

**MECHANISMS OF HUMAN DISEASE: LABORATORY SESSION
PATHOLOGY OF THE PANCREAS LAB**

Friday, January 13, 2012
8:30 – 10:00 am

Faculty Copy

GOAL:

1. Describe the basis morphologic and pathophysiologic changes in various diseases of the Pancreas and Gastrointestinal Tract.
2. Define (Describe) and correlate symptoms and signs of a disease with the structural changes in diseased organs.

OBJECTIVE:

1. Review the normal gross and histologic anatomy of the pancreas.
2. Describe the morphologic characteristics of adenocarcinoma of the pancreas.
3. Describe the morphologic characteristics of acute pancreatitis.
4. Describe the morphologic characteristics of chronic pancreatitis.
5. Describe the morphologic characteristics of appendicitis.
6. Describe morphologic characteristics of colonic diverticula

CASE 1

CHIEF COMPLAINT: “My wife says my eyes look kind of yellow.”

HISTORY: 60 year-old male, who has a past medical history significant for a 30 pack-year history of smoking, presents with a several month history of jaundice, gnawing epigastric pain that radiates to the back, and a 20 lb weight loss.

VITAL SIGNS: BP 140/90 HR 80 RR 18 T 98

PHYSICAL EXAMINATION: Alert and oriented, cachectic-appearing male with yellow sclerae. The abdomen is scaphoid with a palpable upper abdominal mass. No lymphadenopathy is noted.

LAB TESTS:

Alkaline phosphatase 140 U/L (reference range 20-70 U/L)

bilirubin total 4.3 mg/dl (0.0-0.3mg/dl)

AST 21 U/L (8-20 U/L)

ALT 19 U/L (8-20)

1. What is the clinical problem?

Epigastric pain and jaundice

2. What is your clinical differential diagnosis?

Obstructive jaundice secondary to inflammatory lesions (pancreatitis, cholecystitis), gallstones, cancer

3. Identify organ/describe pathology in the virtual microscopy slide.

Pancreas; sections of the pancreas show an adenocarcinoma with clusters of neoplastic glands intermixed with pancreatic ducts. There is extensive fibrosis associated with the neoplasm and the fibrosis and tumor replaces most of the normal pancreas. There are several pancreatic lobules distorted by inflammation and fibrosis near the edge of the section on most slides.

4. What is your diagnosis?

Pancreatic carcinoma

5. Explain the jaundice in this patient.

The neoplasm, in the head of the pancreas, compressed the common bile duct causing an extrahepatic obstruction.

6. Name two genetic mutations commonly described in this disease.

K-RAS gene is the most frequently altered oncogene in pancreatic cancer

- Point mutations occur at codon 12 in 90% of pancreatic carcinomas
- K-*ras* mutation is the early event in carcinogenesis

p16 gene is the most frequently inactivated tumor suppressor gene in pancreatic cancer

- Inactivated in 95% of cases

CASE 2

CHIEF COMPLAINT: “My stomach and back really hurt.”

HISTORY: 47 year-old male presents with a several day history of severe epigastric pain after a “bender with the guys”. The pain radiates to the back and chest. He drinks alcohol daily.

VITAL SIGNS: BP 110/60 HR 110 RR 18 T 99

PHYSICAL EXAMINATION: Thin, malnourished and anxious appearing male who is almost “doubled over” in pain. Sclera are anicteric. There is epigastric tenderness to palpation. No palpable abdominal masses. Stool is brown and hemoccult negative.

1. What is the clinical problem?

Abdominal pain

2. Develop a differential diagnosis.

**Peptic ulcer
Gastritis
Pancreatitis
Cholecystitis**

3. What lab test(s) would be helpful?

**CBC
Amylase, lipase
Alkalkine phosphatase, bilirubin
Liver enzymes**

**WBC 16,000/mm³
Hgb 13gm/dl
serum amylase 450 IU/L (reference range 25-125 IU/L)
serum lipase 130 IU/L (7-58 IU/L)
LDH 350 IU/L (45-90 IU/L)
Alkaline phosphatase 32 U/L (reference range 20-70 U/L)
bilirubin total 0.2 mg/dl (0.0-0.3mg/dl)**

4. Identify organ/describe pathologic changes in the virtual microscopy slide.

Pancreas; the section of pancreas reveals extensive necrosis and acute inflammation. Large areas of the pancreas are necrotic. Neutrophils infiltrate the edge of these areas and extend into the adjacent lobules and fat.

