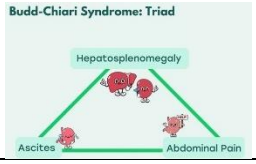
Budd Chiari syndrome



Definition *Thrombus: blood clot formed intravascularly, blood in circulation must be in liquid form. Thrombus circulates until it finds the right diameter of vessel and stop.	Thrombotic occlusion of the hepatic vein, so any condition that has an increased risk of thrombus formation→ pt can develop Budd Chiari *Condition that can be seen in other diseases, liver complications are due to other problems, but we must think of it as a possibility when we see complications. الدكتورة قصدها انه ناتج عن امراض او مشاكل اخرى This process can be: – acute -chronic
Complaints	Hepatomegaly -Wt. Gain -Ascites -Abd. Pain and tenderness *if its acute → severe symptoms , chronic → mild symp.
Causes	We should know that all these cases→ increase the risk of a thrombus so eventually, have a risk to develop into the syndrome, cause can be blood diseases, or others. 1-PCV (polycythaemia vera) 2-Pregnancy (increase likelihood to develop thrombi due to hormonal changes) 3-Postpartum 4-Oral contraceptive 5-PNH (paroxysmal nocturnal haemoglobinuria) 6-Mechanical obstruction (can be compression associated with a tumour for example, keep in mind obstruction + stasis →predispose thrombus formation) 7-Tumors within liver as (HCC) (because tumor enlarges and compress the surroundings. If the tumor for example was close to a portal vein and closed it→ thrombus) (HCC: this type of cancer tend to infiltrate the vessels → tumour growth within a vessel) 8-Idiopathic in 30% of the cases
Morphology	-Swollen liver, red with tense capsule -microscopically: centrilobular congestion and necrosis (but why do we have congestion in central veins? Because they are tributaries of portal veins) (congestion: dilated vessels + stuffed with blood. We should know that congestion level varies depending on the severity of the disease and it is associated with necrosis because once the central vein is filled with blood → compress surrounding hepatocytes → necrosis of hepatocytes, it can be acute or prolonged,, if it is prolonged → fibrosis around the central vein) -Fibrosis -Thrombi
Diagnosis	Clinical and suspicion Because we don't have a specific thing to look for all the symptoms are non-specific It's a serious disease, if not recognized early → liver failure + death Mortality rate is high if not treated.

Primary sclerosing cholangitis

Definition	Disease that affects biliary tract of liver. Not so frequent but important → Inflammation, obliterative fibrosis, & segmental dilation of the obstructed intra hepatic & extra hepatic bile ducts *This fibrosis that surround bile duct -→ segmental dilatation that gives significant appearance of hepatocytes
Notes	The importance arises because it is related to other diseases. (UC: ulcerative colitis, inflammatory bowel disease) -In PSC, UC coexists in 70% of patients. (patient with PSC mostly have UC so we must check on this) -in patients of UC, 4% develop PSC -3rd – 5th decade of life -M: F 2:1
Clinical findings	-asymptomatic pts. -persistent ↑ serum alkaline phosphatase (characteristic feature about this disease, this enzyme is a part of the liver function test, and it reflects the biliary system → this enzyme is excreted by epithelium lining the biliary system) - fatigue, pruritis (severe itching due to deposition of bile salt), jaundice (obstruction of the biliary system), wt loss, ascitis -bleeding, encephalopathy (these are extreme conditions where there is severe biliary damage and eventually development of fibrosis and cirrhosis) -This is an autoimmune disease, we would find antibodies like: Antinuclear cytoplasmic Abs in 80% or more of cases, antimitochondrial Abs < 10% of cases (why are the antimitochondrial Ab less? Because these antibodies are characteristic of other diseases that's why we don't find them at all or we find them at low rates)
Morphology (characteristic)	-Concentric periductal onion-skin fibrosis & lymphocytic Infiltrate (around the bile duct (destructed by inflame. process) → fibrosis in layers + presence of lymphatic infiltrate). -This process of fibrosis is segmental, meaning that not all the tube gets fibrosed rather that certain segments. As a result we would have → segmental obstruction -Atrophy & obliteration of bile ducts -Dilation of bile ducts in between areas of stricture -Cholestasis (because the biliary system is the target)& fibrosis -Cirrhosis, cholangiocarcinoma (10 – 15%)
Pathogenesis	-Exposure to gut derived toxins (exposure of biliary system by toxins produced by the normal flora) -Immune attack -Ischemia of biliary tree

Secondary biliary cirrhosis

Definition	Prolonged obst. To extrahepatic biliary tree, so Disease affecting the biliary→ 2nd biliary cirrhosis.

