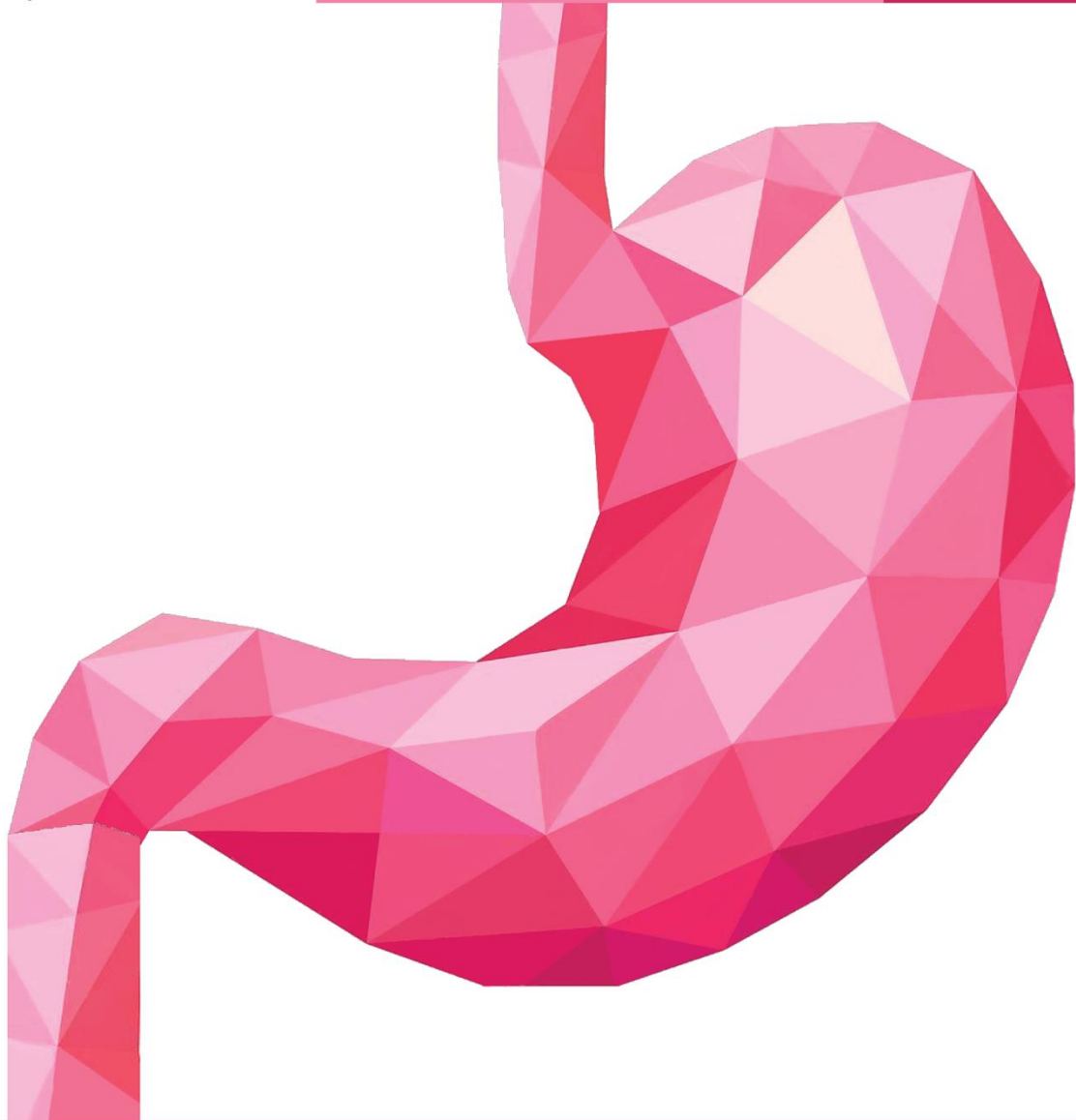




GIS

14

PATHOLOGY



Done by: Leen Hajeer

Scientific Correction: Anas Zayad

Gramatical Correction: Dena Kofahi

Doctor: Dr. Maha Shomaf

In this sheet we are going to discuss peliosis hepatis, liver nodules and liver tumors. Hope you enjoy 😊

The red colored notes are added for further clarification

◆ Peliosis Hepatis

It is a vascular condition characterized by **sinusoidal dilatation** throughout the liver.

