SMALL AND LARGE INTESTINE

IDIOPATHIC INFLAMMATORY BOWEL DISEASE (IBD)

-The two disorders known as inflammatory bowel disease (IBD) are Crohn's disease (CD) and ulcerative colitis (UC).

-These diseases have distinctly different clinical and pathological features.

- Both CD and UC are chronic, inflammatory disorders of obscure origin.

- **CD** is an autoimmune disease that may affect any portion of the gastrointestinal tract from mouth to anus, but most often involves the distal small intestine and colon.

- **UC** is a chronic inflammatory disease limited to the rectum and colon.

- Both exhibit extra-intestinal inflammatory manifestations.

Etiology and Pathogenesis

-In the normal GIT, the mucosal immune system is always ready to respond against ingested pathogens but is unresponsive to normal intestinal microflora .

-The exact cause (s) is still not established, hence the designation idiopathic .

-It is postulated that IBD result from exaggerated local immune responses to microflora in the gut , in genetically susceptible individuals .

Thus, the pathogenesis of IBD involves

1. Failure of immune system
2. Genetic susceptibility
3. Altered composition of the gut micro flora .

Crohn Disease

Pathological features

When fully developed, Crohn disease is characterized pathologically by

1. Sharply segmental (skip lesions) and transmural involvement of the bowel by an inflammatory process with mucosal damage.

2. The presence of

- Small noncaseating granulomas
- Deep fissures that may eventuate in the formation of **fistulae**

Clinical Features

The disease usually begins with intermittent attacks of diarrhea, fever, and abdominal pain, spaced by asymptomatic periods lasting for weeks to many months . In those with colonic involvement, fecal blood loss may lead to anemia .

Extra intestinal manifestations of this disease include

1. Arthritis & finger clubbing
2. Red nodules of the skin
3. Primary sclerosing cholangitis .
4. Renal disorders
5. Systemic amyloidosis
6. increased incidence of cancer of GIT in patients with long standing progressive CD .

ULCERATIVE COLITIS

- Ulcerative colitis is a chronic ulcero-inflammatory disease limited to the colon and rectum.

- its begins in the rectum and extends proximally to colon.

-Affecting only the mucosa and submucosa .

- Well-formed granulomas are absent.

- However, like CD, UC is a systemic disorder associated in some patients with arthritis, uveitis, hepatic sclerosing cholangitis , and skin lesions .

- The onset of disease peaks between ages 20 and 25 years.

Microscopic features

- The basic mucosal alterations in UC are similar to those of colonic CD, with inflammation, mucosal damage, and ulceration.

- There is diffuse lesion , chronic inflammatory infiltrate in the lamina Propria .

