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The EM Educator Series

The EM Educator Series: Why is my patient with gallbladder pathology so sick?

Author: Alex Koyfman, MD (@EMHighAK) // Edited by: Brit Long, MD (@long_brit) and Manpreet Singh, MD (@MprizzleER)

Cases:

#1: A 43-year-old female presents with right upper quadrant pain and nausea. She ate a large meal approximately 2 hours ago. This is the third time this has happened, but each time before the pain resolved spontaneously.

#2: A 74-year-old male presents with jaundice, fever, and right upper quadrant pain for 2 days. He appears toxic.

Questions for Learners:

1) What is the spectrum of gallbladder disease?
2) What sources do you need to consider in sepsis? What about the abdomen?
3) How does cholangitis present? Can it vary? Why do we miss it?
4) What is the ED evaluation of cholangitis?
5) How is cholangitis managed?
6) What complications of ERCP should you consider?

Suggested Resources:

- ✓ Articles:
  - CORE EM – Cholangitis
  - emDOCs.net – So you think it is sepsis: considerations beyond lung and urine in the sick patient without a source
  - emDOCs.net – Cholangitis: Deadly Cause of Right Upper Quadrant Abdominal Pain
  - Ely, Rachel, Brit Long, and Alex Koyfman. "The Emergency Medicine− Focused Review of Cholangitis." The Journal of emergency medicine 54.1 (2018): 64-72.

Answers for Learners:

1) What is the spectrum of gallbladder disease?

Definitions	
Symptomatic cholelithiasis	Wax/waning postprandial epigastric/RUQ pain due to transient cystic duct obstruction by stone, no fever/WBC, normal LFT
Acute cholecystitis	Acute GB inflammation due to cystic duct obstruction. Persistent RUQ pain +/- fever, ↑WBC, ↑LFT, +Murphy's = inspiratory arrest
Chronic cholecystitis	Recurrent bouts of colic/acute chol'y leading to .chronic GB wall inflamm/fibrosis. No fever/WBC
Acalculous cholecystitis	GB inflammation due to biliary stasis(5% of time) and not stones(95%). Seen in critically ill pts
Choledocho-lithiasis	Gallstone in the common bile duct (primary)means originated there, secondary = from GB
Cholangitis	Infection within bile ducts usu due to obstrux of CBD. Charcot triad: RUQ pain, jaundice, fever (seen in 70% of pts), can lead to septic shock

2) What sources do you need to consider in sepsis? What about the abdomen?

➔ Think LUCCASS (Lung, Urine, Cardiac, CNS, Abdomen, Arthritis, Skin, Spine)

Musculoskeletal: Patients with poor vascular circulation, diabetes, and immunocompromise are at the greatest risk for serious musculoskeletal infection. The most common cause of sepsis secondary to skin and soft tissue infections is cellulitis due to Staphylococcus aureus or Streptococcus pyogenes. Many patients will have decubitus ulcers which may become a source for osteomyelitis or systemic infection. A genitourinary exam may reveal a necrotizing infection such as Fournier's gangrene. Consider staphylococcal toxic shock syndrome in the ill-appearing patient with a generalized macular rash. An erythematous, hot swollen joint, especially the hip or knee, should raise suspicion for a septic joint. Aspiration is required for diagnosis of septic arthritis.

Cardiac: While a thorough cardiac exam is often difficult in the chaos of the emergency department, the presence of a new murmur in the acutely ill patient should raise suspicion for endocarditis. Risk factors for endocarditis include the presence of a prosthetic valve, intravascular devices, intravenous drug use, and immunocompromise. If the vegetation is large enough, it may be visible on bedside ultrasound, though this is certainly not sensitive. Other physical exam findings consistent with endocarditis include stigmata of peripheral thromboembolism such as Osler nodes, Janeway lesions, or splinter hemorrhages.

Meningitis and encephalitis: The classic triad of meningitis is altered mental status, nuchal rigidity, and fever, though the majority of patients only have one or two of these symptoms. The most common causes of meningitis in adults in the United States are Streptococcus pneumoniae, group B streptococci and Neisseria meningitidis. Listeria monocytogenes is more common in children, older adults, and the immunocompromised. Meningitis and encephalitis may also be caused by viruses such as herpes, enteroviruses, and CMV.

Spinal infections: Back pain is an incredibly common chief complaint in the emergency department. While the majority of patients presenting with back pain will have fairly benign pathologies including

disc herniation and muscle strain, spinal infection should be considered in all patients presenting with back pain. Risk factors for spinal infection include immunosuppression, recent invasive procedures, spinal implants, and intravenous drug use. Vertebral osteomyelitis, discitis, and epidural abscesses are potential sources of sepsis from a spinal infection.

Urinary tract pathology: If a patient is more ill-appearing than is explained by a simple urinary tract infection, consider a CT to evaluate for a perinephric abscess, infected nephrolithiasis, or emphysematous pyelonephritis.

Abdominal sepsis: Recognition of abdominal sepsis is sometimes hampered by the patient's mental status or body habitus. Conscious patients are able to describe their abdominal pain and may be able to localize their discomfort. In the obtunded patient, an especially thorough abdominal examination is of great diagnostic utility. Absence of bowel sounds, abdominal distention, and rigidity may point to an abdominal cause of sepsis in the acutely ill-patient. While it is difficult to assess pain response in the obtunded or unconscious patient, other markers of discomfort, such as grimacing, guarding, or tachycardia, can be used to localize abdominal pain in a patient with altered mental status. If concern for intra-abdominal source of sepsis, imaging is recommended. Causes of intra-abdominal infection include abscess (perinephric, ovarian abscess), spontaneous bacterial peritonitis, cholecystitis or cholangitis, ruptured hollow viscus, or infection of the gastrointestinal tract (appendicitis, colitis, diverticulitis). Pelvic examination is helpful for the identification of tubo-ovarian abscesses and pelvic inflammatory disease and may help identify the infectious source in toxic shock syndrome. While occult intra-abdominal infections may initially respond to empiric antibiotic treatment, recognition of the presence of these infections is vital as aggressive source control through surgical or vascular interventional means is usually necessary for treatment.

