Infectious Diseases

Lesson 7

GASTROINTESTINAL AND HEPATOBILIARY INFECTIONS

Part B – Intra-abdominal Infections

Bernardino Roca Villanueva

Servicio de Medicina Interna, Hospital General de Castellón
Departamento de Medicina, Universidad Jaume I

broca@uji.es

Objectives and learning goal

Objectives

- To study all clinically relevant intra-abdominal infections
- To understand the differences and similarities that exist among the diverse intra-abdominal infections

Learning goal

To develop enough clinical skills to properly manage a patient with an intra-abdominal infection

Contents

Introduction

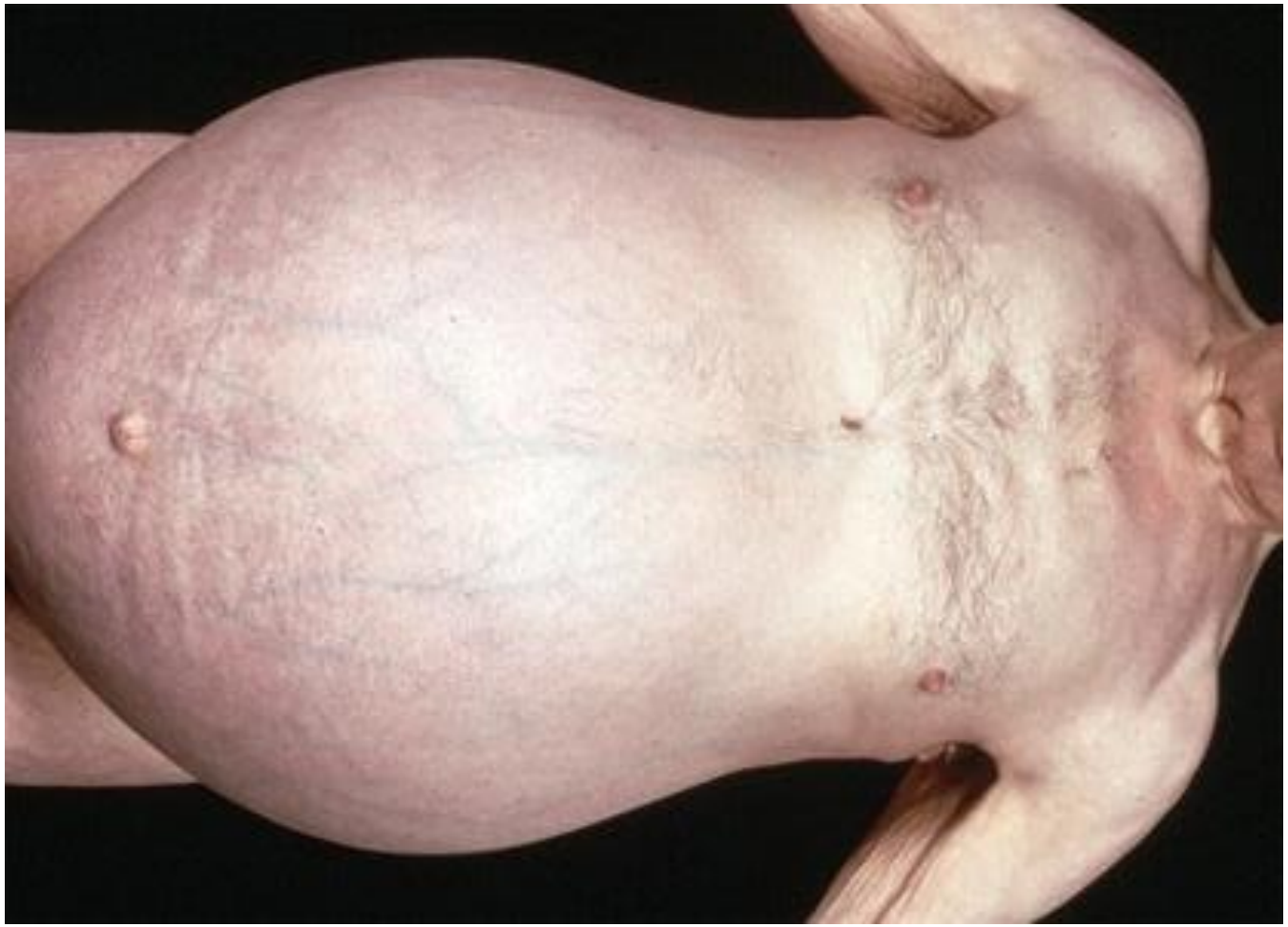
Relevance and main features

- Incidence of intra-abdominal infections is difficult to ascertain
- Provoke a significant number of hospital admissions
- Often at the interface of internal medicine and surgery
- In many cases, the internist, gastroenterologist, radiologist, and general surgeon need to coordinate themselves to assure the most favorable outcome

Primary or spontaneous peritonitis

Pathogenesis

- Occurs in patients with **ascites** due to **severe cirrhosis**, and less frequently in ascites due to heart failure, malignancy, or lymphedema
- Bacteria may enter the peritoneal space by:
  - Hematogenous spread
  - Lymphatic spread
  - Migration through the bowel wall
- Factors favoring infections in severe cirrhosis:
  - The reticuloendothelial system of the liver is often bypassed secondary to shunting, increasing the risk of prolonged bacteremia
  - Bowel motility is also slowed, resulting in bacterial overgrowth



Cirrhosis of the liver

Microbiology

- The most common pathogens are enteric bowel flora: ***E. coli*** and *Klebsiella pneumoniae*
- Also common *Streptococcus pneumoniae* and other streptococci and enterococci
- Rarely *S. aureus,* anaerobes and others

Clinical manifestations

- Initial symptoms and signs may be subtle
- Fever the most common manifestation, initially often low grade
- Abdominal pain diffuse and constant, differs from the usual sensation of tightness with tense ascites
- Development of hepatic encephalopathy
- Diarrhea usually precipitated by overgrowth of bowel flora
- Abdominal tenderness is diffuse and without guarding; in the late stages rebound tenderness may be elicited

