Patho final

First lec 8

Hepatic injury (8)

1. Inflammation
   Hepatitis

2- Degeneration
- feathery degeneration
- accumulation of iron, coper

3- Fibrosis
Bridging fibrosis

4- cirrohsis
- micronodular
- macro nodular

5- Regeneration
- ↑ mitosis, cell cycle markers
- The cell of the canal Hering & the progenerator → hepatocyte
  → bile duct cells

6- Ductular Proliferation

7- Steatosis

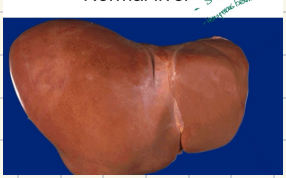
Microviscular:
AFD, Reys syndrome
Acute fatty change during Pregnancy

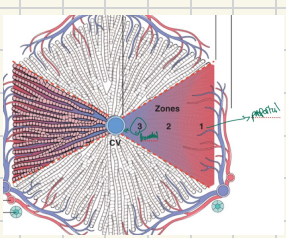
Macroviscular:
DM, obesity

8- Necrosis

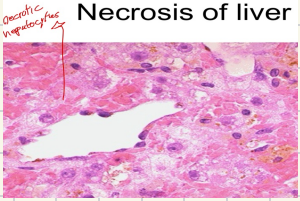
type	location	cause
Coagulative necrosis Councilman bodies Lytic necrosis	Centrilobular necrosis: Mid zonal : Periportal : interface hepatitis Focal: Piece meal necrosis bridging necrosis Diffuse: massive & submassive necrosis	Ischemic Toxic

Normal liver

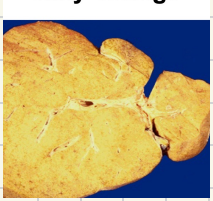




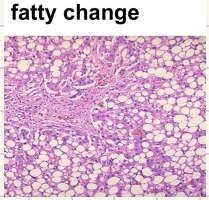
Necrosis of liver



fatty change



fatty change



Past:

The outstanding feature of chronic hepatitis is:
a. Portal lymphocytic infiltrate.
b. Councilman bodies.
c. Steatosis.
d. Fibrosis.
e. Bile duct damage

(d)

Lec.2
Clinical syndromes
1. Hepatic failure 2- cirrhosis 3-Portal hypertension 4- cholestasis

1- Hepatic failure & 3 Categories

1- Acute liver failure with massive hepatic necrosis

× Most common 2 causes: -مدونة اسئلة-
- Drugs. 2nd
- Fulminant viral hepatitis. 1st

× Hepatic insufficiency → hepatic encephalopathy 2-3 weeks
× not common but! life threatening.

× Treatment of massive necrosis:
- liver transplantation.

2- chronic liver disease "most common"

× has relation w/ Cirrhosis.

× more common than acute

× Clinical feature of liver failure
-نفس الاعراض مع اختلاف الاسباب-

- Jaundice -Yellowing-
- hypoalbuminemi Alb ↓
- hyperammonemia → edema NH_3 ↑
- Fetor hepaticas -smell-
- Palmar erythema.. estrogen ↑
- spider angiomas
- Hypogonadism (-) feedback
  = enlargement of breast tissue in men/boys ← on sex hormone

⇓

!! complications !!

- multiple organ failure: Kidney-
- Coagulopathy II, VII, IX, X Clotting factors:
- Hepatic encephalopathy: consciousness ↓, hyperflexia... EEG changes
- Hepatorenal syndrome

3- Hepatic dysfunction without overt necrosis

× No morphological change but! → abnormal function !!

× causes:
- Reye's syndrome
- Acute fatty liver of Pregnancy
- Tetracycline toxicity -drug-

All are true clinical manifestations of chronic liver disease, EXCEPT:
a. Finger clubbing.
b. Dupuytren contracture.
c. Breast atrophy in males.
d. Jaundice.
e. Spider angiomas

(c) في مدونة الـ clinical كل شي عكس الـ concepts

The most common drug that cause acute liver failure is:
a. Isoniazid.
b. Carbon tetrachloride.
c. Rifampin.
d. Halothane.
e. Acetaminophen

لم يذكر في هذه المدونة اسئلة عن الـ drug الي جاي ب (e) paracetamol.

The most common cause of massive hepatic necrosis is:
a. Wilson disease.
b. Acute fatty liver of pregnancy.
c. Autoimmune hepatitis.
d. Viral hepatitis.
e. Drugs and chemicals

(d)

Lec.3

Alcoholic liver disease (ALD):

- widely abused agent !!
- causes accidents, cirrhosis

→ 80-100 mg/dl → legal for driving
→ occasional → 300/400 + coma / death
→ Habitual → 700 → no clinical effect
- metabolic tolerance -

Pathogenesis

short term → mild, reversible hepatic changes
chronic intake → severe injury
women susceptibility to injury >>> men
↳ enzyme activity lower.