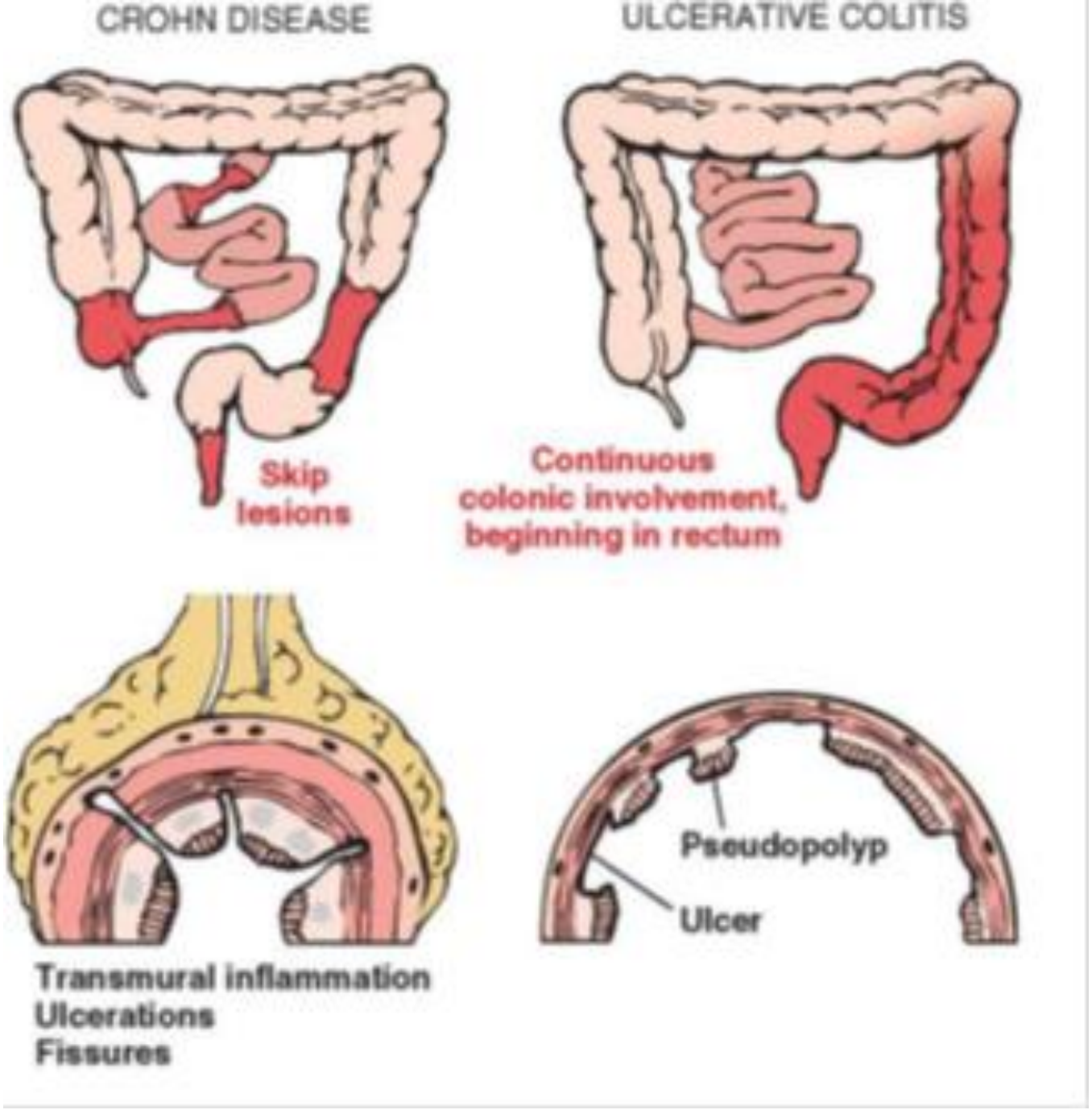
- Neutrophilic infiltration of the epithelial layer may produce abscesses which are not specific for UC and may be observed in CD .

- Unlike CD, there are no granulomas .

- Ulcerations of the mucosa extending to the submucosa .

- Isolated islands of mucosa bulge into the lumen to create small elevations termed **pseudopolyps .**

- Features of healing in disease include submucosal fibrosis; mucosal architectural distortion and atrophy .


CROHN DISEASE
ULCERATIVE COLITIS
Skip lesions
Continuous colonic involvement, beginning in rectum
Transmural inflammation
Ulcerations
Fissures
Pseudopolyp
Ulcer

Tumors of the Colon and Rectum

benign neoplastic lesions of the colo-rectum are collectively known as **polyps in general** , intestinal polyps can be classified as nonneoplastic or neoplastic. The most common neoplastic polyp is **the adenoma**, which has the potential to progress to cancer.

Nonneoplastic colonic polyps can be further classified as

inflammatory, hamartomatous , or hyperplastic. .

Epithelial polyps (adenoma)

that arise as the result of epithelial proliferation and dysplasia are termed adenomatous polyps (adenomas). They are precursors of carcinoma .

Hyperplastic Polyps

These are the most common polyps of the colon and rectum. They are small (usually <5 mm in diameter) and appear as smooth protrusions of the mucosa .

They are often multiple and consists of well-formed glands and crypts lined by non-neoplastic epithelial cells.

Adenomas (Adenomatous polyps)

Adenomas are intraepithelial neoplasms that range from small, often pedunculated lesions to large neoplasms that are usually sessile .