Diagnosis

- Paracentesis, 4 samples of ascitic fluid for:
  - Culture, 10 mL inoculated into a blood flask
  - Cell counts and cytology analysis, tube containing anticoagulant
  - Total protein, albumin, LDH, glucose, and amylase levels
  - Gram stain
- Leukocyte count > 250 cells/mm^3 with predominance of polymorphonuclears
- Urinalysis leukocyte esterase strips, a reading > 20 indicates acute inflammation and probable infection
- Gram stain is positive in 20-40 % of cases
- High total protein, LDH, and amylase, and low glucose, suggest **secondary** peritonitis, due to bowel perforation

Treatment and outcome

- Empiric cefotaxime or ceftriaxone, as an emergency
- If secondary peritonitis is suspected, anaerobic coverage with metronidazole should be added
- Mortality 60-70%
- Spontaneous peritonitis is a marker of terminal liver disease, and sufferers should strongly be considered for liver transplant
- Antibiotic prophylaxis, initiated after the first episode with trimethoprim-sulfamethoxazole, oral norfloxacin, or oral ciprofloxacin

Secondary peritonitis

Pathogenesis

- Spillage of bowel flora into the peritoneal cavity
- Causes include:
  - Perforation of a gastric ulcer
  - Appendicitis with rupture
  - Diverticulitis
  - Bowel neoplasm
  - Gangrenous bowel resulting from
    - Strangulation
    - Mesenteric artery insufficiency
  - Pancreatitis

Microbiology

- Stomach perforation → infection with mouth flora, including **streptococci**, *Candida* spp., lactobacilli, and anaerobes
- Bowel perforation → mixed enteric flora, including:
  - **Anaerobes** such as ***Bacteroides fragilis***
  - Aerobic gram-negative bacteria such as ***E. coli***, *Klebsiella* spp., *Proteus* spp., and *Enterobacter* spp.
  - Gram-positive bacteria such as *S. viridans*, enterococci, and *C. perfringens*

Peritoneal response to infection

- Rapid and exuberant
- Large quantities of **proteinaceous exudate** are released into the peritoneum → wall off infection → abscesses
- Massive influx of **polymorphonuclears** and **macrophages**
- Massive influx of **fluid** that can result in intravascular fluid losses of 300-500 mL hourly
- Lymphatics clear large numbers of bacteria quickly, but finally bacteria invade the bloodstream
- Host defense may be overwhelmed → metabolic acidosis, tissue hypoxia, shock, multiorgan failure, and death

Clinical manifestations: symptoms

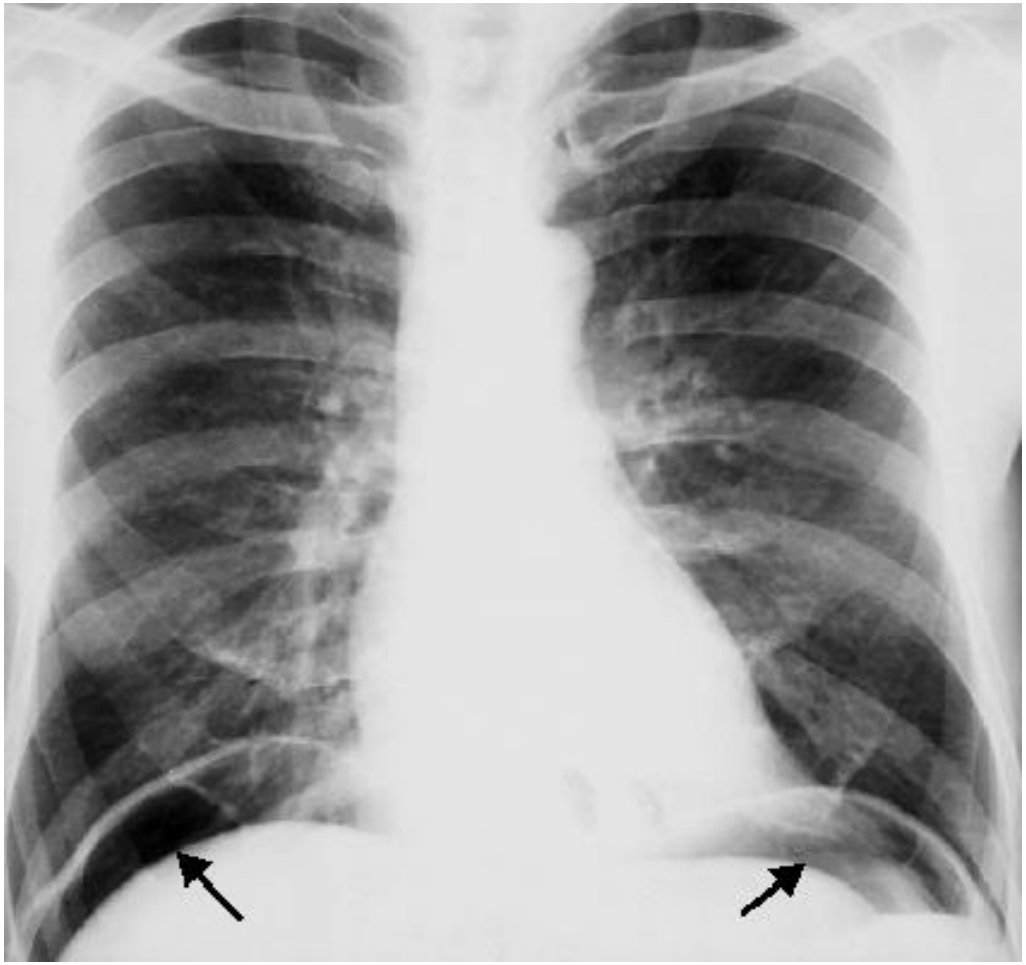
- Anterior peritoneum is richly enervated, and the first manifestation is **pain**, usually sharp, localized to the site of spillage, and aggravated by motion
- Loss of appetite, nausea, fever, chills, constipation, and abdominal distension
- Patients usually lie still in bed, breathing with shallow respirations
- Generalized abdominal pain, tachycardia, and hypotension develop in the later stages