Indwelling devices: Indwelling devices such as central venous catheters, ports, and dialysis access may be a nidus for infection. Physical examination of the septic patient with invasive devices should include examination of the site of the device, taking particular note of any erythema or purulent drainage. Though specific, signs of exit-site infection are not sensitive for the presence of line-associated bacteremia. One study found that only 4.6% of catheter-associated bacteremia was associated with purulent drainage at the exit site. In the absence of clear physical exam findings for line-associated bacteremia, clinical suspicion must remain high for line infection in patients with indwelling devices. If possible, the device should be promptly removed and cultured.

3) How does cholangitis present? Can it vary? Why do we miss it?

Always think about cholangitis in any ill-appearing patient with RUQ pain or undifferentiated sepsis. Abdominal pain is the most common complaint and is seen in about 80% of patients with cholangitis. Similarly, fever and jaundice are also variable in presentation. Studies show that anywhere between 40 and 80% of patients with cholangitis will have fever. Jaundice may not manifest itself initially. It is also less common than abdominal pain and fever, occurring in 50-70% of patients with cholangitis. So reliance on clinical signs alone is not helpful and thus, imaging is recommended.

Charcot's triad and Reynold's pentad are not reliable. Charcot's triad is anywhere between 72 and 95% specific for cholangitis, although there is about an 11% false positive rate in cholecystitis. Reynold's pentad signifies more severe disease, but it is rare and shows up in less than 10% of patients with cholangitis. Despite its low sensitivity rate of 26%, providers were forced to use the absence of Charcot's triad to rule out the diagnosis of cholangitis.

Absence of these clinical findings does not rule out cholangitis. Use the total picture with clinical exam, labwork, and imaging studies.

4) What is the ED evaluation of cholangitis?

The Tokyo Guidelines 2013 (TG13). These criteria are as following:

Category	Threshold
A. Systemic Inflammation	
Fever or Shaking Chills	Body Temperature >38°C
Laboratory evidence of inflammatory response	WBC <4,000 or >10,000
	CRP >1
B. Cholestasis	
Jaundice	T-Bili ≥2 mg/dL
Abnormal LFT	Alk Phos >1.5 x upper limit normal
	GGT >1.5x upper limit normal
	AST >1.5x upper limit normal
	ALT >1.5x upper limit normal
C. Imaging	
Biliary dilatation	
Evidence of etiology on imaging	
Diagnosis should be suspected if one item from A plus one item from B or C are present	
Diagnosis is considered definite if one item from, A, B and C are present.	

Using the TG13, the sensitivity increased to 91% and the specificity only decreased slightly to 78% and the false positive rate decreased to 5%. The TG13 criteria can be applied to patients with and without abdominal pain who present with undifferentiated sepsis. Now, practitioners have reliable criteria consisting of data that is obtainable in an emergency department workup.

5) How is cholangitis managed?

Resuscitation, antibiotics and consultation for early biliary decompression are the mainstays of cholangitis treatment.

Resuscitation is important to maintain hemodynamic stability. Hemodynamic stability is also necessary to make sure that antibiotics perfuse the infected regions, namely the biliary tree. Cardiac and blood pressure monitoring should be reassessed frequently as tachycardia and hypotension due to sepsis can quickly develop. Patients should be treated early with intravenous fluids and, if needed, vasoactive agents. Laboratory studies directed at cholangitis are important, but other laboratory markers for sepsis will help with directing therapy as well. Obtain serial lactate measurements, venous blood gas for acid-base disturbance, and urine output measurements to help direct any hemodynamic therapy. Blood cultures are not routinely useful unless disease severity is high where multi-organ dysfunction is present. Although blood cultures are positive in anywhere between 22 and 71% of cholangitis cases, typical causative organisms are not known to cause vegetations and are often susceptible to the antibiotic regimen. Therefore, blood cultures often do not provide any additional information.

Antibiotic regimens should be directed toward Gram-negative species and, less commonly, anaerobes and Gram-positive species. Cultures taken from biliary fluid and blood in patients with cholangitis reveal Escherichia coli in more than 50% of cases. Other culprits are typically other Gram-negative species and anaerobic species. In recent years, there has been an increase in resistance of Gram-negative bacilli to typical antimicrobials and occasional Gram-positive organisms (i.e. Enterococcus), especially in hospital-

acquired infections. Antibiotics need to be effective at treating the causative organisms but also need to be concentrated in the bile in order to be effective. First generation cephalosporins and fluoroquinolones are adequate in mild disease. Once organ failure begins to manifest, coverage for hospital-acquired infections should occur. **Third or fourth generation cephalosporins or piperacillin-tazobactam are better options. Vancomycin or linezolid should be administered to cover Gram-positive organisms and metronidazole should be given to cover anaerobes.20 The carbapenems or aztreonam are acceptable alternatives.**

Early biliary decompression will also help with source control. Before antimicrobial therapy was introduced, biliary decompression was the only way to treat cholangitis. Gastroenterology consultation for ERCP should occur early if suspicion is high. ERCP is usually effective at diagnosing and relieving obstructions that may be present.

6) What complications of ERCP should you consider?

➔ pancreatitis // cholangitis // hemorrhage // perforation