The prevalence of colonic adenomas increases progressively with age . Males and females are affected equally .

All adenomas by definition arise as the result of dysplastic epithelial proliferation. The dysplasia ranges from low-grade to high-grade.

There is strong evidence that adenomas are precursors for invasive **colorectal adenocarcinomas**.

COLORECTAL CARCINOMA

- Most carcinomas arise from preexisting **adenomas** .

- A great majority (98%) of all cancers in the large intestine are **adenocarcinomas**.

- The peak incidence for colorectal cancer is 60 to 70 years of age .

- Both genetic and environmental influences contribute to the development of colorectal cancers.

- When colorectal cancer is found in a young person, preexisting ulcerative colitis or one of the polyposis syndromes must be suspected .

-Tumors in the proximal colon tend to grow as polypoid , exophytic masses that extend along the wall of the cecum and ascending colon .

- Obstruction is uncommon .

- All colon carcinomas are microscopically similar. Almost all are adenocarcinomas that range from well-differentiated to undifferentiated, anaplastic masses.

- Many tumors produce mucin , which is secreted into the gland or into the interstitium of the gut wall. Because these secretions dissect through the gut wall, they facilitate extension of the cancer and worsen the prognosis.

- Cancers of the anal zone are predominantly squamous cell in origin .

Appendix

ACUTE APPENDICITIS is inflammation of appendix .

Occur in the second and third decades .

Males are affected more than females.

Causes

Obstruction in the form of a fecolith and, less commonly, a gallstone, tumor, or ball of worms (Oxyuris vermicularis).

some cases have no demonstrable lumenal obstruction, and the pathogenesis of this inflammation remains unknown .

MORPHOLOGY

At the earliest stages, only a neutrophilic exudate may be found throughout the mucosa. Submucosa , and muscularis .

Histological appearance

there is abscess formation within the wall, ulcerations and foci of necrosis in the mucosa . This state called **acute suppurative appendicitis** .

Appendiceal compromise leads to large areas of hemorrhagic green ulceration of the mucosa, and green-black gangrenous necrosis through the wall extending to the serosa, creating **acute gangrenous appendicitis** .

The histologic criterion for the diagnosis of acute appendicitis is neutrophilic infiltration of the muscularis propria .

TUMORS OF THE APPENDIX

Carcinoids are the most common form of neoplasia in the appendix .

Mucocele of the appendix

Mucocele refers to dilation of the lumen of the appendix by mucinous secretion .

Mucinous neoplasms Mucinous neoplasms range from the benign **mucinous cystadenoma** , to malignant **mucinous cystadenocarcinoma** , which invades the wall, to a form of disseminated intraperitoneal cancer called **pseudomyxoma peritonei .**

PANCREAS

- ACUTE PANCREAIITIS Inflammation of the pancreas, almost always associated with cell injury of acini

Acute pancreatitis is characterized by the acute abdominal pain resulting from enzymatic necrosis and inflammation of the pancreas .

there is an elevation of pancreatic enzymes in blood and urine .

The release of pancreatic lipases causes fat necrosis in and about the pancreas .

Etiology.

A variety of predisposing conditions for acute pancreatitis .

1) gallstones and alcoholism, which together are responsible for approximately 80% of the cases.

2) The remaining specific causes are unusual, and 10% to 20% of cases of acute pancreatitis are without apparent predisposing influences .

- CHRONIC PANCREATITIS is characterized by repeated bouts of mild to moderate pancreatic inflammation, with continued loss of pancreatic parenchyma and replacement by fibrous tissue.

Etiology.

hypercalcemia and hyperlipoproteinemia predispose to chronic pancreatitis. Almost

half of the patients have no apparent predisposing influences and are therefore said to have **idiopathic pancreatitis .**

Pathogenesis Hyper secretion of protein from acinar cells in the absence or decreased fluid secretion permits the precipitation of proteins that admixed with cellular debris , form ductal plugs. This plugs are observed in all forms of chronic pancreatitis , but in alcoholic patients, these plugs may enlarge to form stones containing calcium carbonate precipitates .