Clinical manifestations: signs

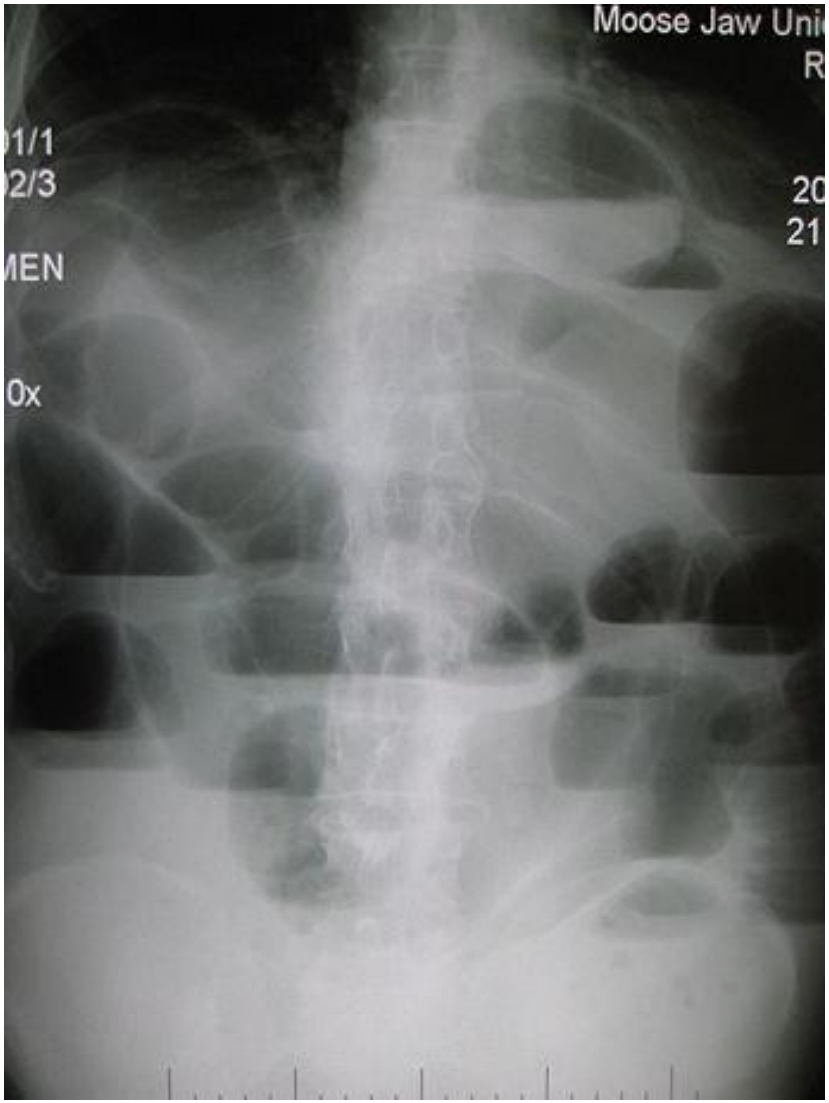
- Bowel sounds are decreased or absent
- Abdomen is tender to palpation, with **guarding** and **involuntary muscle spasm**: board-like abdomen
- **Rebound tenderness** (slow compression of the abdomen followed by rapid release of pressure causes severe pain), indicates peritoneal irritation
- Tenderness on rectal examination
- Elderly patients often fail to present with the classic findings of peritonitis

Diagnosis I

- Leukocytosis, 17,000-25,000 per mm^3, with left shift
- Supine and upright abdominal X-rays:
  - Free air under the diaphragm (bowel or gastric perforation)
  - Assess the bowel gas pattern
  - Search for areas of thickened edematous bowel wall
- Chest X-ray must always be performed to exclude lower lobe pneumonia, which can cause ileus and upper quadrant tenderness mimicking peritonitis



