LECTURE 6

Primary sclerosing cholangitis

Inflammation, obliterative firosis, &-segmental dilation of the obstructed intra hepatic & extra hepatic bile ducts

In PSC, UC coexists in 70% of patients-

In patients of UC, 4% develop PSC-

3-5th decades-

-M: F 2:1

Clinical presentstion

- asymptomatic
- persistent ↑ serum alkaline phosphatase
- fatigue, pruritis, jaundice, wt loss, ascitis, bleeding, encephalopathy

- antimitochondrial Abs < 10% of cases
- **Antinuclear cytoplasmic Abs** in 80% of cases

Morphology

-Concentric periductal onion-skin fibrosis & lymphocytic infiltrate

Atrophy & obliteration of bile ducts-

Dilation of bile ducts inbetween areas of stricture-

Cholestasis & fibrosis-

Cirrhosis-

Cholangiocarcinoma (10–15%)-

Pathogenesis

Exposure to gut derived toxins-

Immune attack-

Ischemia of biliary tree-

Secondary biliary cirrhosis

-Prolonged obstruction to extrahepatic biliary tree

-Causes:

1-cholelithiasis

2-biliary atresia

3-malignancies

4-stricutres

Primary biliary Cirrhosis

- Chronic, progressive & often fatal cholestatic liver disease
-Non-suppurative granulomatous destruction of medium-sized intrahepatic bile ducts, portal inflammation & scarring

-Age 20-80yrs (peak 40-50yrs)
-F>M
-Insidious onset
-Pruritis, jaundice
-Cirrhosis over 2 or more decades

-↑Alkaline phosphatase & cholesterol

-Hyperbilirubinemia = hepatic decompansation

-Antimitochondrial Abs > 90%

Antimitochondrial pyruvate dehydrogenase

-Associated conditions: sjogern synd. Scleroderma thyroiditis, RA, Raynauds phenomenon. MGN, celiac disease.

- **Morphology**
- Interlobular bile ducts are absent or severely destructed (florid duct lesion)
- Intra epithelial inflammation
- Granulomatous inflammation
- Bile ductular proliferation
- Cholestasis
- Necrosis of parenchyma
- Cirrhosis

Sinusoidal Obstruction Syndrome (Veno-occlusive disease)

-Originally described in Jamaican drinkers of bush-tea containing pyrrolizidine alkaloids

-This occurs in the first 20-30 days after bone marrow transplantation

. Which is caused by:

1-Drugs as cyclophosphamide

2-Total body radiation

-Incidence

-20% in recepients of allogeneic marrow transplant

-Clinical presentation

Mild–severe

Death if does not resolve in 3 months

Mechanism

Toxic injury to sinusoidal endothelium
→emboli

→blockage of blood Flow

Passage of blood into space of Disse
→↑stellate cells → fibrosis

Liver tumors

- **Benign**
- **Cavernous hemagioma**
- Most common is
- Usually <2cm
- Subcapsular
- **Liver cell adenoma**
- Young female
- History of oral contraceptive intake
- May rupture esp. during pregnancy causing severe intraperitoneal hemorrhage
- Rarely may contain HCC
- Misdiagnosis Of HCC

Liver Nodules

Focal noudular hyperplasia

- Well demarcated hyperplastic hepatocytes with central scar.
- Non-cirrhotic liver
- Not neoplasm but nodular regeneration
- Local vascular injury
- Females of reproductive age
- No risk of malignancy
- 20% of cases have cavernous hemagnioma

Macroregenerative Nodules

- Cirrhotic liver
- Larger than cirrhotic nodules
- No atypical features,
- Reticulin is intact
- No malignant potential

Hepatocellular carcinoma

- **5.4% of all cancers**
- **Incidence:**
  <5/100000 population in N&S America
  N& central Europe
  Australia
  15/100000 population in Mediterranean
  36/100000 population in Korea, Taiwan
  mozambique, china

- **Blacks > white**
- **M:F ratio**
  3:1 in low incidence areas. >60yr
  8:1 in high incidence areas. 20-40yr

Predisposing Factors

1. **Hepatitis carrier state**
   vertical transmission increases the risk 200X
   cirrhosis may be absent
   young age group (20-40yr)
2. **>85% of cases of HCC occur in countries with high rates of chronic HBV infection**

3-Cirrhosis

In western countries cirrhosis is present in 85-90% of cases

>60yr

HCV & alcoholism

4. Aflatoxins

5. Hereditary tyrosinemia (in 40% of cases)

6. Hereditary hemochromatosis

Pathogenesis

1. Repeated cycles of cell death & regeneration
   HBC, HCV, gene mutations, Genomic instability
2. Viral integration
   HBV DNA intergration which leads to clonal expansion
3. HBV DNA intergration which leads to genomic instability not limited to integration site.

4. HBV

X-protein which leads to transactivation of viral & cellular promoters,

Activation of oncogenes,

Inhibition of apoptosis

5. Aflatoxins (fungus Aspirgillus flavus)

mutation of p53

6. Cirrhosis

HCV

Alcohol

Hemochromatosis

Tyrosinemia (40% of pts. Develop HCC despite adequate dietary control

Morphology

1. Hepatocellular carcinoma
2. Cholangiocarcinoma
3. Mixed

- Unifocal
- Multfiocal
- Diffusely infiltrative

- Vascular invasion is common in all types.
- Well ---- Anaplastic

- **Fibrolamellar carcinoma**
  20-40 yr. M=F
  No relation to HBV or cirrhosis
  better prognosis
  single hard scirrhous tumor
- Cholangiocarcinoma are desmoplastic

Metastasis

,Vascular – lungs, bones, adrenals, brain

- C/P
  abd. Pain, malaise, wt. loss
  increase α-feto protein in 60–75% of cases.

- α-feto protein increases also with:
  1-yolk sac tumor
- 2-cirrhosis
- 3-massive liver necrosis
- 4-chronic hepatitis
- 5-normal pregnancy
- 6-fetal distress or death
- 7- fetal neural tube defect

Prognosis

- Death within 7 -10 months
- **Causes:**

1-Cachexia

2-GI bleeding

3-Liver failure

4-Tumor rupture and hemorrhage

THE END