CYP2E1 : increase metabolism of Ethanol

Forms of ALD

Hepatic steatosis ← independently → Alcoholic hepatitis

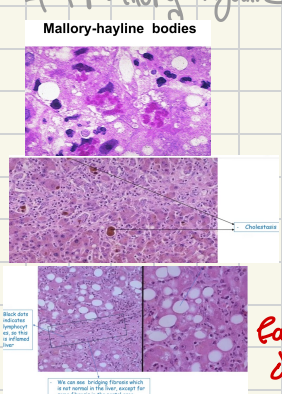
Cirrhosis

Hepatic steatosis

most common

x microvascular steatosis
reversible
- around central vein -
diffuse
yellow-greasy
fibrosis
cirrhosis
- irreversible -

++ Mallory hyaline



Fatty change

Alcoholic hepatitis

2nd must common

1- cell injury
(Necrosis, swelling...)

2- mallory-hayline bodies
eosinophilic cytoplasmic inclusion
Characteristic but not
Pathognomonic.

3- Neutrophilic reaction

4- Fibrosis
5- cholestasis
within hepatocyte / biliary system

6- mild deposition of hemosiderin

Cirrhosis

3rd

- "not every patient with cirrhosis is alcoholic"

- slowly development
- become shrunken
- not fatty
↙ ↘
micronodule macro.

- hepatitis will accelerate the progress of cirrhosis

- fibrosis ↑
- diffuse
++ Mallory-hayline

Alcoholic hepatitis notes

1- cell injury (Necrosis, swelling...)
↓
Accumulation of fat, water
Proteins
↓
cholestasis
↓
Hemosidrein (iron↑)

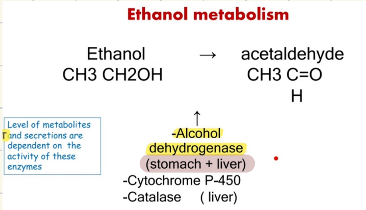
2- Malory-hayline bodies
eosinophilic cytoplasmic inclusion
- cytokeratin
- other Proteins
Characteristic but not Pathognomonic.

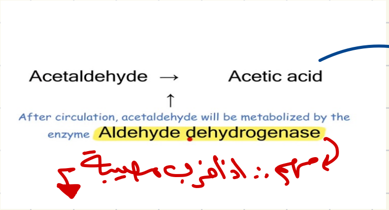
imp. note about mallory: موجودة في كل ال ALD وفي 4 غيره

- can also be in: -
. Primary biliary cirrhosis
. wilson disease
. chronic cholestatic syndrome
. Hepatocellular carcinoma.

2 related to bile
1 Carcinoma
1 wilson

Ethanol metabolism





مهم :: اذا فيه مصيبة

بعدين بتوزع بالجسم

* Genetic Polymorphism
women > men
Susceptibility

x Some of the absorbed ethanol → does not metabolized.
(Asian) ↳ excreted uncharged in urine, sweat, breathe.
x Easterner People have lowered enzyme activity due to Point mutation
∴ facials Flushinge, tachycardia, hyperventilation

Ethanol toxicity

- Fatty change
. NADH production >> NAD
. Acidaldehyde w/ tubulin :
↓ microtubule function.
↓ Lipoprotein transport from liver ∴ ↑ Lipo in liver.
. ↑ Peripheral catabolism of fat ∴ ↑ FFA delivery to liver
. ↓ oxidation of FFA mitochondria

- Induction of P-450
toxic metabolite

- free radical
affect mit./microtubule
∴ Protein damage !!

- Acetaldehyde
- lipid peroxidation
- antigenic alteration.
∴ Immune attack

- Superimposed HCV infection
بتزيد احتمالية اصابة ال alcoholic ب HCV

- Alcohol → release endotoxins → inflammation
- Alcohol → release endothelins → regional hypoxia → ↓ hepatic Perfusion
- Alteration in cytokine regulation → ↑ inflammation → ↑ injury

clinical features !!