	**All these diseases have characteristics of abnormality bile ducts, narrowing of bile ducts, bleeding of hepatocytes due to toxins of bile
causes	1-cholelithiasis (stone formed in bile ducts, however some stones can be formed in the biliary system, these stones can fall in biliary system and cause obstruction which means all the bile secreted from this system is stagnant → damage hepatocytes → if not treated early → cirrhosis) 2-biliary atresia (narrowing of the biliary system, can be intrahepatic- extrahepatic, most common: atresia of bile duct) 3-malignancies (these malignancies can be primary or secondary and as they grow slowly →causing pressure from outside →obstruction) 4-stricutres (congenital or induced by surgeries → fibrous band that would eventually contract→ entrap the common bile duct or the hepatic duct)

Primary Biliary cirrhosis

Definition	Characterized by cirrhosis related to biliary disease (inflammation + destruction). Chronic, progressive & often fatal cholestatic liver disease, non-suppurative granulomatous destruction (MAIN CHARACTERISTIC) of medium-sized intrahepatic bile ducts, portal inflammation & scarring.
Presentation	Patient presents late, because the condition takes along time to develop in addition to having non-specific manifestations at the beginning. This process is graded. -Age 20-80yrs (wide range) (peak 40-50yrs) -F>M -Insidious onset -Patients mostly suffer from: Pruritis, jaundice -Cirrhosis over 2 or more decades (2-3 yrs. up to decades)
Notes	↑Alkaline phosphatase & cholesterol (because cholesterol is excreted through bile, that's why any biliary problem → increase in cholesterol) -Hyperbilirubinemia = hepatic decompensation - progression of the disease is inevitable + it can be prolonged that's why they can develop jaundice -Antimitochondrial Abs > 90% Antimitochondrial pyruvate dehydrogenase is the characteristic
Associated conditions	High probability of having other autoimmune diseases like: Sjogren synd., Scleroderma thyroiditis, RA, Raynaud's phenomenon. MGN, celiac disease
Morphology	-interlobular bile ducts are absent or severely destructed (florid duct lesion) -intra epithelial inflammation -Granulomatous inflammation (usually surrounding the biliary system) -Bile ductular proliferation -Cholestasis (EXTENSIVE) -Necrosis of parenchyma (depending on the severity) -Cirrhosis

A student asked, dr. how can we differentiate between primary and secondary biliary cirrhosis?

-Primary biliary cirrhosis is characterized by the presence of granulomas

Sinusoidal Obstruction Syndrome

Another name for this disease	Veno-occlusive disease
Notes	Originally described in Jamaican drinkers of bush-tea containing pyrrolizidine alkaloids. Not frequent but we should be aware of it because it can occur in malignant pts.
When does it occur	Pts with malignancies especially leukemic , because most of them receive bone marrow transplantation. This occurs in the first 20-30 days after bone marrow transplantation. Before receiving the new BM they undergo radiation to remove leukemic cells and clear their system, and because the radiation is systemic→ can damage the hepatocytes and the sinusoids. It can also be because of chemotherapy. (also, after the alkaloids ingestion). -Why does it occur 20-30 days after transplantation? Because that's the time needed for the end process of preparation, or in other words the time needed for the cells to damage and cause obstruction of the sinusoids.
Causes	1 Drugs as cyclophosphamide 2 Total body radiation
Incidence	-20% in recipients of allogeneic marrow transplant
Clinical Presentation	Mild – severe Death if does not resolve in 3 months, however if he survived → death is avoided.
Mechanism	Toxic injury to sinusoidal endothelium →death of the lining endothelial cells→ desquamation/separation of these cells forming clusters → emboli blockage of bl. Flow →Passage of blood into space of Disse →↑stellate cells → fibrosis. *REMEMBER: sinusoids are very delicate vascular structures, any collection of cells within →obstruction →impede the blood flow

Peliosis Hepatis

Definition	Causes	Pathogenesis	Features
Sinusoidal dilatation (it's a vascular disease)	1-anabolic steroids (taken for muscle building) 2-oral contraceptive 3-danazol	Unknown	-Asymptomatic, -reversible -Intra abdominal haemorrhage (Due to stagnation of blood flow the fluid →leaves to abdomen→its one of the causes of intraabdominal haemorrhage) -Liver failure

Liver tumours

Liver tumours can be benign or malignant, however most liver tumours are a result of metastasis (secondary tumours). Our main aim in diagnosing liver tumours is not to find if they're malignant or not, HOWEVER our main concern is its presence IN THE LIVER. WHY? Any liver mass should be followed up, especially because it's a common site of metastasis + liver plays a big role → carry on body functions (that's why we will focus on benign tumours as well)

MOST COMMON TUMORS OF LIVER? SECONDARY

MOST COMMON PRIMARY TUMOR OF LIVER? HEPATOCELLULAR CARCINOMA

Morphology of cancers:

Most common, HCC however we have CC (biliary carcinoma called cholangiocarcinoma, a cancer a rising from biliary epithelium) or mixed.