- Causes:
 - 1) Anabolic steroids: **Synthetic androgenic hormones that are used to grow muscles and for body building. Overdose of these drugs may lead to peliosis hepatis.**
 - 2) Oral contraceptives.
 - 3) Danazol: **A form of synthetic anabolic steroids.**
- Pathogenesis is unknown.
- Asymptomatic disease, however, may cause complications of **intraabdominal hemorrhage** and **liver failure**.
- It is reversible once the underlying cause is stopped.

Liver Tumors and Nodules

Liver tumors can be benign or malignant.

◆ Benign Liver Tumors:

1) Cavernous Hemangioma

- The most common benign liver tumor.
- **It's a vascular liver tumor characterized by a collection of dilated blood vessels forming a lesion.**
- Usually small in size, less than 2 cm in diameter.
- Subcapsular in location.

2) Hepatocellular Adenoma (HA)

- Usually occurs in young females with history of oral contraceptive intake.
 - It may rupture, especially during pregnancy when it can enlarge rapidly, causing severe intraperitoneal hemorrhage.
 - Rarely may contain hepatocellular carcinoma (HCC).
 - May be misdiagnosed as HCC.
- ✂ **Estrogen stimulates the development of hepatocellular adenoma, thus HA is associated with oral contraceptive intake and pregnancy.**

◆ Liver Nodules:

1) Focal Nodular Hyperplasia (FNH)

- Well demarcated hyperplastic hepatocytes with a central scar, forming localized non-diffused nodules.
- Present in **non-cirrhotic liver**.
- Not a neoplasm but present nodular regeneration.
- Occurs due to local vascular injury.
- Most common in females in reproductive age.
- No risk of malignancy.
- 20% of cases have cavernous hemangioma.

2) Macroregenerative Nodules

- Present in **cirrhotic liver**, but they are larger than cirrhotic nodules.
- Reticulin background of the parenchyma is intact.
- No atypical features.
- No malignant potential.

3) Dysplastic Nodules

- Present in **cirrhotic liver**.
- Larger than 1mm in diameter.
- Have atypical features, pleomorphism and crowding, with high proliferative activity.
- Can be high or low grade dysplasia.
- They are considered **precancerous** since they are **monoclonal** in nature and present with some **gene mutations** that are seen in malignant tumors.
- They are of two types: **small-cell dysplastic nodules** and **large-cell dysplastic nodules**.

◆ Malignant Liver Tumors

○ Morphology of primary liver carcinoma:

- ✓ Hepatocellular carcinoma (HCC) or cholangiocarcinoma (CC) or a mix of both.
- ✓ Can be unifocal or multifocal.
- ✓ Diffusely infiltrative.
- ✓ Vascular invasion is common in all types.
- ✓ Tumor grade varies from well differentiated to anaplastic.

1) Hepatocellular Carcinoma (HC)

- Represents 5.4% of all cancers.
- Incidence: <5/100,000 population in North and South America, north and central Europe, and Australia.

15/100,000 population in the Mediterranean.

36/100,000 population in Korea, Taiwan, Mozambique, and China.

- It affects the black race more than whites.
- M:F ratio is variable:
3:1 in low incidence areas, with the age of incidence >60 years.
8:1 in high incidence areas, with the age of incidence between 20-40 years.

➤ **Predisposing Factors:**

1) Hepatitis carrier state

- ✓ Vertical transmission increases the risk of malignancy 200 times.
- ✓ In this case cirrhosis may be absent.
- ✓ The affected age group is 20-40 yrs.

2) Chronic hepatitis B infection

- ✓ > 80% of cases of HCC occur in countries with high rates of chronic HBV infections.