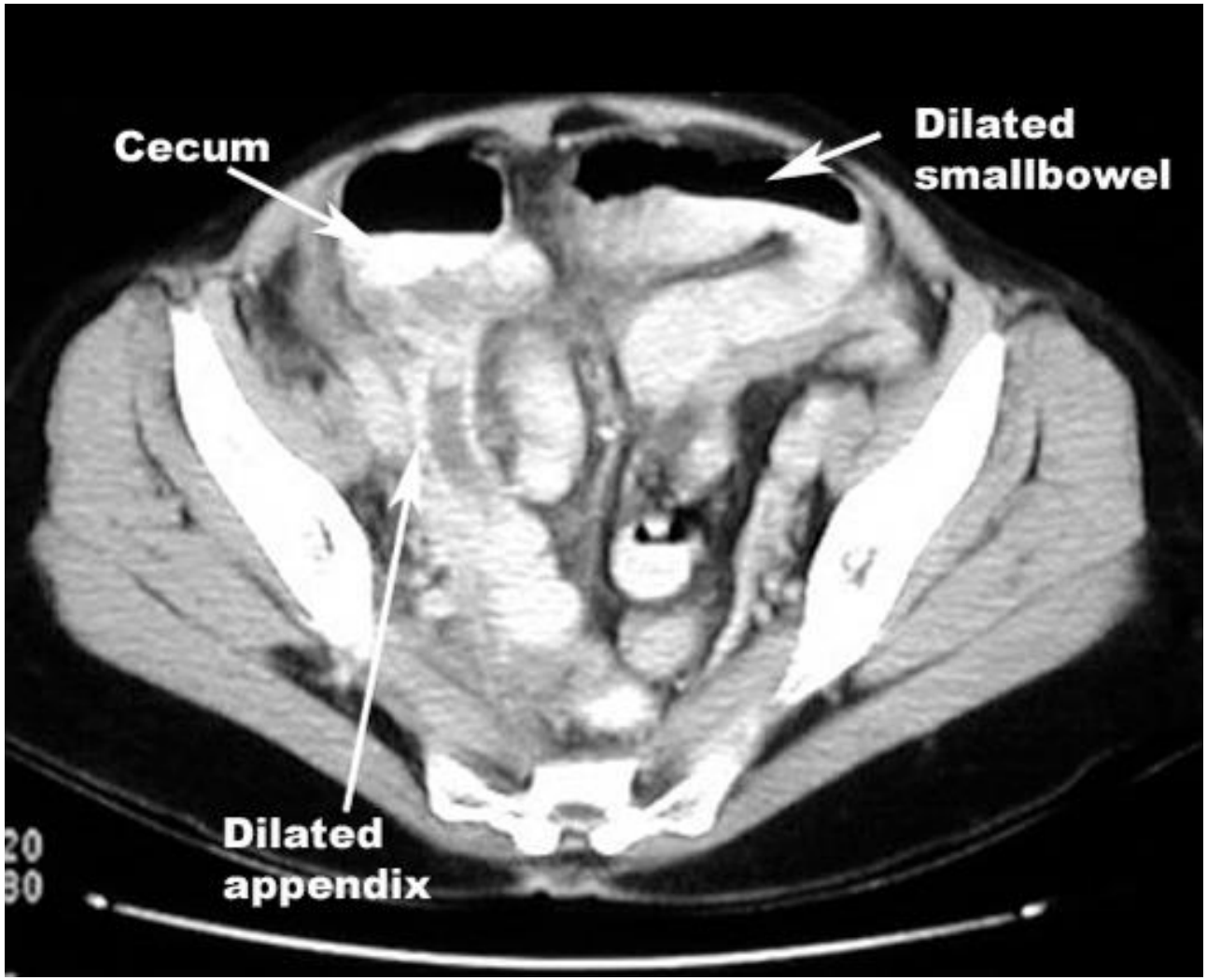
Free air under the diaphragm



Bowel obstruction, air-fluid levels

Diagnosis II

- CT scan of the abdomen and pelvis, after oral and intravenous contrast, test **of choice** for suspected intra-abdominal infection:
  - Often obviates the need for exploratory laparotomy
  - Accurate diagnosis of appendicitis
  - Localization and needle aspiration of abscesses
  - Identification of areas of bowel obstruction
- Abdominal examination, vital signs, basic blood analyses, and image tests help in deciding whether an **exploratory laparotomy** is necessary



Acute appendicitis

Treatment

- Antibiotics emergently initiated in suspected secondary peritonitis: **imipenem**, piperacillin-tazobactam, etc.
- A general **surgeon** should be consulted emergently, exploratory laparotomy is often required for diagnosis, drainage, and bowel repair
- Intraoperative cultures may be helpful
- Peritoneal **irrigation** is performed intraoperatively, and **drains** are placed at sites where purulent collections are noted
- Multiple operations are often required for purulent peritonitis

Secondary peritonitis associated with peritoneal dialysis

Pathogenesis and clinical features

- Frequent complication of chronic ambulatory peritoneal dialysis and the most frequent reason for discontinuation of that therapy
- ***S. aureus***, including MRSA, or **gram-negative bacteria**, fungi, mycobacteria, etc.
- Fever and diffuse abdominal pain
- Peritoneal dialysis fluid becomes cloudy

Diagnosis and treatment

- Peritoneal fluid leukocyte counts > 100/mm^3, with a predominance of polymorphonuclears; predominance of lymphocytes in fungal or mycobacterial infection
- Peritoneal fluid gram stain and culture
- Blood cultures
- Antibiotic added to the dialysate, cefazolin, or vancomycin + tobramycin.
- If the patient fails to improve within 48 hours, removal of the dialysis catheter should be considered

Hepatic abscess

Pathogenesis: sources of infection

- **Biliary tract infection**
- Portal vein bacteremia due to intra-abdominal infections:
  - **Appendicitis**
  - Diverticulitis
  - Inflammatory bowel disease
- Extension from a contiguous infection
  - Perforation of the gallbladder or duodenal ulcer
  - Perinephric, pancreatic, or subphrenic abscess
- Penetrating wounds and postoperative complications
- Bacteremia from any source
- In one quarter of cases, a cause cannot be determined

Microbiology

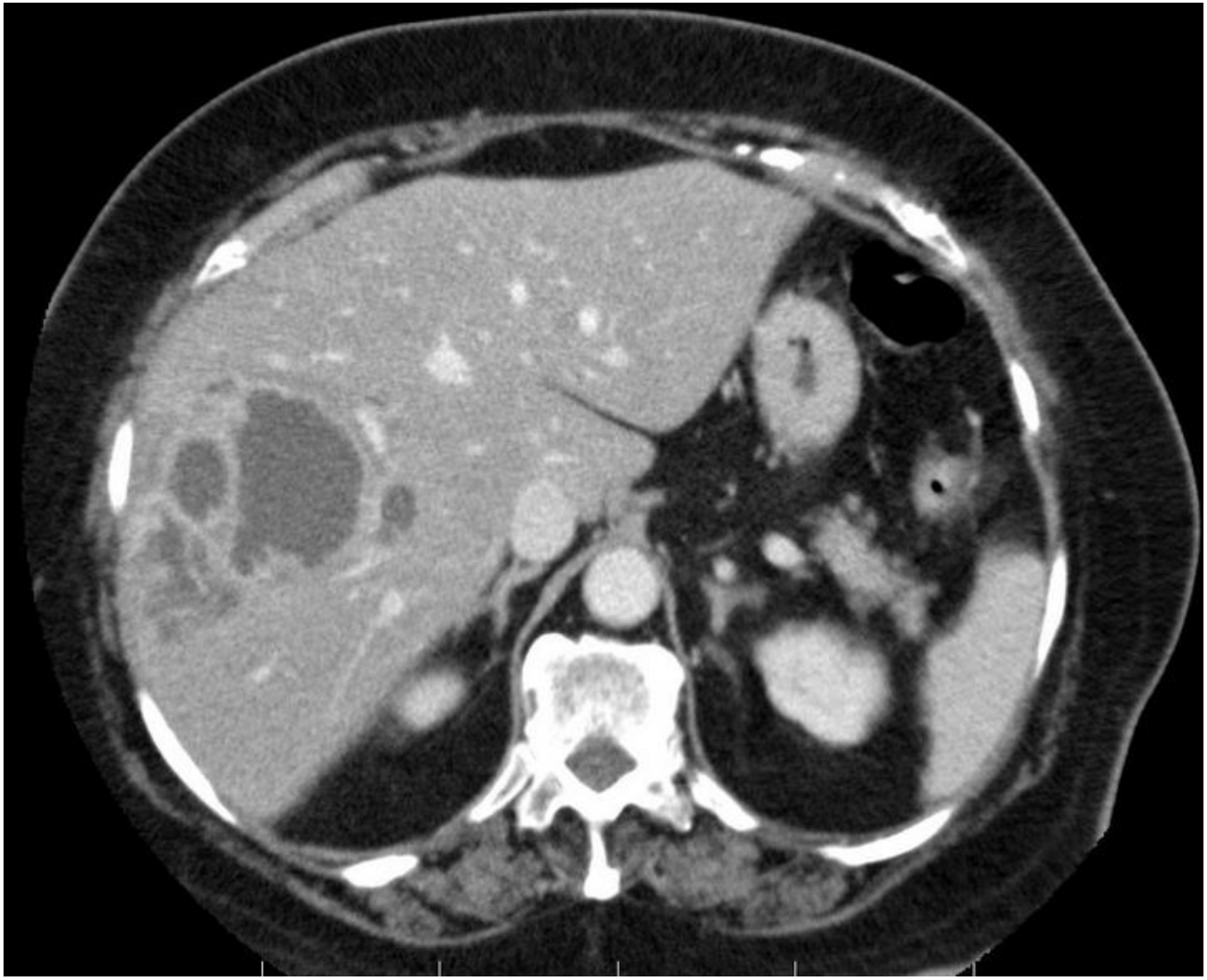
- Reflects the primary site of infection
- Usually polymicrobial:
  - Anaerobes: ***Bacteroides* spp.**, *Fusobacterium* spp., *Peptostreptococcus* spp., and *Actinomyces* spp.
  - Microaerophilic streptococci, ***S. milleri***, etc.
  - Gram-negative rods: ***K. pneumoniae*** (particularly K1 serotype)
  - *Candida* spp., in patients with leukemia following chemotherapy-induced neutropenia
  - Amoebic liver abscess, rare, complicates 3-9 % cases of amoebic colitis

