GIS

Pathology no. 6

| Modified slides

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Words in Blue color: extra information

Words in Green color: from doctor

Primary Sclerosing Cholangitis (PSC)

- characterized by **Inflammation obliterative fibrosis, & segmental dilation of the obstructed intra hepatic & extra hepatic bile ducts.**
- **In PSC, UC** (ulcerative colitis) **coexists in 70% of patients.**
- **In patients of UC, 4% develop PSC.**
- **3-5th decades of life.**
- **M: F 2:1** males are affected twice as females.

Clinical presentation:

- **Asymptomatic.**
- **Persistent** elevated serum **alkaline phosphatase.**
- Symptoms include: **fatigue, pruritus, jaundice, weight loss, ascites, bleeding and encephalopathy.**
- This condition is characterized by presence of auto-antibodies:

*Fluid accumulation in the abdomen.

Anti-mitochondrial antibodies are present in < 10% of cases.

Anti-nuclear cytoplasmic antibodies are present in 80% of cases.

- This is important in differentiating it from the primary biliary cirrhosis manifestations.

Morphology :

- **1) Concentric periductal onion-skin fibrosis and lymphocytic infiltrate.** Surrounding the bile duct.
- **2) Atrophy and obliteration of bile ducts.** Due to their destruction.
- **3) Dilation of bile ducts in between areas of stricture.**
- **4) Cholestasis** (blockage of bile flow by accumulation of bile salts within small bile duct) **and fibrosis.**
- **5) Cirrhosis**
- **6) cholangiocarcinoma can be seen in 10 –15% of the cases.** (Increase risk of malignancy for the liver, particularly this type)

Pathogenesis:

- Exposure to gut derived toxins
- Immune attack by auto-antibody
- Ischemia of biliary tree

Extra note 018 sheet : PSC is thought to be an autoimmune disease; it does not demonstrate a clear response to immunosuppressants. Thus, many experts believe it to be a complex, multifactorial disorder.

Extra note 018 sheet : biliary tree is the system which directs secretions from the liver, gallbladder and pancreas through a series of ducts, into the duodenum).

Secondary biliary cirrhosis:

- **Prolonged obstruction to extra hepatic biliary tree.**
- Any condition which is responsible for obstruction of the biliary tree end up with developing of cirrhosis as :
- Causes:

1) Cholelithiasis (The formation of gallstones).

2) Biliary atresia (One or more bile ducts are congenitally narrow, blocked, or absent).

3) Malignancies.

4) Strictures (The common bile duct is abnormally narrow)

Primary biliary Cirrhosis:

- **A chronic, progressive and often fatal cholestatic liver disease.**
- Characterized by the formation of: **Non-suppurative granulomatous destruction of medium-sized intra-hepatic bile ducts** with **Portal inflammation and scarring.**
- This condition affect the: **Age 20-80yrs (peak 40-50yrs).**
- Much more common in females **F>M.**
- **Insidious onset and** it can present with **Pruritis, jaundice.**
- **It may cause cirrhosis over 2 or more decades** after initial presentation.

Primary biliary Cirrhosis

Also it's characterized by:

- **Increase alkaline phosphatase and cholesterol.**
- **Hyperbilirubinemia which is due to hepatic** decompensation and the inability for the liver to deal of the load of bilirubin in hepatocytes.

failure of the liver to compensate for the functional overload resulting from the disease.

- Presence of auto-antibody **Anti-mitochondrial antibodies** most common.
- **Antimitochondrial - pyruvate dehydrogenase are present in more than 90% of the patients**

Associated conditions: Sjogren syndrome, Scleroderma thyroiditis,

RA (rheumatoid arthritis), Raynaud's phenomenon,

MGN (membranous glomerulonephritis), and celiac disease.

Morphology

- **Interlobular bile ducts are absent or severely destructed (florid duct lesion).**
- **Intra-epithelial inflammation.**
- **Granulomatous inflammation** that usually centered around destructed bile duct it can be associated with Bile ductular proliferation.
- **Cholestasis** (blockage of bile flow).
- **Necrosis of parenchyma**
- **Cirrhosis**

* The florid duct lesion, defined as a granulomatous destruction of the bile ducts, is the histological hallmark of PBC.

Sinusoidal Obstruction Syndrome(Veno-occlusive disease)

- A condition in which some of the small veins in the liver are obstructed.
- **Originally described in Jamaican drinkers of bush-tea containing pyrrolizidine alkaloids** which associated with the infection of the liver.
- **This occurs in the first 20-30 days after bone marrow transplantation**
- **due to(causes):**

1) Drugs as cyclophosphamide.

2) Total body radiation.

In other words, it is a complication of radiation to the whole body or high-dose chemotherapy given before a bone marrow transplant.

- **Incidence :**

- **20% in recepients of allogeneic marrow**
- **transplant**
- **Clinical presentation:**
- **Mild–severe**
- In sever forms it can cause **Death if does not resolve in 3 months.**

Mechanism:

- **Toxic agents** (e.g. cyclophosphamide) causes injury to the hepatic venous endothelium.

sinusoidal endothelium → emboli formation → blockage of blood flow → passage of blood into space of Disse → stellate cells activation → fibrosis

Some Recommended videos for the previous slides promise it WILL help!

- (1512) Primary sclerosing cholangitis causes, symptoms, diagnosis, treatment & pathology – YouTube
- (1512) Primary biliary cholangitis causes, symptoms, diagnosis, treatment & pathology – YouTube

Liver tumors

start with it !