3) Cirrhosis

- ✓ In western countries cirrhosis is present in 85-90% of cases of HCC.
- ✓ These cases are usually associated with individuals of old age (>60 years).
- ✓ Remember that HCV and alcoholism are common predisposing factors for development of cirrhosis.

4) Aflatoxins (poisonous carcinogens and mutagens that are produced by *Aspergillus flavus*).

5) Hereditary tyrosinemia: An amino acid metabolic disorder that involves impaired break down of the amino acid tyrosine. It affects the liver and kidneys.

- ✓ It is present in 40% of cases.
- ✓ Even with adequate dietary control of their condition, they sustain high risk of developing HCC.

6) Hereditary hemochromatosis

➤ **Pathogenesis:**

1) Repeated cycles of cell death and regeneration due to HBV and HCV infections.
They are associated with increased risk for the development of mutations and genomic instability that is required for cancer development.

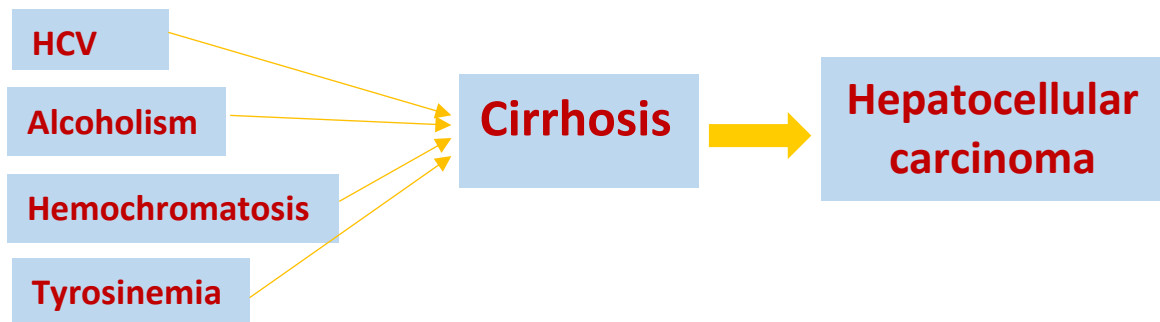
2) Viral integration

HBV DNA integration in the host DNA leads to clonal expansion. It also leads to genomic instability that is not limited to the integration site.

3) The viral protein of HBV, called X-protein, leads to transactivation of viral and cellular promoters, activation of oncogenes, and inhibition of apoptosis, all of which are early steps in carcinogenesis.

4) Aflatoxins can cause mutations in P53.

5) Cirrhosis



2) Fibrolamellar Carcinoma

- A specific form of hepatocellular carcinoma.
- Presents as single, hard scirrhous tumor.
- Affects individuals in a young age group: 20-40 years. M=F.
- Has no relation to HBV or cirrhosis.
- Has better prognosis than the conventional type of HCC.

3) Cholangiocarcinoma (CC)

- **Cancer in the epithelial cells of hepatic bile ducts.**
- It is characterized by the fibrous background of the tumor.
- In 50% of cholangiocarcinoma cases, vascular metastasis to the lungs, bones, adrenals, and brain occurs.

○ Clinical picture of liver tumors:

- ✓ Abdominal pain, malaise, and weight loss (non-specific symptoms).
- ✓ Increase in α -fetoprotein levels in 60-75% of patients.

○ α -fetoprotein also increases with:

- ✓ Yolk sac tumor, cirrhosis, massive liver necrosis, chronic hepatitis, normal pregnancy, fetal distress or death, and fetal neural tube defect.
- ➔ So, it's not specific to HCC, but the age and presentation of HCC are totally specific. Thus, the increase in α -fetoprotein should in particular patients (those with the specific age and presentation of HCC) indicate the presence of a liver tumor.

○ Prognosis:

- ✓ Death within 7-10 months after diagnosis.
- ✓ Due to: Cachexia, GI bleeding, Liver failure, tumor rupture and hemorrhage.