Hepatic steatosis -reversible- → liver size ↑
→ liver enzyme ↑

Alcoholic hepatitis -nonspecific sym- → liver ± spleen
-for long time- → LFT ↑ enzyme

Cirrhosis → Portal hypertension

The most common form of alcoholic liver disease is
a. Massive necrosis.
b. Hepatic steatosis.
c. Ductular proliferation.
d. Cirrhosis.
e. Alcoholic hepatitis •

b>e>d *

Mallory-hyaline bodies (damaged intermediate filaments) can be seen in which of the following conditions?
A. Wilson disease
B. Primary biliary cirrhosis
C. Alcoholic hepatitis •
D. HCC
E. All of the above

(E)

Mallory hyaline bodies can be seen in hepatocytes in all the following conditions EXCEPT:
a. Hepatocellular carcinoma.
b. Submassive hepatic necrosis.
c. Alcoholic cirrhosis.
d. Primary biliary cirrhosis.
e. Wilson disease

(b)

A mutation in aldehyde dehydrogenase could lead to accumulation of acetaldehyde, which of the following could be an outcome of this toxic accumulation?
A. Fascial flushing
B. Hyperventilation •
C. Tachycardia
D. B+C
E. All of the above

(E)

Causes of death in ALD:

- Hepatic failure
- Massive GI bleeding
- Infections
- Hepatorenal syndrome
- HCC in 3-6% of cases -carcinoma-

Cirrhosis

- diffuse fibrosis
- nodules : fibrosis surrounds Hepatocyte

main characteristics:

- Bridging fibrous : severe fibrosis always present
- nodules → micro.
  → macro. disfiguration
- Diffuse : must include whole liver if not → ∴ not cirrhosis.

× Causes of Cirrhosis (٩) باقي الحاجات بتكون خرج عن كل سبب بالتنزيل

chronic alcoholism	chronic viral infection HBV, HCV	Biliary disease
Hemochromatosis	Autoimmune hepatitis	Wilson disease
α-1 antitrypsin deficiency	-Rare causes-	cryptogenic cirrhosis

Pathogenesis of cirrhosis:

Hepatocellular death → regeneration → Fibrosis → Vascular changes

+scars

Fibrosis → cell death over long time → porenchyma / connective tissues

Vascular changes → Portal vein-hepatic, hepatic artery portal

In normal liver the ECM collagen I, III, V, XI only on:

- liver capsule
- Portal tract
- Around central vein

∴ اذا انوجدت هذه الانواع من الكولاجين جنب مكانها = Fibrosis

space of Disse

↑ stimuli of stellate cells (ito's cell) → Production of collagen = Fibrosis ٩

Stimulants !!

1. ROS
2. Growth factors
3. cytokines TNF, IL-1, lymphotoxins

Clinical Features of cirrhosis

Silent
Anorexia, wt loss, weakness
Complications:
- Progressive hepatic failure
- Hepatocellular carcinoma!
- Portal hypertension
  - sinusoid
  - central vein

Causes of Portal Hypertension

Pre-hepatic
- Portal vein thrombosis
- splenomegaly

Post-hepatic
- Rt. side of heart failure
- Constrictive pericarditis
- Hepatic vein out flow obstruction

Hepatic
- cirrhosis
- schistosomiasis (Parasite)
- Fatty change
- Diffuse granulomatosis, TB

Clinical consequence of Portal Hypertension (4)

- Ascitis
- edema
- fluids ↑ ≥ 500 mL

Features:
serous fluid
contain Protein
same conc. as blood of:
glucose, Na^+, K^+
Neutrophil = infection
RBCs = disseminated cancer ← مش دائماً موجودين

- Portosystemic shunt

↑ Portal venous Pressure

sites:
- rectum
- gastroesophageal junction
- Retroperitoneum
- Falciform lig. → caput medusae

- Splenomegaly ← سبب / ناتج

× Normal function:
destruction of blood

Hypersplenism:

Pancytopenia / anemia
Immunity ↓

Pathogenesis of Ascitis

- ↑ Sinusoid BP
- Hypoalbumenia
- leakage of lymph
- Renal retention → hyperaldosteronism
  - Na^+, H_2O

- Hepatic encephalopathy

NH_3 normally metabolized in liver

↓

when liver def. ** = NH_3↑

= cerebral edema

∴ coma, Death

Pathogenesis:

severe loss of function

exposure brain to toxic

Acute insult. NH_3↑

↓

chronic insult. CNV in Ad metab

Pasta

A pathologic study of hepatic cirrhosis is performed. There is collapse of reticulin with bridging fibrosis from deposition of collagen in the space of Disse to form fibrous septa. Which of the following cell types is activated under the influence of cytokines to give rise to collagen-producing cells?
A. Bile duct cell
B. Endothelial cell
C. Hepatocyte
D. Macrophage
E. Stellate cell

(E) (ito's cell)

A longitudinal study is conducted of non-alcoholics with type 2 diabetes mellitus, dyslipidemia, and BMI >30. There is an increasing prevalence of liver disease in these persons over time. Which of the following microscopic pathologic findings is most characteristic for the livers of these persons?
A. Apoptosis
B. Cholestasis
C. Cirrhosis
D. Hemosiderosis
E. Steatosis

* حالة على عزوقيل.