Clinical manifestations

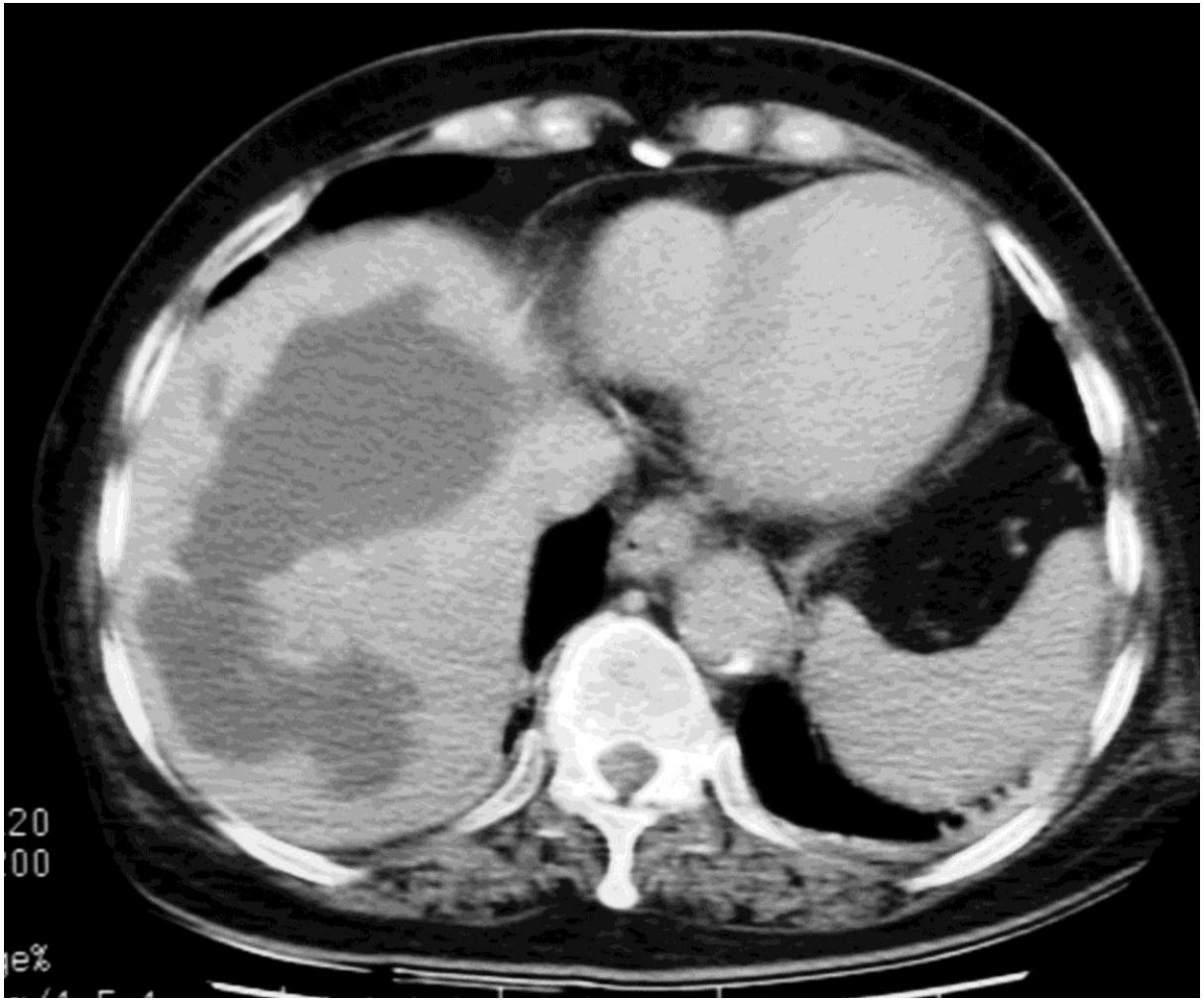
- **Fever** with or without chills; a common infectious cause of fever of undetermined origin
- Abdominal pain, often in the right upper quadrant, dull and constant
- Weight loss
- Physical examination:
  - Tenderness over the liver
  - Jaundice is rare
  - Abscess in upper regions of liver, decreased lung breath sounds because of atelectasis or pleural effusion

Diagnosis

- Leukocytosis, over 20,000/mm^3, with neutrophilia and increased immature forms
- ↑ serum alkaline phosphatase
- Blood cultures positive in up to half of patients
- Abdominal CT scan, the most sensitive test, shows a discrete area of low attenuation at the abscess site
- Ultrasound is somewhat less sensitive
- Found most commonly in the right lobe
- If a single large abscess is noted, amoeba serology should be ordered



