**Lecture 19 General pathology Dr. Ali H. Murad**

***CIRRHOSIS***

Cirrhosis is the end-stage of chronic liver disease & is defined by three characteristics:

**1-Bridging fibrous septae** in the form of delicate or broad bands of fibrosis that link portal tracts with one another and portal tracts with centrilobular veins.

1. **Parenchymal nodules** containing regenerating hepatocytes encircled by fibrosis, with diameters varying from very small micronodules to large macronodules.

1. ***Disruption of the architecture of the entire liver***

***Classification of cirrhosis***

The only satisfactory classification of cirrhosis is based on the underlying etiology.

**The established causes of cirrhosis**:-

1. Alcoholic liver disease (70% in Western countries)
2. Viral hepatitis (a very common cause in our country)
3. Biliary diseases
4. Primary hemochromatosis
5. Wilson disease
6. α1-Antitrypsin deficiency
7. Cryptogenic cirrhosis

**Pathogenesis of cirrhosis**

The central pathogenetic processes in cirrhosis are progressive fibrosis and reorganization of the vascular microarchitecture of the liver. In cirrhosis, types I and III collagen are deposited in the lobule, creating delicate or broad septal tracts. New vascular channels in the septae connect the vascular structures in the portal region (hepatic arteries and portal veins) and terminal hepatic veins .

***In cirrhosis death is usually due to one or more of the following***

1. Progressive liver failure
2. Portal hypertension related complications
3. The development of hepatocellular carcinoma

***TUMORS AND HEPATIC NODULES***

The most common hepatic neoplasms are metastatic carcinomas, with colon, lung, and breast heading the list as sites of the primary tumor. Solitary or multiple benign hepatocellular nodules may develop in the liver.

These include

1. Focal nodular hyperplasia
2. Macroregenerative nodules
3. Dysplastic nodules

**Benign Tumors**

**Cavernous hemangiomas** are most common benign lesions of the liver are.

These well-circumscribed lesions consist of vascular channels and intervening stroma. They appear as discrete red-blue, soft nodules, usually less than 2 cm in diameter, often directly beneath the capsule.

**Hepatic (liver cell) Adenoma** usually occurs in women of childbearing age who have used oral contraceptive steroids, and it may regress on discontinuance of hormone use. The tumor is yellow-tan, well demarcated nodules, up to 30 cm in diameter and is often located beneath the capsule . It is composed of sheets and cords of cells that may resemble normal hepatocytes with prominent arteries and veins.

**Hepatocellular Carcinomas (HCC)**

The incidence (generally 5% of all cancers) varies widely in different areas of the world.

More than 85% of cases occur in countries with high rates of chronic HBV infection e.g.Asian and African countries

***Pathogenesis***

Three major etiologic associations have been established:

1. Infection with HBV or HCV
2. Alcoholic cirrhosis
3. Aflatoxin exposure, substances made by a fungus that contaminates peanuts, wheat, soybeans, ground nuts, corn, and rice is a major risk factor for liver cancer

***Gross features***

There are three gross forms of HCC

1. *Unifocal,* usually a massive tumor
2. *Multifocal* i.e. made of variably sized nodules
3. *Diffusely infiltrative* i.e. permeating widely and sometimes involving the entire liver

***Microscopic features***

 1-HCCs range from well-differentiated to poorly differentiated lesions. In well differentiated HCC the neoplastic hepatocytes are arranged in broad trabeculae, which are separated by sinusoids.

 2-Central necrosis in the broad trabeculae may produce a pseudoglandular pattern.

 3-Poorly differentiated tumors are composed of large multinucleate anaplastic tumor giant cells.

 4- In the better differentiated variants, globules of bile may be found within the cytoplasm of cells and in pseudocanaliculi between cells.

 5- Mallory bodies(rregular, ropelike eosinophilic intracytoplasmic strings that represent aggregates of cytokeratin intermediate filaments) may be found within the cytoplasm of the neoplastic cells.

 6-HCC displays scant connective tissue stroma (that is why it is soft in consistency**)**

**Upon completion *The dominant primary diseases of the liver are***

1. *Viral hepatitis*
2. *Alcoholic liver disease (in the Western world; rare in Iraq)*
3. *Hepatocellular carcinoma*

***GALLBLADDER DISEASES***

**Cholelithiasis (Gallstones)**

Gallstones trouble up to 20% of adult populations and are mainly of two types

1. *Cholesterol stones* composed of crystalline cholesterol monohydrate

(80%)

1. *Pigment stones* composed predominantly of bilirubin calcium salts (20%)

***Pathogenesis and Risk Factors***

The majority of individuals with gallstones (80%) have no identifying risk factors

 **Contributory risk factors include**

*1. Age and gender:* the incidence of gall stones increases with age in that only 5% of the population younger than age 40 but 25% of those older than

80 years develop stones. The prevalence in women is about twice as high as in men.

1. *Ethnic and geographic*: gallstones are more prevalent in Western industrialized societies and uncommon in developing ones.
2. *Heredity:* family history imparts increased risk.
3. *Environment:* estrogenic influences, including oral contraceptives and pregnancy***,*** increase hepatic cholesterol uptake and synthesis, leading to excess biliary secretion of cholesterol.
4. *Obesity*, *rapid weight loss*.

**Cholecystitis**

This may be acute, chronic, or acute superimposed on chronic, and almost always occurs in association with gallstones. Its epidemiologic distribution closely parallels that of gall stones.

**Chronic Cholecystitis**

may be the sequel to repeated bouts of acute cholecystitis, but in most instances it develops de novo, ***it is almost always associatedwith gallstones*** but these do not seem to have a direct role in the initiation of inflammation.

***Pathological feature***

1-The changes are extremely variable and sometimes minimal.

2-The mere presence of stones within the gallbladder, even in the absence of acute inflammation, is often taken as sufficient justification for the diagnosis.

3-The gallbladder may be contracted, of normal size, or enlarged.

4- The submucosa and subserosa are often thickened from fibrosis.

**TUMORS**

**Carcinoma of the Gallbladder** is the most frequent malignant tumor of the biliary tract.

***Gross features***

 The cancer is either *exophytic (fungating) or infiltrative* growth.

***Microscopic features***

*Well- to poorly-differentiated infiltrative adenocarcinomas* that is sometimes *papillary*.

By the time gallbladder cancers are discovered, *most have invaded the liver directly* and many have extended to the cystic duct and adjacent bile ducts and lymph nodes .