(1513) Benign liver tumors causes, symptoms, diagnosis, treatment & pathology – YouTube

Liver tumors can be benign or malignant.

- **Benign**

1- Cavernous hemagioma

- **The most common benign liver tumor.**
- Usually small in size**, less than 2 cm in diameter.**
- **Subcapsular** in location.

2-Liver cell adenoma

- 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.**
- Usually they are benign **Rarely may contain(HCC)**hepatocellular carcinoma **.**
- **May be misdiagnosed as HCC.**

✳ Estrogen stimulates the development of hepatocellular adenoma, thus **Liver cell adenoma** is associated with oral contraceptive intake and pregnancy.

Liver Nodules

1-Focal Nodular Hyperplasia

- **Well demarcated hyperplastic hepatocytes with a central scar,** forming localized non-diffused nodules.
- Present **in non-cirrhotic liver**
- **Not a neoplasm but shows 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**.

Diagnosis of liver nodules is very important because these can be misdiagnosed with malignant one!

2-Macroregenerative Nodules.

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

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وأتوب إليه.

Malignant Liver Tumors

1-Hepatocellular carcinoma(HCC).

- 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 more than whites** Blacks >white
- **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 young 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).
- 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 (in 40% of cases)

- An amino acid metabolic disorder that involves impaired break down of the amino acid tyrosine. It affects the liver and kidneys.

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 gene mutations and genomic instability that is required for cancer development.

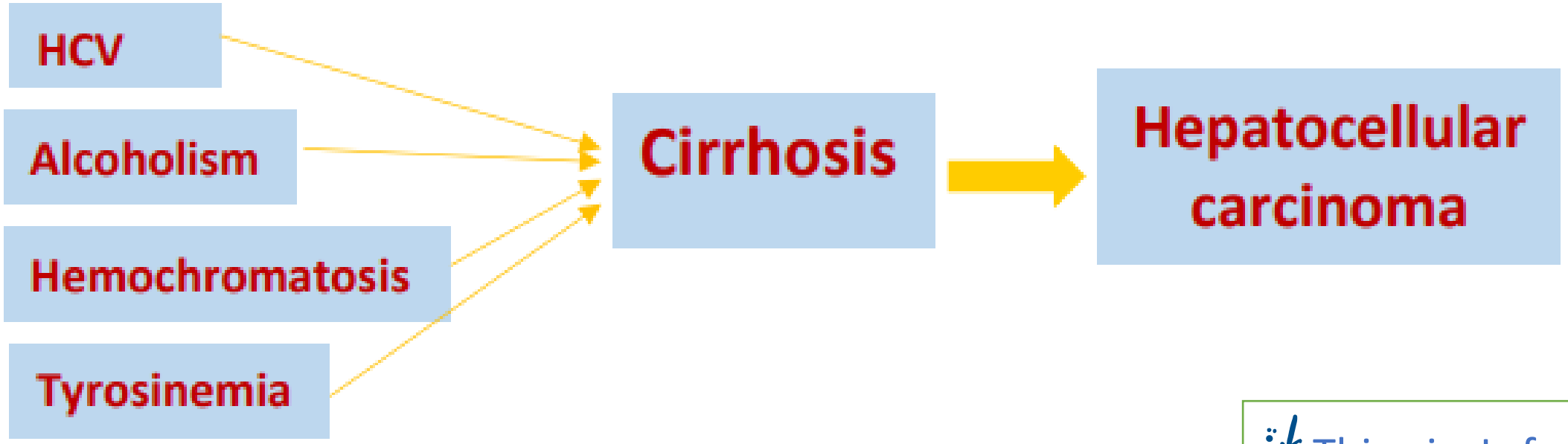
2-Viral integration HBV DNA integration in the host DNA. leads to clonal expansion.

3-It also leads to genomic instability that is not limited to the integration site.

4-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.

5- Aflatoxins (fungus Aspirgillus flavus**).** Can cause **mutation of p53.**

6- Cirrhosis.



This pic. Is from 018 sheet.

Morphology:

1-Hepatocellular carcinoma. (hepatocyte origin)

2-Cholangiocarcinoma. (epithelium of biliary duct origin)

3-Mixed of both type.

Liver tumor can be :

- **Unifocal.**
- **Multifocal.**
- **Diffusely infiltrative.**
- **Vascular invasion is common.** mode of metastasis in all types.
- Regard grad liver tumor can be **Well** —to— **Anaplastic** differentiation.

Continuation of Malignant Liver Tumors:

2-Fibrolamellar Carcinoma specific form of hepatocellular carcinoma.

- 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.**
- **Presents as single, hard scirrhous tumor.**

3- Cholangiocarcinoma (CC). Cancer in the epithelial cells of hepatic bile ducts.

- **They are desmoplastic.** That's why we should think of any metastatic tumor with high desmoplastic reaction to be of biliary system.

Metastasis:

➢**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:

1- Yolk sac tumor

2-cirrhosis

3- massive liver necrosis

4-chronic hepatitis

5-normal pregnancy

6- fetal distress or death

7-and fetal neural tube defect

It's not specific to HCC, **but** the age and presentation of HCC are totally specific. Thus, the increase in α-fetoprotein (**in patients with the specific age and presentation of HCC**) **MUST** indicate the presence of a liver tumor.

Prognosis of liver cancer:

- **Death within 7-10 months.** after diagnosis.
- Due to(causes):

1)Cachexia

2) GI bleeding

3) Liver failure

4) tumor rupture and hemorrhage

The end

wish you all the best !

يجعلها نهاية أحزانكن،