Tumours are typically→ unifocal in contrast of that of metastasis which are →multifocal. Tumours → diffusely infiltrative

Does that mean primary tumours are ALWAYS unifocal and secondary tumours always MULTIFOCAL? NO

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

Name	Type /Definition	Description	Presentation	Causes- Prognosis
Cavernous hemagioma	Benign (MOST COMMON BENIGN TUMOR) *Haemangioma: tumor of BV	Made of vessels filled with blood especially because they are Subcapsular (surface of liver)→ they can bleed. SO ANY PROCEDURE THAT MAY IRRITATE THESE BV → BLEEDING They are usually <2cm.		Once diagnosed by radiology, don't think of taking a biopsy, why? BLEEDING So if it was known to be hemagioma → bx are not indicated
Liver cell adenoma	Benign tumor that produces secretory cells By definition of adenoma: tumor of glands or tumours that produces secretory cells however, liver doesn't have glands that why we didn't say that this type of tumor is tumor of gland, instead we said IT PRODUCES SECRETORY CELLS	May be misdiagnosed as HCC. But it rarely may contain HCC. These tumours are also subcapsular so they can be ruptured	Young female on oral contraceptives because they are hormone dependent	-Hx of oral contraceptive intake -May rupture esp. during pregnancy causing severe intraperitoneal haemorrhage
Hepatocellular carcinoma	PRIMARY Malignant cancer, it's the faith of many conditions and it forms, makes up 5.4./.of all cancers (tend to metastasize through hematogenous spread that's why it can grow within the hepatic vein or even reach the IVC and causes →obstruction)		Incidence: --<5/100000 population in N&S America N& central Europe Australia (NOT FREQUENT) --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 (B) carrier state: vertical transmission (most common CARRIER RATE), increases the risk 200X. These patients may develop cancer early in life when it gets superimposed by Hep D or when the virus gets reactivated. This type of cancer is associated with HEP B / C cirrhosis itself regardless the cause increases the risk of cancer and may be absent young age group (20-40yr) (due to high supervision on the transmission of HEP B→ we reduced the incidence of cirrhosis caused by Hep B however Hep C is HARD to control) 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 (toxins produces by fungi found in improperly stored grains, these toxins can induce gene mutation (immunosuppressant gene) → imp in carcinogenesis → In African countries the exposure to these toxins is from early age that's why they have high incidence of cancer 5. Hereditary tyrosinemia (in 40% of cases) (even with the control → high risk of HCC) 6. Hereditary hemochromatosis
Pathogenesis of hepatocellular carcinoma: 1-Repeated cycles of cell death & regeneration HBC, HCV, gene mutations, Genomic instability 2-Viral integration HBV DNA integration which leads to inducing the synthesis of new protein → clonal expansion 3-HBV DNA integration 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 Aspergillus flavus) mutation of p53(tumor suppressive gene) 6-Cirrhosis (itself is a degenerative-regenerative process) HCV Alcohol Hemochromatosis Tyrosinemia (40% of pts. Develop HCC despite adequate dietary control				
Fibrolamellar carcinoma	This tumor is different that primary, its imp bec it occur in young individuals. No relation to HBV or cirrhosis better prognosis THAN HCC	Single hard scirrhous tumor. Characteristics: -LARGE CELLS -EOISINOPHILIC CYTOPLASM -FIBROTIC BACKGROUND(hence its name)	20-40 yr. M=F	**metastasis** Vascular – lungs, bones, adrenals, brain, in 50% of cholangiocarcinoma **C/P** abd. Pain, malaise, wt. loss increase α-feto protein in 60 – 75% of pts. BUT ITS TOTALLY UNSPECIFIC • 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 OF DEATH :** **1 Cachexia** **2 GI bleeding** **3 Liver failure** **4 Tumor rupture and haemorrhage**

Cholangiocarcinoma	Tumor of biliary system (adenocarcinoma)	Desmoplastic(tumor is associated with fibrosis, tumor based fibrosis) IMP BECAUSE IF WE FIND A TUMOR IN THE ABDOMEN FORMING SEVERE DYSPLSIA WE SHOULD THINK OF → pancreas or biliary system tumours		

NON-NEOPLASTIC TUMORS THAT FORMS NODULES

Name	Description	Cause	Presentation	Prognosis
Focal nodular hyperplasia	-Well demarcated hyperplastic hepatocytes nodules with central scar. -Non-cirrhotic background of liver -Not neoplasm but nodular regeneration	Local vascular injury to liver causing arichtecture loss + parenchymal degeneration + fibrosis. This injury can be because of a vascular problem	--Females of reproductive age --20% of cases have cavernous hemagnioma	No risk of malignancy
Macro regenerative nodules	Background of Cirrhotic liver (so, we have cirrhotic nodules and WE FIND AN ENLARGED OUTSTANDING NODULE, So we have to see what caused it to enlarge (to check if its malignant)) -Larger than cirrhotic nodules -No atypical features (microscopically) -Reticulin is intact			No malignant potential
Dysplastic nodules	Larger than 1 mm Background of a Cirrhotic liver -Atypical features, pleomorphism and crowding With high proliferative activity -High or low dysplasia -Has two types, small – cell dysplastic nodules Large – cell dysplastic nodules			Precancerous (monoclonal, +ve gene mutations) **gene mutations are what makes it precancerous