Liver abscess



Liver abscess

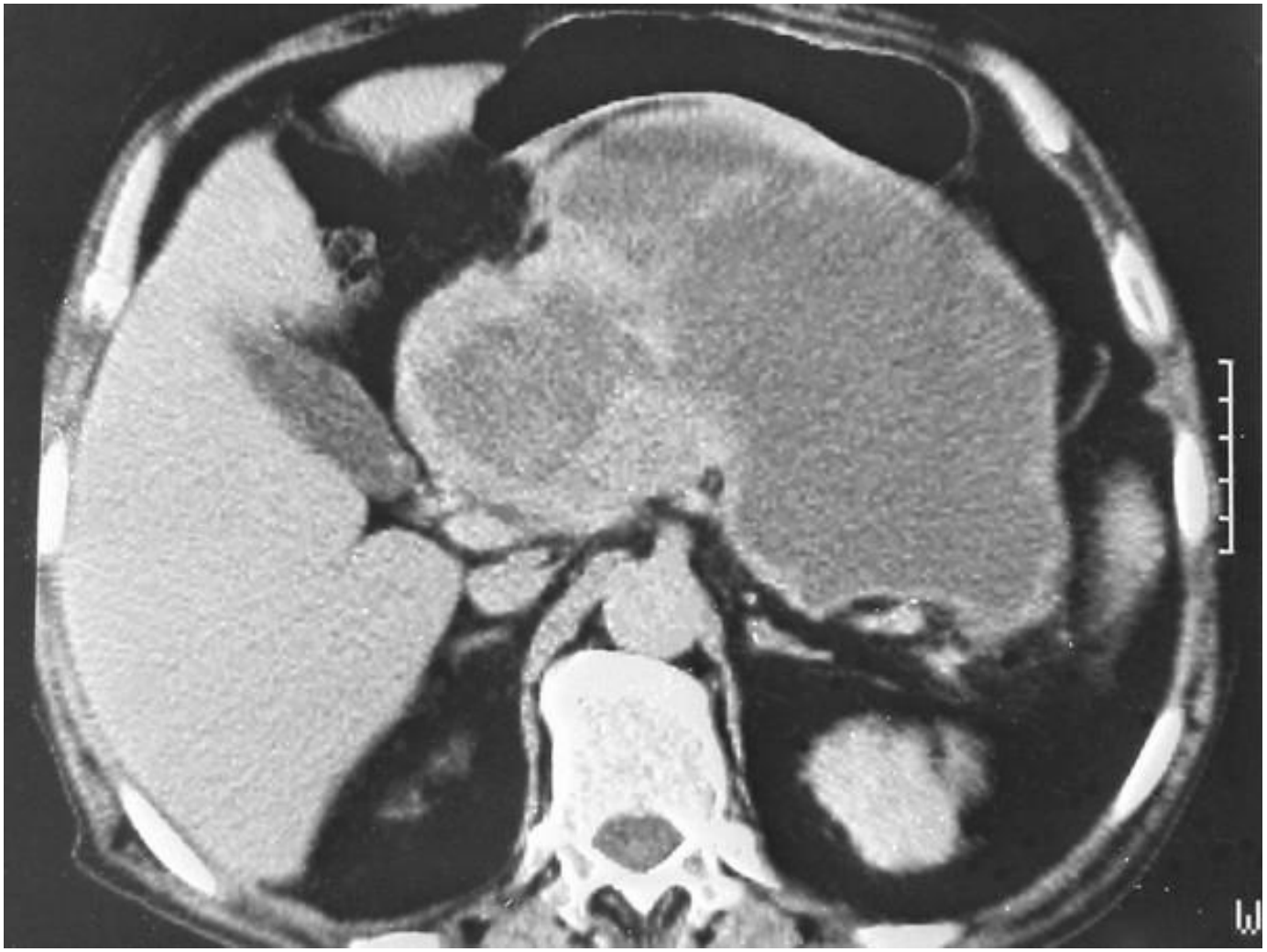
Treatment and outcome

- Ultrasound and CT can both be used to guide needle aspiration for culture and drainage
- A finding of brownish fluid **without a foul odor** suggests **amoebic** abscess
- Antibiotic therapy identical to that for secondary peritonitis
- Open surgical drainage:
  - Persistent fever after 2 weeks of treatment
  - Biliary obstruction
  - Multiloculated abscesses, other than *Echinococcus granulosus*
  - Highly viscous abscesses
- Nearly 100% of patients are now cured

Pancreatic abscess

Characteristics

- Pancreatitis → release of pancreatic enzymes → tissue necrosis that becomes infected by:
  - Reflux of contaminated bile
  - Hematogenous spread
- Usually polymicrobial
- Ultrasound and CT scan for diagnosis, culture and drainage
- The same antibiotic used for secondary peritonitis
- Open drainage and debridement are usually required