BMI >30 → over weight

(E) fat accumulation

The most like complication of cirrhosis that could lead to thrombocytopenia is?
A. Ascites
B. Hemorrhoids
C. Esophageal varices
D. Splenomegaly
E. Hepatic Encephalopathy

↓ blood count ∴ (D)

Hepatorenal syndrome : عشان اقدر اوصفه بعد الرمي لازم يكون السبب idiopathic, unknown.

Secondary to liver failure

CCL4 will cause damage → liver / kidney

mycotoxins / wilson disease

→ not hepatorenal

Advanced hepatic failure → tubular necrosis, acute renal failure

All have a known cause so → they won't cause Hepatorenal syndrome

- Kidney function Promptly improves if hepatic failure is reversed ✓
- The exact cause is unknown, could be → vasoconstriction → ↓ renal blood flow
- ↓ urine output → blood urea nitrogen ↑, creatinine values ↑
- Renal failure → ↑ risk of death.

Drug - Induced liver disease

Drug reaction

Predictable

- dose dependent
- Acetaminophen
- Alcohol
- Tetracycline
- CCl_4
- Antineoplastic

Unpredictable → بتعتمد عالHost عشان هيك صعب توقعه!

idiosyncrasies of Host
- Immune response
- rate of metabolism

- chlorpromazine
- Halothane
- sulfonamide
- Methyldopa
- Allopurinol

Drug induced chronic hepatitis could be → viral hepatitis / → autoimmune hepatitis] → serolog (الحل)

Mechanism of injury

direct

the drug itself:
- Acetaminophen
- CCl_4
- mushroom toxins

indirect

Immune-mediate damage
حاملة اله → - foreign antigen -

Patterns of injury

- Hepatocellular necrosis
- cholestasis
- steatosis
- steatohepatitis
- Fibrosis
- Vascular lesions
- Granuloma
- Neoplasms benign / malignant

Pattern of Injury	Morphology	Examples
Cholestatic	Bland hepatocellular cholestasis, without inflammation	Contraceptive and anabolic steroids
Cholestatic hepatitis	Cholestasis with lobular necroinflammatory activity	antibiotics; phenothiazines
Hepatocellular necrosis	Spotty hepatocyte necrosis	Methyldoya, phenytoin
	Submassive necrosis, zone 3	Acetaminophen, halothane
	Massive necrosis	Isoniazid, phenytoin
Steatosis	Macrovesicular	Ethanol, methotrexate, corticosteroids, total parenteralnutrition

Steatohepatitis	Microvesicular Mallory bodies	Amiodarone, ethanol
Fibrosis and cirrhosis	Periportal and pericellular fibrosis	Methotrexate, isoniazid enalapril
Granulomas	non-caseating	Sulfonamides
Vascular lesions	Sinusoidal obstruction syndrome (veno-occlusivedisease)	High-dose chemotherapy bush teas
	Budd-Chiari syndrome	Oral contraceptives(OCP)
	Sinusoidal dilatation	Oral contraceptives (OCP)
	Peliosis hepatis (blood-filled cavities)	Anabolic steroids tamoxifen

- Neoplasms

Hepatic adenoma	OCP anabolic steroids
HCC	Thorotrast
Cholangiocarcinoma	Thorotrast
Angiosarcoma	Thorotrast, vinyl chloride

Drugs that may cause acute liver failure:

Past!

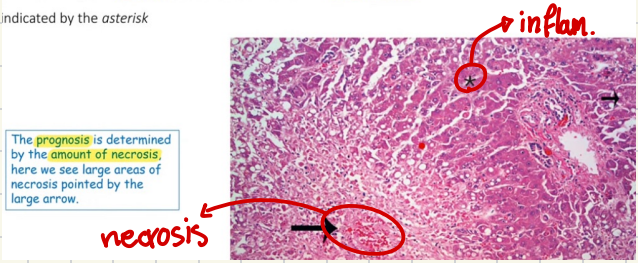
- Acetaminophen → most common cause
- Halothane
- antituberculosis (rifampin, isoniazid)
- antidepressant
- toxins as CCl4, Mushroom

Morphology:

massive
sub massive
Patchy

] necrosis

Hepatocellular necrosis caused by acetaminophen overdose. Confluent necrosis is seen in the perivenular region (zone 3 ;*large arrow* .(There is little inflammation. The residual normal tissue is indicated by the *asterisk*



Past:

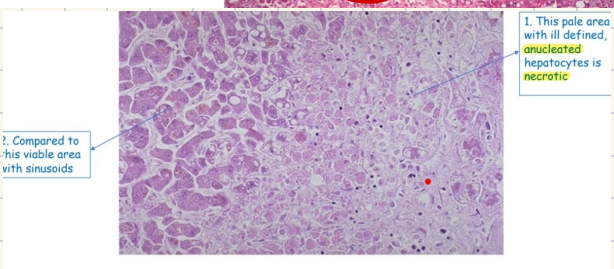
Which of the following statements is false?
A. Hepatic encephalopathy caused by the increased amount of NH3 in the blood because damaged hepatocytes cannot metabolize ammonia through urea cycle
B. High doses of rifampin and isoniazid may lead to acute liver failure
C. 50-60% of Fulminant hepatitis cases are caused by viral hepatitis.
D. Chlorpromazine considers one of the causes of predictable drug induced liver disease.
E. Acetaminophen is the most common cause of drug induced liver failure.

(D)

A 65-year-old man presented with malaise and weight loss. On physical examination, he was found to have enlarged abdomen and skin yellowish discoloration. An abdominal CT scan showed uniformly enlarged liver. Liver biopsy microscopically showed abundant Mallory hyaline bodies, neutrophilic infiltrates, necrosis of hepatocytes, and extensive macrovesicular steatosis . Which of the following is the most likely diagnosis?
a.Acetaminophen toxicity.
b.Sclerosing cholangitis.
c.Chronic hepatitis B infection.
d.Acute hepatitis.
e.Alcoholic hepatitis

علامتين سألها

(E)



A 55 year old man with a history of chronic alcoholism diagnosed with early cirrhosis.
The development of which of the following conditions is associated with high mortality rate in this patient?
a.Caput medosa
b.Upper GIT bleeding.
c.Ascitis.
d.Hemorrhoids.
e.Splenomegaly

(B)

Compl. to cirrhosis causes:

- Autoimmune hepatitis:

Chronic, similar to viral hepatitis

mild - sever

Dramatic response to immunesuppressive therapy

Features:

- Female predominance > male.
- Negative serology for viral infection (Autoimmune!)
- the presence of A.I.D increase the A.I.D chance to occur
- serum immunoglobulin ↑
- Auto_Antibodies ↑

Types of Auto-Antibodies:

1- Anti-smooth muscle: most common!
   Anti: actin
   troponin
   tropomyosin
2- liver / kidney:
   Anti: cytochrome P. 450
   UDP-glucuronosyl
3- Anti-soluble liver / pancreas antigen.

Outcomes of Autoimmune:

- mild → severe chronic
- Full remission is unusual.
- cirrhosis → death.

- Non-alcoholic fatty liver disease

- Steatosis → only fat
  - steatohepatitis → fat + inflam.
  - Hepatocyte destruction → DAMPs.
    on Parenchymal ← → Fibrosis
  - especially metabolic causes -
  - reversible →

Predisposing Factors:

- Type 2 DM
- Obesity BMI > 30
- Dyslipidemia:
  Imbalance of fat

* mechanism of fatty accumulation:

Impaired oxidation of f.A → ↑ synthesis, uptake of FFA on liver
∴ ↳ hepatic secretion of VLDL

↑ TNF, IL-6, chemokine → liver inflammation, damage.

Clinically:
↑ transaminases: AST, ALT ↑
- Most → Asymptomatic
- fatigue symptoms → (right upper quadrant enlargement) discomfort.

Past:

A 31-year-old woman has experienced increasing malaise for the past 4 months. Physical examination yields no remark-able findings. Laboratory studies show total serum protein of 6.4 g/dL, albumin of 3.6 g/dL, total bilirubin of 1.4 mg/dL, AST of 67 U/L, ALT of 91 U/L, and alkaline phosphatase of 99 U/L. Results of serologic testing for HAV, HBV, and HCV are negative. Test results for ANA, anti-liver kidney microsome-1, and anti-smooth muscle antibody are positive. A liver biopsy is done; microscopically, there are minimal portal mononuclear cell infiltrates with minimal interface hepatitis and mild portal fibrosis. What is the most likely diagnosis?
A. α1-Antitrypsin deficiency
B. Autoimmune hepatitis
C. Chronic alcoholism
D. HDV infection
E. Isoniazid ingestion

Antibody liver/kidney → Autoantibody
(B)

Non-alcoholic fatty liver disease is seen in all of the following conditions EXCEPT one:
a.Insulin resistance
b.Obesity
c.Diabetes mellitus type 2
d.Dyslipidemia
e.Chronic anemia

(e)

- another cause of cirrhosis:

Hemochromatosis (50 - 60 y.old)

iron ↑ → liver
→ pancreas

Causes of hemosiderosis (secondary)

- multiple transfusions
- ineffective erythropoiesis (thalasemia).
- increased iron intake
- chronic liver disease
- Genetic:
  (HFE gene on Ch.6) close to → HLA gene
  mutation!