The liver

Hepatitis :-mean any inflammatory lesion of the liver . This term is not used for local lesions such as an abscess but only when there is diffuse inflammatory involvement of the liver .

Etiology

There are many etiological factors that causing hepatitis such as alcoholic hepatitis, drug induce hepatitis and viral hepatitis .

Viral hepatitis:- mean infection of the hepatocytes by virus that produces necrosis and inflammation of the liver and presented with jaundice .

It caused mainly by hepatotropic viruses (which are hepatitis virus A,B,C,D,E).

Hepatitis viruses C &B are the most common cause of chronic hepatitis , liver cirrhosis and hepatocellular carcinoma .

1-Hepatitis A Virus (HAV)

Acute viral hepatitis A is a benign, self-limited disease with incubation period of 4 weeks. HAV does not cause chronic hepatitis or a carrier state .

In children, the disease tends to be mild or asymptomatic .

HAV spreads by ingestion of contaminated water and foods .

The viremia is short-lived, thus, blood-borne transmission occurs rarely; therefore, donated blood is not screened for this virus .

HAV is a small, RNA virus. It reaches the liver from the intestinal tract after ingestion, replicates in hepatocyte, and is shed in the bile and feces .

Detection of anti-HAV IgM antibody is the best diagnostic marker for the disease .

2-Hepatitis B Virus (HBV) this can produce

1. Acute viral hepatitis B with recovery and clearance of the virus

2. Chronic viral hepatitis B

-Is an important precursor of hepatocellular carcinoma.

-HBVremains in blood along the incubation period (4-26weeks).

-It is also present in all body fluids, with the exception of stool .

-The main mode of transmission of virus is vertical transmission from mother to child during birth .

- After exposure to the virus, there is a long incubation period (average 16 weeks)

HBsAg appears before the onset of symptoms and then declines in 3 to 6 months .

Anti-HBs persist for life, conferring protection; this is the basis for current vaccination .

Hepatitis C Virus (HCV) is another major cause of liver disease .

-The major route of transmission is through blood inoculation, with low rates of sexual and vertical transmissions.

-HCV infection has a much higher rate (than HBV) of progression to chronic hepatitis and eventual cirrhosis.

-It is a single-stranded RNA virus .

-Based on the genetic sequence, HCV is subclassified into six genotypes. An infected person may carry many HCV variants. This variability seriously hinders development of HCV vaccine.

-The incubation period for hepatitis C is 6 to 12 weeks.

-The clinical course of acute viral hepatitis C is usually asymptomatic .

-Strong immune responses involving CD4+ and CD8+ cells .

-Persistent infection is the hallmark of HCV; in 80% of such cases it complicates subclinical acute infection (infection without sing s and symptoms) .

-Cirrhosis develops in 20% of patients .

Pathological features of viral hepatitis

Acute viral hepatitis

1-The normal radial array of the lobules is lost.

2- hepatocytes are swollen with wispy cytoplasm.

3-Hepatocytes necrosis

4-Inflammation is prominent feature of acute hepatitis.

5-The portal tracts are infiltrated predominantly by lymphocytes.

6-Hypertrophy& hyperplasia of Kuppfer cells

7-Cholestasis may be present

Chronic hepatitis

1-Hepatocyte necrosis may occur in all forms of chronic hepatitis.

2-The inflammatory component consists mainly of lymphocytes, macrophages, and occasional plasma cells.

3- periportal necrosis (interface hepatitis)

4-The hallmark of serious liver damage is the deposition of fibrous tissue. periportal fibrosis occurs then followed by bridging fibrosis that links fibrous septa between lobules.

5-Continued loss of hepatocytes with fibrosis results in cirrhosis .

ALCOHOLIC LIVER DISEASE

Chronic heavy drinkers are predisposed to 3 distinctive forms of alcoholic liver disease; these may overlap.

1. Fatty change or Hepatic steatosis (almost all heavy drinkers 90-100%)
2. Alcoholic hepatitis (10-35%)
3. Cirrhosis (8-20%)

Alcoholic Fatty Liver :- accumulation of fat begin in centrilobular hepatocytes .the lipid droplets range from small to large vesicles ,the largest filling the cell and displace the nucleus .