Clinical cases

- 1) A 40-year-old man has a long history of chronic alcohol abuse. On physical examination his liver edge is firm on palpation of the abdomen, but liver span does not appear to be increased. An abdominal CT scan reveals a cirrhotic liver. He joins a support group for persons with chronic alcohol abuse and he stops drinking. Despite his continued abstinence from alcohol, he most likely remains at risk for development of which of the following diseases?
 - A) Hepatic adenoma
 - B) Focal nodular hyperplasia
 - C) Hepatocellular carcinoma
 - D) Hemangioma
 - E) Cholelithiasis

- 2) A 28-year-old woman with recent onset of a major depressive disorder ingests an entire bottle (100 capsules, 500 mg each) of a medication containing acetaminophen. She becomes progressively obtunded over the next 8 hours. Which of the following microscopic findings is most likely to be present in her liver 3 days following this ingestion?
 - A) Normal histology
 - B) Extensive necrosis
 - C) Bridging fibrosis
 - D) Severe steatosis
 - E) Portal chronic inflammation

- 3) A 54-year-old Asian man has had malaise with a 6 kg weight loss over the past 7 months. On physical examination he has a firm, nodular liver edge. His stool is negative for occult blood. Laboratory studies show a positive serology for hepatitis B surface antigen, but negative serologies for hepatitis B surface antibody, hepatitis A IgM antibody, and hepatitis C antibody. His serum alpha-fetoprotein is 109 ng/mL. Which of the following neoplasms is he most likely to have?
 - A) Hemangioma
 - B) Hepatic adenoma
 - C) Cholangiocarcinoma
 - D) Hepatocellular carcinoma
 - E) Hepatic angiosarcoma

- 4) A 41-year-old man is found in an obtunded state and taken to the hospital. On admission physical examination he is icteric. His abdomen is enlarged with a fluid wave. An abdominal CT scan shows extensive intraperitoneal fluid and a uniformly enlarged liver that has decreased attenuation (decreased brightness). A liver biopsy is performed and microscopically demonstrates abundant Mallory hyaline, neutrophilic

infiltrates, hepatocyte necrosis, portal fibrosis, and extensive macrovesicular steatosis. Which of the following is the most likely diagnosis?

- A) Autoimmune hepatitis
- B) Sclerosing cholangitis
- C) Alcoholic hepatitis
- D) Hepatitis B virus infection
- E) Diabetes mellitus

ANSWERS

1) C

Hepatocellular carcinoma occurs most often in the setting of cirrhosis (which occurs most often from chronic alcoholism and from chronic viral hepatitis B and C). The liver remodels itself over years, so the cirrhosis is slowly reversible, with decreasing carcinoma risk.

2) B

This is a massive overdose of acetaminophen, which causes extensive hepatic necrosis. Administration of N-acetylcysteine helps increase glutathione to counter the toxicity.

3) D

Chronic hepatitis and both micro- and macronodular cirrhosis carry an increased risk for liver cancer. Most often this is hepatocellular carcinoma. Either chronic hepatitis B or C infection increases the risk for primary liver cancer. An elevated AFP is characteristic for hepatocellular carcinoma.

4) C

This is the typical appearance of acute sclerosing hyaline necrosis with alcoholic hepatitis. It is usually seen in the setting of chronic alcoholism with a superimposed recent episode of binge drinking. It is the one condition intrinsic to liver in which many neutrophils are present. Ammonia is most likely to be increased with acute liver failure.

وَكُلُّ بَابٍ وَإِنْ طَالَتْ مَغَالِقُهُ .. يَوْمًا لَهُ مِنْ جَمِيلِ الصَّبْرِ مِفْتَاحُ
كَمْ مِنْ كُرُوبٍ ظَنَنَّا لَا انْفِرَاجَ لَهَا .. حَتَّى رَأَيْنَا جَلِيلَ الْهَمِّ يَنْزَاحُ
فَاصْبِرْ لِرَبِّكَ لَا تَيَاسُ فَرَحَمَتُهُ.. لِلخَلْقِ ظِلٌّ وَلِلْأَيَّامِ إِصْبَاحُ 🍷

Good luck