Features of Hemochromatosis:
- cirrhosis
- DM
- skin pigmentation
- Cardiomegaly, joint disease
  testicular atrophy

Pathogenesis:
- def. in absorption
- Normally → total body iron 2-6 g
  .5 stored
- In the disease > 50 gm → 1/3 → on liver

HFE gene: translation of Hepcidin (normal)

Hepcidin: negative Fe. absorption from intestine

∴ HFE deletion ⟶ iron overload.

Two mutation can occur in HFE gene.

- 845 nucleotide (C282Y)
- histidine... (H63D)
  - most common
  - highest iron acc.

* Excessive Fe deposition ⟶ toxicity

1- ↑ Lipid peroxidation
2- ↑ collagen formation
3- ↑ DNA damage

Male >> Female
كانت الـ female عندهم الدورة الشهرية بتنزل فيها الحديد مع الدم = يقل.

morphological changes

1- Deposition of hemosidrin in diff. organs:
- Liver
- Pancreas
- Glands ∴ endocrine insufficiency
- myocardium

2- cirrhosis
3- Pancreatic fibrosis

One of the following regarding hepcidin is CORRECT:
a.Spleen is the main source.
b.Reduced hepcidin levels associated with increased iron absorption.
c.It enhances iron efflux from intestine into plasma.
d.Its levels increased in hemochromatosis.
e.It enhances cupper deposition

(b)

Patients with hereditary hemochromatosis have a mutation in:
A. MHC Class I
B. ATP7B
C. HFE
D. HNF1-α
E. DMT1

(c)

- Wilson Disease
- Autosomal recessive
- Cu accumulation !! , α-2 globulin
  ↓
- ↑ free radical Production
- bind to sulfhydryl group → changing their antigenicity
  ∴ Immune attack to hepatocyte
- Displacement of other metals in hepatic metalloenzymes

ATB7B mutation

Morphology:
for liver
- Fatty change
- cirrhosis
- Acute hepatitis ⟶ chronic hepatitis
- Massive hepatic necrosis

* Orcein stain / Rodanine stain ⟶ show the copper deposition within cytoplasm. (H&E) is not useful here.

- Mallory bodies: من الصبغة اللي بتكونها

Morphology:

For Brain:

Toxic injury to basal ganglia causing → atrophy
→ cavitation

For Eye:

(Kayser-Fleischer rings)

Green-brown → cornea

Clinically: > 6 yrs. of age

- most common presentation → acute Hepatitis
→ chronic
- Neuropsychiatric Presentation → behavioral changes
→ Parkinson disease-like syndrome.

∴ ceruloplasmin level ↓
∴ urinary exc. of Cu ↑
∴ hepatic content of cu ↑

Past:

One of the following is FALSE regarding Wilson disease:
a. Decreased serum ceruloplasmin.
b. Decreased urinary cupper excretion.
c. Mallory hyaline bodies.
d. Fatty change in liver.
e. Kayser-Fleischer ring

(b)

A girl come to your clinic complains of a tremor at rest, which becomes progressively worse over the next 6 months. She exhibits auditory hallucinations and is diagnosed with an acute psychosis. A slit lamp examination shows corneal Kayser-Fleischer rings. Which of the following serologic test findings is most likely to be reported in this patient?
A. Decreased α1-antitrypsin level
B. Decreased ceruloplasmin level
C. Increased α-fetoprotein level
D. Increased ferritin level
E. Positive antimitochondrial antibody

(B)

Ceruloplasmin is copper complexed with which of the following :
A. Albumin
B. Alpha globulin
C. Bilirubin
D. Acetaldhyde

(B)

Comp. of cirrhosis causes:

α-1 antitrypsin deficiency.

normal function: Protease inhibitor as → elastase
→ cathepsin G.
→ Proteinase 3

(ch. 14)

most common sites → lung → Smoking increase the risk
→ liver

Autophagocytic response.

normal genotype Pi. MM → Pi. ZZ mutation in both alleles

Morphology:

- Intracytoplasmic inclusions → acidophilic in H&E

PAS +ve

Usually present in:

Neonatal Hepatitis cholestasis - jaundice chronic hepatitis

Cirrhosis Fatty change Mallory bodies

High risk of HCC

Reye's syndrome

Fatty change microvisicular → in liver & encephalopathy.