Lipid accumulation spread from central vein to midlobe and then to periportal region .

Within hepatocyte , ethanol

1. increases fatty acids synthesis
2. decreases mitochondrial oxidation of fatty acids
3. increases the production of the triglycerides
4. impairs the release of lipoproteins .

Morphological Features:-

Grossly the liver become large (4-6 weight or more) ,soft ,yellow ,and greasy.

Microscopically: fat accumulation as minute droplets in the cytoplasm of a hepatocytes these droplets coalesced lead to distention of the entire cytoplasm of these cells .

The hepatocytes become just like adipocyte with distended clear cytoplasm and the nucleus is displaced to the periphery and become flattened

Alcoholic Hepatitis:- is superimposed on fatty liver & appear as an acute necrotizing lesion characterized by

1) ballooning and necrosis of hepatocytes predominantly in the centrilobular region

2) presence of hyaline cytoplasmic inclusions within damaged hepatocyte called **Mallory-denk bodies**

3-neutrophilic infiltration around the damaged hepatocytes that containing Mallory-denk bodies

4) If alcoholic hepatitis is continued, fibrosis & scaring in centrilobular region and then spread outward. And finally the liver architecture is distorted and **liver cirrhosis** is established.

Liver Cirrhosis

The end stage of chronic liver disease is cirrhosis.

Cirrhosis is a condition in which the entire liver parenchyma exchanged into a large number of nodules separated from one an other by irregular branching & anastomosing sheets of fibrous tissue.

Classification of liver cirrhosis:

Aetiological classification:-

* Acquired

1. alcoholic
2. post viral
3. Biliary cirrhosis

* Inherited

1. haemochromatosis
2. wilsons' disease
3. alpha-1 antitrypsin deficiency

Morphological classification

1- micronodular cirrhosis in which the nodules are approximately up to 3mm in diameter.

2. macronodular cirrhosis in which the nodules are of variable size & may be ranged up to 1 cm diameter.

3. Mixed type in which both small & large nodules are present. This pattern is most frequently seen in end stage cirrhosis.

Pathogenesis:- cirrhosis results from long continuous loss of liver cells, with a persistent inflammatory reaction accompanied by fibrosis & compensatory hyperplasia .

complications of cirrhosis:-

1. Hepatic failure
2. Portal hypertension
3. Liver cell carcinoma which arise in 10-15% of all cirrhotic patients.

TUMORS OF LIVER

Benign tumors:-

1. cavernous hemangioma:- it is a well demarcated lesion consist of endothelial cells-lined vascular channels & intervening stroma.

They appear as discrete red-blue soft nodule less than 2cm in diameter and commonly it located just beneath the capsule.

2. adenoma:- occurs in young females who are on oral contraceptive drug. Histologically composed of sheet or cords of cells resemble normal hepatocytes. When the adenoma presented as intrahepatic mass it may be mistaken with hepatocellular carcinoma. Subcapsular adenoma are at risk of rupture specially during pregnancy (due to estrogenic stimulation) and may lead to life threatening intraabdominal hemorrhage.

Malignant:-

1. Hepatoblastoma:- aggressive hepatocellular tumor of childhood & it usually fatal.

2. Hepatocellular carcinoma:-malignant tumor of hepatocytes that's closely linked to HBV infection, HCV, alcoholic liver cirrhosis & haemochromatosis. In 85% of patients there is raising in serum level of α-fetoprotiens. Hepatocellular carcinoma may appear grossly as:-

i) Unifocal usually massive tumor.

ii) Multifocal (malignancy made of widely distributed nodules of variable size

iii)Diffusely infiltrative(cancer may involve the entire liver).

Microscopically; either well differentiated to anaplastic, but

trabecular, acinar , pseudoglandular patterns may present.

3. cholangiocarcinoma:-it is of adenocarcinoma type typically with abundant fibrous stroma (desmoplastic)that why the tumor grossly appear firm and gritty in consistency.