gas within gallbladder wall in emphysematous cholecystitis usually from E.coli or Clostridium

### Differential Diagnosis

#### 1. Key DDx

- Biliary colic
  - Transient obstruction of cystic duct, pain subsides after <3 hrs and patient feels well, usually afebrile
- Choledocholithiasis
  - Obstruction of the common bile duct by a stone
  - Pain, jaundice, LFT elevations
- Ascending cholangitis

- Acute obstruction of biliary tree causing infection and inflammation; patients appear toxic, fevers and chills, jaundice, leukocytosis, elevated alk phos and total bilirubin
  - Chronic cholecystitis
    - Chronic inflammation after recurrent acute cholecystitis, thickened gallbladder, long-standing postprandial discomfort
  - Hepatitis
    - Jaundice, fever, + hepatitis serologies
- 2. Extensive DDX
  - Other GI causes of abdominal pain
    - PUD, gastritis, pancreatitis, infectious colitis, diverticulitis, IBD, SBO, appendicitis, DKA gastroenteritis
    - Spontaneous bacterial peritonitis, amoebic hepatic abscess
  - Non-GI causes of abdominal pain
    - MI, intestinal ischemia, renal colic, pyelonephritis, PID, right lower lobe

### **Acute Treatment (SOR:B)**

1. Admit to hospital
2. Conservative treatment for 24-48 hr then cholecystectomy
3. NPO, NG tube if vomiting
4. IV hydration, correct electrolyte abnormalities
5. Analgesia
  - Ketorolac 30-60 mg IM (adjusted for age and renal function)
  - IV narcotic analgesia may be required
6. Antibiotics
  - Benefit unclear
  - Cover enterococcus, anaerobes and gram-negatives
  - Administer if
    - Systemic signs: fever, tachycardia, hypotension
    - No improvement after 12 hr conservative tx
  - Ampicillin 2 g IV q4hr plus gentamicin (dosed by weight and renal function)
  - Piperacillin/tazobactam 3.375 g IV q6 or 4.5g IV q8hr
  - Ampicillin sulbactam 3 g IV q6hr
  - Ticarcillin clavulanate 3.1 g IV q6hr
  - 3rd gen cephalosporin
    - Ceftriaxone 1 g IV q24hr + metronidazole 500 mg IV q8hr
  - Fluoroquinolones
    - Ciprofloxacin 400 mg IV q12hr / levofloxacin 500 mg IV q24hr AND metronidazole 500 mg IV q8hr
  - If life-threatening, imipenem 0.5 g IV q6hr or meropenem 1 g IV q8hr or ertapenem 1 g q24hr
7. Immediate cholecystectomy
  - If patient appears toxic, or gangrene or perforation suspected

### **Further Management (SOR:C)**

1. Low surgical risk patients
  - 24-48 hr supportive care followed by laparoscopic cholecystectomy
  - Early lap chole has some surgical risk as late lap chole, but lower cost and lower morbidity by reducing recurrent Sx/readmission
2. High surgical risk patients
  - Severe cardiovascular or pulmonary disease, or patients with sepsis
  - Conservative management
  - If fail to improve
    - Percutaneous cholecystostomy to drain gallbladder plus continued antibiotics
    - Once inflammation resolved, elective cholecystectomy
    - If not surgical candidates
      - Gallstone dissolution therapy with ursodiol via cholecystostomy catheter
3. Contraindications for laparoscopic cholecystectomy
  - Cirrhosis, coagulopathy, pancreatitis, pregnancy, morbid obesity, severe cardiorespiratory insufficiency, signs of gallbladder perforation

### **Prognosis (SOR:B)**

1. Mortality for single episode of acute cholecystitis is 3%
  - <1% mortality in young, otherwise healthy patients
  - 10% mortality in high-risk patients or those with complications

### **Prevention (SOR:C)**

1. Prevention of gallstones
2. NSAIDs for biliary colic
  - Single dose ketorolac 30-60 mg IM (adjusted for age and renal function) followed by ibuprofen 400 mg PO for subsequent attacks
  - Indomethacin and diclofenac have shown promise in some studies
  - May reduce progression to acute cholecystitis

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