- Viral infection + salicylate -
∴ enlargement in liver → liver failure fatty change ✓

* inflammation → absent x

- Vomiting ↑↑
- mitochondrial abnormalities increase the risk of Reye's syndrome

* Vascular diseases *

1) Budd - chiari syndrome

Hepatic vein → blocking of blood flow from liver → Heart
not Portal vein !!

- enlargement of liver (Hepatomegaly)

- Wt. gain - Ascites - abd. Pain

Causes of Budd:

- PCV (Polycythemia Vera) → malignancy in RBC ∴ thrombosis
- Pregnancy - Postpartum.
- oral contraceptive
- HCC
- PNH (Paroxysmal nocturnal Hemoglobinuria).
- Mechanical obstruction

Idiopathic in 30% of cases

Morphology:

- swollen liver, red w/ tense capsule
- Congestion → necrosis
- Fibrosis
- Thrombi

2] Primary sclerosing cholangitis. (PSC)

Autoimmune biliary disease → inflammation → intra / extra Hepatic bile duct

↓

Fibrosis

↓

Stenosis

∴ obstruction of bile duct.

clinical Presentation:

alkaline phosphatase, biliary duct → enzyme will be released

Wt. loss على عكس الـ Budd

most common

Antimichrocondrial Abs., Antinuclear cytoplasmic Abs.

x لازم افرق بينها وبين PBC

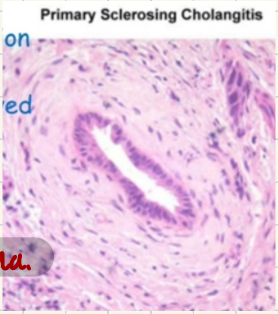
بناخذها باخر محاضرة.

Morphology:

lymphocytic infiltration

cirrhosis

- High risk of cholangiocarcinoma.



3] Secondary biliary cirrhosis.

∴ more common than PBC ⟶ they are treatable if diagnosed early

∴ obstruction only ⟶ extra hepatic

Causes:

- cholelithiasis (stones)
- Biliary atresia
- Malignancy

Past: Pay attention!

Which of the following statements is false?
A. α-1-Antitrypsin deficiency is an AR disorder that lead to pulmonary emphysema and hepatic damage.
B. liver function tests (LFTs) are abnormal in Rey's syndrome.
C. Budd–Chiari Syndrome characterized by occlusion of the portal veins.
D. Primary Sclerosing Cholangitis caused by fibrosis and obstruction of both intra-hepatic and extra-hepatic bile ducts
E. Anti-mitochondrial antibodies is associated with Primary biliary cirrhosis

(C)

Primary biliary cirrhosis:

Auto-immune disease
⟶ cholestatic liver disease.
⟶ non-suppurative granulomatous ⟶ intrahepatic only

- Pruritus, Jaundice حكة واصفرار

Biliary disease not the liver itself... : بدي اقول ب.. لو اجابوا عنده هاي الاعراض

- Alkaline ↑, cholesterol ↑
- Hepatic decompensation ⟶ Hyperbilirubinemia (Jaundice).
- Antimitochondrial Abs.

Morphology:

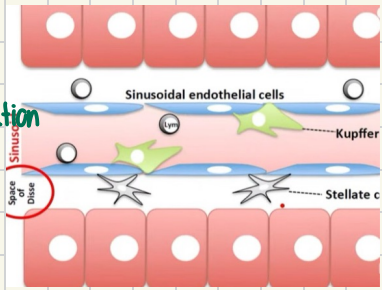
- Florid duct lesions
- Granulomatous
- cholestasis
- Bile ductular Proliferation.
- Necrosis
- cirrhosis

Sinusoidal Obstruction Syndrome

1] Bush-tea contains → Pyrrolizidine alkaloids
occurs after Bone marrow transplantation
20-30 days

2] cyclophosphamide

3] Radiation



Mechanism

Toxic injury to sinusoidal endothelium
↓
emboli formation
↓
blockage of blood Flow
↓
Passage of blood into space of Disse
↓
↑stellate cells activation in the space of disse
↓
Fibrosis occurs

Peliosis Hepatis

- Sinusoidal dilatation

Causes:
- Anabolic steroid
- oral contraceptive
- Danazol

Reversible disease.

Past عن اجزاء سابقة

- A study of persons with increased risk for ischemic heart disease reveals that some of them also have liver disease. Risk factors include lack of exercise and increased consumption of fast-food products containing high fructose corn syrup. Laboratory studies show that their blood glucose averages 117 mg/ dL. Serum AST and ALT are elevated. Abdominal CT imaging shows hepatomegaly with diffusely decreased attenuation but no focal lesions. Some of them go on to develop hepatocellular adenoma. Which of the following underlying disorders do these persons most likely have?