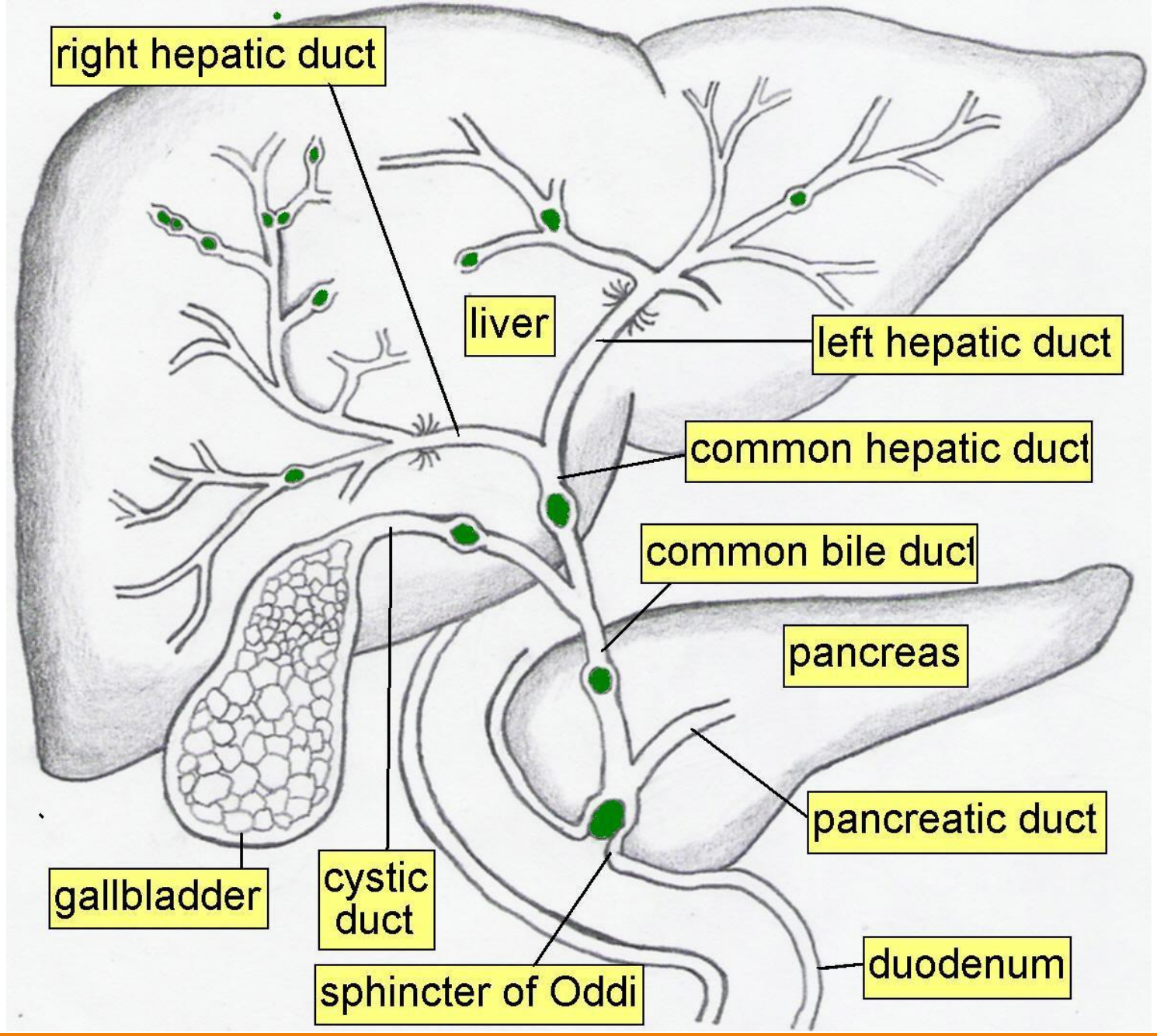


Pancreatic abscess after acute necrotizing pancreatitis

Cholecystitis and cholangitis

Pathogenesis

- Gallstones → biliary obstruction → ↑ pressure and distension of the gallbladder → blood flow compromise and interfere with lymphatic drainage → tissue necrosis and inflammation → cholecystitis → cholangitis
- Infection is not the primary cause of acute cholecystitis and cholangitis, obstruction prevents flushing of bacteria from the gallbladder → infection in more than half of all cases


right hepatic duct
liver
left hepatic duct
common hepatic duct
common bile duct
pancreas
pancreatic duct
gallbladder
cystic duct
sphincter of Oddi
duodenum

Microbiology

- Organisms of the bowel flora, similar to those in secondary peritonitis
- The most frequently cultured:
  - *E. coli*
  - *Klebsiella* spp.
  - Enterococci
  - Anaerobes

Clinical manifestations

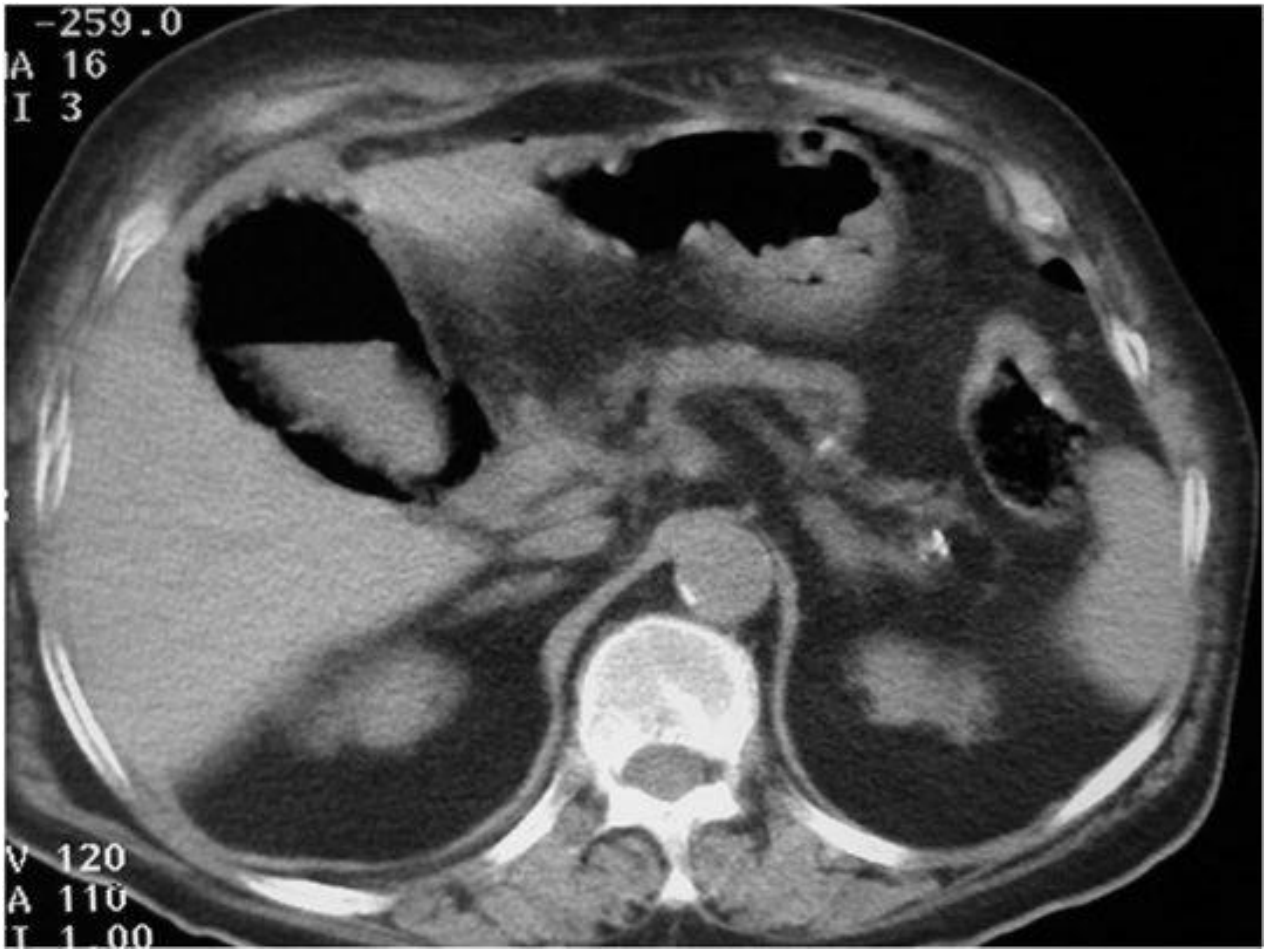
- Charcot triad (**fever**, **right upper quadrant pain**, and jaundice)
- Marked tenderness over the liver
- Hypotension suggests gram-negative etiology
- Elderly patients may not complain of pain
- Marked leukocytosis with left shift
- ↑ **alkaline phosphatase**, **gamma-glutamyl transpeptidase**, **bilirubin**, aminotransferases
- Blood cultures frequently positive