5. What is your diagnosis?

Acute pancreatitis

6. Discuss the lab tests in the context of the pathologic findings.

Damage to pancreatic acinar cells by inflammation causes release of amylase and lipase (which are absorbed into the blood stream)

Serum LDH (isoenzyme 4) is present in the pancreas and is released with pancreatic inflammation/necrosis. Values >350 are a poor prognostic factor (one of the Ranson criteria)

Leukocytosis occurs frequently in patients with acute pancreatitis (marker of inflammation)

7. What are potential complications of this process?

Infection, abscess/pseudocyst, GI obstruction, pancreatic rupture/hemorrhage, obstructive jaundice, pulmonary complications (ARDS) in severely ill patients, acute renal failure with severe intravascular volume depletion.

CASE 3

CHIEF COMPLAINT:

Abdominal pain

HISTORY:

A 53 year-old chronic alcoholic with 20 pack-year history of smoking has been hospitalized several times in the past for acute pancreatitis. He has a dull abdominal pain much of the time and steatorrhea.

PHYSICAL EXAMINATION:

Alert and oriented male who appears older than his stated 53 years. His abdomen is soft with no palpable masses or organomegaly. He has mild epigastric tenderness.

1. Identify organ/describe pathologic changes in the slide.

Pancreas; sections show distortion of the normal architecture. Extensive fibrosis replaces the acini. Some ducts show dilatation and calcium precipitates. Many slides show compression and distortion of small ducts and ductules by fibrous tissue.

2. What is your diagnosis?

Chronic pancreatitis

3. What are potential complications?

Chronic pain,

Exocrine insufficiency (weight loss due to malabsorption, steatorrhea)

Endocrine insufficiency (destruction of islet cells: glucose intolerance, diabetes –late in the disease)

CASE 4

CHIEF COMPLAINT:

None

HISTORY:

An asymptomatic 60 year old male patient presents for a routine screening physical. A colonoscopy is done.

LAB TESTS:

Hgb 14.0 g/dL Hct 42%

1. Identify the organ/describe the pathologic changes in the slide.

Colon; sections show a diverticulum. The mucosa and submucosa herniate through the muscularis propria.

2. What is your diagnosis?

Diverticulosis; blind pouch leading off the alimentary tract; congenital diverticula have all three layers of the bowel wall; others are acquired and lack or have an attenuated muscularis propria. In Western world, 50% adults >60 yrs have colonic diverticulae. Possible etiologic factors: focal weakness in colonic wall and increased luminal pressure.

3. What are major complications of this process?

Inflammation (with or without perforation or obstruction - diverticulitis), chronic blood loss/rarely acute hemorrhage, abdominal discomfort/constipation/diarrhea

CASE 5

CHIEF COMPLAINT:

“My stomach really hurts.”

HISTORY:

A 13 year-old girl presents to her physician with fever and right lower quadrant abdominal pain. She had a preceding episode of nausea and vomiting.

VITAL SIGNS:

BP 125/80 HR 90 RR 18 T 100

PHYSICAL EXAMINATION:

The patient is a healthy, anxious appearing girl who has abdominal rebound tenderness to palpation .

1. Identify the organ/ describe the pathologic findings in the slide.

Appendix; sections show acute and chronic inflammation. The lumen is filled with neutrophils and the mucosa is ulcerated. The submucosa, muscularis propria and serosa are infiltrated with inflammatory cells, including neutrophils, eosinophils and monocytes. The serosa is edematous and covered by fibrin and neutrophils. Note the perivascular infiltrate and margination of neutrophils.

2. What is your diagnosis?

Acute appendicitis

3. Correlate the clinical findings with the pathology.

Inflammation of visceral and parietal peritoneum stimulates nerve endings which caused localized pain, and tenderness to palpation (rebound tenderness). Appendiceal inflammation is associated with obstruction in 50 to 80% of cases (due to fecolith, gallstone, tumor or ball of worms - Oxyuriasis vermicularis).

4. What are potential complications of this disease process?

Perforation most serious, pyelophlebitis with thrombosis of the portal venous drainage, liver abscess, and bacteremia. Surgeons have a false-positive diagnosis rate of 20 to 25% - risks associated with exploratory laparotomy are far outweighed by the risks of perforation.