- A Type 1 diabetes mellitus
- B Familial hypercholesterolemia
- C Hepatitis C virus infection
- D Hereditary hemochromatosis
- E Metabolic syndrome

سؤال فيرس: مكتب وشوطالي

(E)

Is not associated with chronic liver disease
a- portal hypertension
b- cirrhosis
c- testicular hypertrophy

C

Wilson disease by cu accumulation is caused by?
a- increased absorption from renal
b- decreased absorption from hepatic
c- decreased excretion from renal
d- increase absorption from hepatic

(d)

All of the following cause fatty changes in the liver except :
A. Sinusoidal obstruction
B. Obesity
C. DM
D. Reye's syndrome
E. Viral hepatitis

A

hypo not hyper

A woman with Inflammatory bowel disease and hepatitis like symptoms with no viral load, what's elevated in her blood
a- Antimitochondrial antibodies
b- antinuclear cytoplasmic antibodies
c- anti pyruvate dehydrogenase

* a → true
But the answer is B → most common

liver tumors

Secondary tumors (metastatic) >> Primary one

Cavernous hemangioma

most common benign liver tumor

rupture+hemorrhage

liver nodules (3)

1-Focal nodular hyperplasia

Well-demarcated ⟶ central scar
Non-cirrhotic, nonmalignant
result from ⟶ local vascular injury related w/ cavernous.

Macro-regenerative Nodules

cirrhosis liver nodules
No presence of Atypical Features
Non-malignant

Dysplastic Nodules

Pre-cancer < small / large
cirrhotic liver
Atypical Feature

Hepatocyte Adenoma

- found in young female
- oral contraceptive intake
- Pregnancy women
- miss-diagnosed w/ HCC

Past

A 41-year-old, previously healthy woman has noted abdominal discomfort for the past month. Laboratory studies show normal serum total protein, albumin, AST, ALT, and bilirubin, but her alkaline phosphatase level is elevated. Serologic testing for hepatitis A, B, and C viruses is negative. Abdominal CT scan shows a 9-cm right hepatic lobe mass with irregular borders. The lesion is resected, and gross inspection reveals a central stellate scar with radiating fibrous septa that merge into surrounding hepatic parenchyma and there is a local vascular injury. What is the most likely diagnosis?
A. Metastatic adenocarcinoma
B. Focal nodular hyperplasia
C. Hepatic adenoma
D. Hepatocellular carcinoma
E. Macronodular cirrhosis

B

central scar + local vascular

One of the following is NOT true about hepatic focal nodular hyperplasia:
a. Nodular regeneration of hepatocytes.
b. High risk of malignant transformation.
c. Females predominance.
d. Not related to cirrhosis.
e. Can be associated with cavernous hemangioma

B

One of the followings combinations is FALSE:
a- liver adenoma - Acetaminophen
b- Wilson disease -ATP7B gene mutation
c- Budd-Chiari syndrome- Oral contraceptive
d- Sinusoidal obstruction syndrome-Cyclophosphamide
e- Reye syndrome- Microvesicular fatty change

A

Predisposing factors of Hepatocellular carcinoma: HCC

- Hepatitis carrier → 200 folds ↑ risk
- most common cases of HCC is usually endemic → (HBV)
- cirrhosis - alcoholism (HCV)
- Aflatoxin → P53 → ↓ of apoptosis
- hereditary tyrosinemia
- Hereditary hemochromatosis

Pathogenesis:

- repeated cycle of cell death ⟺ regeneration.
- viral integration of HBV DNA
- not limited to integrated site.

Morphology of HCC : 3 types of liver malignancy

HCC

(Vascular invasion is common.)

CC

↓

lining epi. in biliary ducts

Mixed

X Fibrolamellar Carcinoma:

develops in normal liver

hard scirrhous (fibrous)

X Cholangiocarcinoma : desmoplastic → (fibrosis)

developed in fibrotic background.

most common malignancy:

X metastasis :

→ hematogenously

AFP

Increase α-feto protein

but not specific

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 :

- Cachexia (wt. loss related to cancer)
- GI bleeding
- liver failure
- Tumor rupture.

Past

The most common predisposing factor of HCC is:
A. HBV infection
B. metastasis to the liver
C. alcohol abused
D. Drugs
E. hereditary hemochromatosis

(A)

Cholangiocarcinoma arises from which of the following ?
A. Kupffer cells
B. Hepatocytes
C. Ito cells
D. Endothelial cells
E. Biliary duct epithelium

(E)

اللهم علمنا ما ينفعنا, وانفعنا بما علمتنا

سي ابوزيد ♡.

Most common malignancy of the liver
a- Hepatocellular carcinoma
b- metastatic tumors
c- adenocarcinoma

B