Diagnosis and treatment

- Ultrasonography, preferred diagnostic study for:
  - Gallstones
  - Dilatation of the gallbladder
  - Dilatation of the biliary ducts
- CT scan and magnetic resonance imaging
- Endoscopic retrograde cholangiopancreatography (ERCP)
  - Diagnosis
  - Dilatation of sphincter of Oddi, removal of stones, placement of stents, etc.
  - Under antibiotic coverage
  - Avoided in cases of cholangitis → high-level bacteremia

Treatment

- Imipenem, ampicillin + gentamicin, immediately
- Prompt surgical intervention for
  - Gangrenous gallbladder
  - Gallbladder perforation
- Acute cholecystitis: **decompression** of the gallbladder and stone removal with:
  - ERCP
  - Percutaneous drainage
  - Urgent if hypotension, mental confusion, etc.
- Outcome favorable in uncomplicated cases

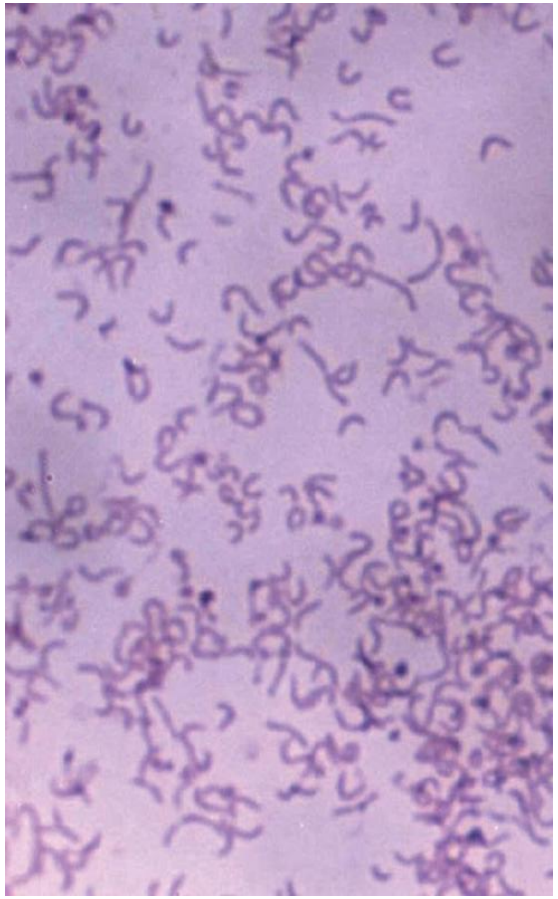


Gangrenous cholecystitis: markedly distended gallbladder with presence of air fluid level

Helicobacter pylori-associated peptic ulcer disease

Microbiology

- *Helicobacter pylori*
  - Small, curved
  - Microaerophilic gram-negative rod
  - Corkscrew-like motility
  - Closely related to *Campylobacter* spp.
- Survive and multiply within the gastric mucosa



Pathogenesis

- Adheres to gastric mucosa, with pedestals similar to those of enteropathogenic *E. coli*
- Have urease → ammonium ions that buffer the gastric acid
- *H. pylori* →↑ inflammatory cells in the lamina propria of gastric wall → cytokines → ↓ somatostatin levels →↑ **gastrin** levels → peptic ulcers
- *H. pylori* → chronic inflammation → **aplastic** changes in the gastric mucosa → gastric carcinomas

Clinical manifestations and diagnosis

- *H. pylori* peptic ulcer:
  - Burning pain several hours after meals, relieved by food
  - Belching, indigestion, and heartburn
- Testing for *H. pylori*, only in symptomatic patients:
  - Urease breath test, patient ingests ^{13}C- or ^{14}C-labeled urea, and their breath is analyzed for ^{13}C or ^{14}C
  - Stool antigen test
  - Measurement of IgG antibody levels by ELISA
  - Endoscopic biopsy:
    - Tested for urease (CLO test)
    - Cultured in selective media, antibiotic sensitivities in refractory cases
    - Silver, gram, or Giemsa stain, and immunofluorescence test

Treatment

- Lansoprazole or omeprazole + amoxicillin + clarithromycin
- Penicillin-allergic, metronidazole can be substituted for amoxicillin
- Sequential therapy: rabeprazole + amoxicillin → rabeprazole + clarithromycin + tinidazole
- Quadruple therapy, one “-prazol” + bismuth + two oral antibiotics (amoxicillin, clarithromycin, metronidazole, tetracycline, etc.)

Key messages

To remember…

Most intra-abdominal infections are produced by bacteria of the intestinal flora, have a similar pathogenesis and must be treated with antibiotics that cover the three main groups of bacteria: gram-positive cocci, gram-negative rods and anaerobes. Drainage is also frequently needed

Further reading

Used references

- Southwick F. Infectious disease. A clinical short course. 3rd Edition. New York: McGraw-Hill, 2014. Chapter 8.
- Sartelli M, Catena F, Ansaloni L et al. Complicated intra-abdominal infections worldwide: the definitive data of the CIAOW Study. World J Emerg Surg 2014; 9: 37. doi: 10.1186/1749-7922-9-37.
- Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's principles of internal medicine. 18th ed. New York: McGraw-Hill, 2012. Chapter 127.

Preparing the exam

- Southwick F. Infectious disease. A clinical short course. 3rd Edition. New York: McGraw-Hill, 2014. Chapter 8.
- These slides