Ascending cholangitis
Acute bacterial cholangitis

Symposium A: Endoscopic Emergencies

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Case

- 62 y/o M with hilar cholangiocarcinoma
- Admitted through ED with fever, chills, jaundice, RUQ abdominal pain
- In the ED, T = 102.5° F, P 124, BP 82/60
- BP 100/78 after 2 L IV NS, ABX given
- Exam: sclerae icteric, mucosae dry, heart / lungs normal, abdomen with mild RUQ tenderness; there are bilateral 8.5 Fr PTC drains, capped
- You are on call, and you’re awakened 03:15
Case

- Labs
- WBC 15.2
- AST 250, ALT 303, ALP 198, TB 5.9
- Imaging?

Case

- Do you get dressed and head in, or crawl back under the covers?
- What’s your game plan, and what’s it based on?
True, *de novo* pancreaticobiliary emergencies

- **Biliary emergencies**
  - Cholangitis
  - Cholecystitis
  - Bile leak
  - Hemobilia
  - (Jaundice)

- **Pancreatic emergencies**
  - Acute pancreatitis
  - Systemic complications
    - Cardiopulmonary
    - Renal
    - Infectious
  - Pancreatic/GI complications
    - Pancreatic necrosis
    - Fluid collections
    - Vascular complications
      - Hemorrhage
      - Thrombosis

- **Chronic pancreatitis**

Jean-Martin Charcot
1825-1893

1877
Acute obstructive cholangitis...a distinct clinical syndrome...requires urgent surgical decompression of the biliary tract...this report...demonstrates the dramatic results of emergency surgical decompression of the biliary tract."

What is cholangitis?

- Bacterial infection in the setting of biliary obstruction → systemic infection: 1° obstructive, 2° infectious
- Symptoms
  - Fever
  - Abdominal pain
  - Jaundice
  - Hypotension
  - Mental status changes

Charcot 1877

Reynolds 1955
Diagnosis of cholangitis

circa 2007:

Definitive diagnosis
Clinical signs of infection and finding of purulent bile during these procedures:
- ERCP
- Surgery
- Percutaneous puncture

The Charcot triad
- Fever
- Abdominal pain
- Jaundice

Tokyo guidelines
Two of three criteria of the Charcot triad plus
- Inflammatory response, for example:
  - Abnormal white blood cell count
  - Elevated C-reactive protein level
- Abnormal liver test results, for example:
  - Alkaline phosphatase
  - y-Glutamyl transpeptidase
  - Aspartate aminotransferase
  - Alanine aminotransferase
- Imaging evidence of etiology, for example:
  - Stone
  - Stricture
  - Stent

Obstructive etiologies of cholangitis

- Choledocholithiasis
  - Primary or secondary
- Mirizzi
- Parasites
- Pancreatitis
- PSC
- Ampullary neoplasm
- Other luminal obstructions
  - Tumor / tumor cast
  - Clot / hemobilia

- Iatrogenic etiologies
  - Stent occlusion, migration, malfunction
  - ERC-opacified, but undrained, ducts
  - Hemobilia
  - Post-surgical
    - Luminal content reflux
    - Stricture
      - Anastomotic
      - Ischemic ± cast
      - Extrinsic
Microbiology of cholangitis

- Gram negative rods
  - E. coli
  - Klebsiella
  - Enterobacter
  - Pseudomonas
- Gram positive cocci
  - Enterococcus
- Anaerobes
  - Clostridium

**Treatment of cholangitis**

- **Supportive care**
  - Hospitalization: ward vs ICU
  - Volume resuscitation
- **Antibiotic therapy**
  - Immediate
  - Intravenous
- **Drainage**
  - Urgent if severe (unstable)
  - 24 – 48 hours if mild or moderate (stable)

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**Treatment of cholangitis**

- **Antibiotic therapy**
  - Guidelines differ
  - Broad-spectrum PCN with beta-lactamase inhibitor
  - Fluoroquinolone ± metronidazole
  - 3rd generation cephalosporin + metronidazole
  - Monobactam
  - Tailor to blood / bile culture results
  - Consider metronidazole particularly if biliary-enteric anastomosis is present

Treatment of cholangitis

• Antibiotic therapy
  – Consider whether infection is community- or hospital-acquired when tailoring empiric therapy
  – Cover pseudomonas in hospital-acquired cholangitis
  – Resistance to common antimicrobial regimens is increasing
  – Patients known to be colonized with MRSA or VRE: vancomycin, linezolid
  – De-escalation as soon as antibiotic susceptibilities are reported out
  – Duration of therapy not well-studied: IDSA 2010 recommends 4-7 days after source controlled; 2 weeks if gm+ cocci

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Antimicrobial agents with high prevalence of resistance among Enterobacteriaceae</th>
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<tbody>
<tr>
<td>Antimicrobial class</td>
<td>Antimicrobial agents</td>
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<tr>
<td>Penicillin</td>
<td>Ampicillin/subactam</td>
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<td>Cephalosporins</td>
<td>Cefazolin</td>
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<td>Cefuroxime</td>
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<td>Flomoxef</td>
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<td>Cettriadone* or cefotaxime*</td>
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<td>Fluoroquinolones</td>
<td>Ciprofloxacin</td>
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<td>Levofloxacin</td>
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<td>Moxifloxacin</td>
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References [4–11]
* This resistance indicates the global spread of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae

Treatment of cholangitis

• Drainage (the most important and definitive element of treatment); in order of preference:
  – Endoscopic
    • Definitive
      – Sphincterotomy
      – Duct clearance
    • Temporizing
      – Stent placement
      – Nasobiliary drainage
  – Percutaneous
    • Salvage
  – Surgical

Treatment of cholangitis

- ERCP drainage options
  - Sphincterotomy with definitive duct clearance
    - Single procedure
    - Greater risk of complications
    - Longer procedure time
- Temporizing stent placement
  - Requires later stent removal / duct clearance
- Temporizing nasobiliary drain placement
  - Technically challenging, fussy, prone to displacement


Treatment of cholangitis

- ERCP drainage: expert technique
  - Expert, efficient cannulation imperative
  - Drain bile before injecting contrast
  - Minimize contrast volume / pressure
  - Dilute contrast if duct dilated
  - Avoid proximal migration of stones
  - Beware of cystic / intrahepatic duct stones
  - Size sphincterotomy appropriately
  - Expert technique for basket, balloon, stent

Treatment of cholangitis

- Biliary drainage caveats
  - What is the anatomy?
  - How sick is the patient?
  - Surgically-altered anatomy
    - Roux-en-Y gastric bypass
      - Other bariatric procedures
    - Roux-en-Y hepaticojejunostomy
      - For biliary disease
      - For liver transplantation
    - Whipple procedure
    - Billroth II

What’s wrong with Charcot?

- Specific, but…
- Insensitive
- No severity assessment to direct urgency of intervention
- International consensus guideline development group: TG07
Severity of cholangitis: The Tokyo Guidelines

• Mild: responsive to
  – Supportive therapy
  – Antibiotics

• Moderate
  – Not responsive to medical therapy
  – No other organ dysfunction

• Severe
  – Associated with at least one sign of organ dysfunction


More about these severity assessment criteria to follow…

Treatment of cholangitis


The updated Tokyo Guidelines

- TG07 inadequately sensitive/specific
  - TG13 has higher sensitivity without sacrificing specificity
- TG13 provides more accurate and reliable diagnostic criteria
- Severity assessment criteria for TG07 are unsuitable for clinical use
  - TG13 provides more accurate and reliable severity assessment criteria for determination of proper timing of biliary drainage

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<th>TG07</th>
<th>1st draft*</th>
<th>TG13</th>
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<tbody>
<tr>
<td>Sens</td>
<td>26.4</td>
<td>82.6</td>
<td>95.1</td>
<td>91.8</td>
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<td>Spec</td>
<td>95.5</td>
<td>79.8</td>
<td>66.3</td>
<td>77.7</td>
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<td>Pos rate in acute cholecystitis</td>
<td>11.9</td>
<td>15.5</td>
<td>38.8</td>
<td>5.9</td>
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TG13

- Elements
  - Diagnostic criteria
  - Severity assessment criteria
  - Management flowcharts / algorithms: “at-a-glance outline of disease management strategy
  - Disease management bundles (new): “checklist” of mandatory interventions: “what to do and when to do it”

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TG13

TG 13 Diagnostic criteria for acute cholangitis

A. Systemic Inflammation
   A-1. Fever and/or shaking chills
   A-2. Laboratory data: Evidence of Inflammatory response

B. Cholestasis
   B-1. Jaundice

C. Imaging
   C-1. Bilary dilatation
   C-2. Evidence of the etiology on imaging (stricture, stone, stent etc)

Suspected diagnosis: One item in A + one item in either B or C
Definite diagnosis: One item in A, one item in B and one item in C

Note: Other factors which are helpful in diagnosis of acute cholangitis include abdominal pain (Right upper quadrant [RUQ] or upper abdominal) and a history of biliary disease such as gallstones, previous biliary procedures, and placement of a biliary stent. In acute hepatitis, marked systemic inflammatory response is observed infrequently.

Calculator of Severity Assessment of Acute Cholecystitis of TG13

I. Does a patient fulfill any of following 6 conditions?
   1. Hypotension requiring dopamine ≥5μg/kg/min. or any dose of Norepinephrine
   2. Decreased level of consciousness
   3. PaO2/FiO2 ratio <300
   4. Olbuntin, Serum creatinine >2.0mg/dl
   5. PT-INR >1.5
   6. Platelet count <100,000/mm3

II. Does a patient match the following findings?
   1. Elevated WBC count (>18000/mm3)
   2. Palpable tender mass in the right upper abdominal quadrant
   3. Duration of complaints >72h

What to do...
Severity-based management of cholangitis

- Mild cholangitis: responsive to
  - Supportive therapy
  - Antibiotics
- Continue supportive therapy
- Continue antibiotics
- Drainage the next day if possible

Severity-based management of cholangitis

- Moderate cholangitis
  - Not responsive to medical therapy
  - No other organ dysfunction
- Continue supportive therapy
- Continue antibiotics
- Monitor vigilantly for deterioration
- Drainage: definitely in the morning; sooner if condition worsens
Severity-based management of cholangitis

• Severe
  – Associated with at least one sign of organ dysfunction
  – Continue supportive care: ICU
  – Continue antibiotics
  – Urgent drainage: time to get out of bed and get in to the endoscopy unit (or even the ICU)
  – Strongly consider quick stent placement with minimal contrast opacification