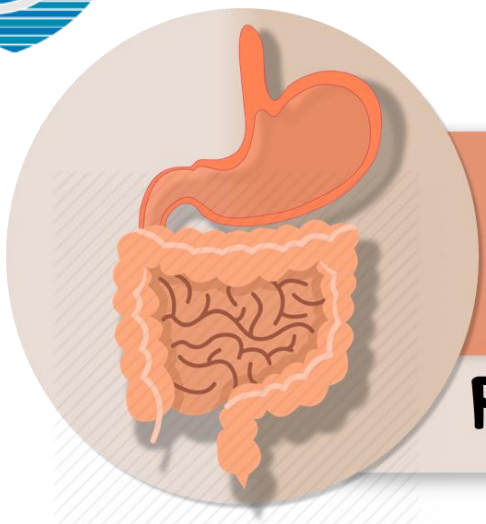

GI system

Pathology

◉Sheet ○Slide

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Viral hepatitis

have many types each type is associated with different outcomes "complication", some can result in acute one ,others result in chronic one, and some of them can result in severe complications called "fulminant hepatitis". It's important to know which viruses can lead to chronic infections and which can cause cirrhosis.

We have hepatitis A, B, C, D and E. Each one has its own characteristic features, inoccupation period and rout of transmission.

fulminant hepatitis

It's the development of hepatic inflammation, insufficiency or failure; which occur in short period of time "2-3 weeks" in this case the main thing to occur in liver is **necrosis**

sometimes the failure may take longer and this called **sub-fulminant** hepatitis "3 months" (the period between acute infection and development of hepatic failure).

causes

- most common cause is hepatitis B virus, especially when its associated with co-infection with hepatitis D virus "also C can cause fulminant hepatitis "

- Drugs and chemicals can also cause fulminant hepatitis.

"how can we exclude viral presence in order to prove that fulminant hepatitis is caused by drugs ??

by serology and looking for antibodies against viruses "Not PCR because its coasty and takes a long time"

- obstruction of hepatic vein can cause fulminant hepatitis.

also Wilson disease, fatty change and autoimmune hepatitis can cause fulminant hepatitis.

IF we look at it we will notice that the liver size is small, because it's necrotic which is the main feature of fulminant hepatitis.

It's a very serious condition and can be associated with liver failure and the death of the patient "some lucky patient can survive and show regeneration "

We can notice that the colour is pale and presence of yellowish areas that represent necrotic tissues .

chronic hepatitis

what's dangerous about viral hepatitis is the probability of developing chronic hepatitis; and that's because chronicity is associated with fibrosis which is irreversible.

Definition of chronic hepatitis: the persistence of viral antigen in the patient's serum beyond the 6 months.

constant levels of antibodies and antigens also indicate chronic hepatitis

most common cause is hepatitis B and C viruses " most of the patients with hepatitis C develop chronic hepatitis"

also the co-infection of HBV with HDV increase the risk of developing chronic infection.

features of chronic hepatitis : "all features of inflammation "

- inflammatory infiltrate including lymphocytes that can cause lymphoid follicles which indicate severe necrosis "same as the one we see in lymph nodes "

- necrosis : hepatitis C cause destruction of the bile duct, in addition to the inflammation.

- steatosis : infiltration of liver cells with fat.

Inflammation in the liver starts in portal areas, and if it is limited to the portal area usually it's mild; but if its spread to parenchyma, producing cell death and necrosis that's what we call **interface hepatitis**

Interface hepatitis can develop into bridging necrosis"the stage where liver parenchyma develops to fibrosis" that can progress into cirrhosis.

-ground glass appearance: homogeneous eosinophilic appearance of the cytoplasm "caused by HBV antigen presence within the hepatocyte cytoplasm"

nowadays it's easy to know whether the infection is caused by HBV or HCV and that's achieved by serology.

-Sanded nucleoli: appear like sand –chromatin start to form small particles.

-In term of gross appearance you can notice dark areas with pale inflamed area which is parenchyma and can be necrotic. Microscopically the hallmark of inflammation is the infiltration by lymphocytes (which appear as single cells with dominant nuclei, and the cytoplasm is minimal and may not be apparent).

NOTE: REFERE TO THE SLIDES FOR PICTRURES

-Death of cells (councilman bodies) which are dead cells that suffered from the infection creating scattered cells, with disappeared nucleus,

and they are associated with gross necrosis of hepatocytes.
if the body can't decrease the antigen and raising the antibodies, antibodies remain high and this can progress into chronic hepatitis (which is characterized by fibrosis) that transform the parenchyma into nodules which can progress into complete cirrhosis!! "Seen as rounded nodules under the microscope" and the treatment in that case is delaying the fibrosis to avoid cirrhosis (one approach of treatment is directed towards delaying the developing of fibrosis).

So cirrhosis isn't achieved until complete nodules are formed.

in order to detect fibrosis more obviously there is a special stain for fibrous tissues that stain fibrous tissue blue.

chronic hepatitis have five grades according to its severity and the degree of development into cirrhosis

A very important part of viral infections is the carrier state "have positive serology without clinical symptoms and can transmit the infection" and that why before blood donation we do serology test for hepatitis B to the donator and if he is positive then he cant donate blood

The most common cause of carrier state is vertical transmission "during delivery", this transmission is because of the opening of blood vessels during delivery that can expose maternal blood to the fetal blood. Carrier state also happens when there is any sort of immunodeficiency.

Hepatitis B and C viruses can cause carrier state.

check the end of the slide "liver 1" for chronic hepatitis pictures

Auto immune hepatitis

-it's a form of clinical hepatitis with histologically similar features to the viral one "inflammation , necrosis , cell death ,etc."

-it can be slowly progressive disease or the progression may be more severe.

-the important thing about auto immune hepatitis is to be diagnosed because the patient would largely benefit from early immunosuppresses "on the other hand in viral case there won't be a response; that's why its important to differentiate between the two forms "

Features

-Females are affected more (like most of the autoimmune diseases)

-They are negative to the viral infection after serological tests

-increased serum liver Ig antibodies levels "some patients won't have this feature"

-History of autoimmune diseases "as we know autoimmune diseases present together"
-The **most common** type of antibodies is the anti-smooth muscles antibodies "which are either actin, the most common, or troponin or anti-troponin"
-Other type of antibodies that can be seen in those patients liver-kidney antibodies, which are directed against certain enzymes in these cells; but it is less frequent. The rarest are antibodies directed toward liver-pancreas antigen.

Outcomes

Variable outcomes are encountered, it might be mild or severe and patient with severe type can progress into chronic hepatitis

Because its an autoimmune disease its considered not curative and the

only thing to do is try to suppress the immunity and decrease the effect of the antibodies.

Risk of developing cirrhosis is about 5%.

fatty infiltration "non-alcoholic fatty liver diease"

we used to thing its not a disease but now we recognize that it could progress so its consider as a disease

It has a grading system to evaluate the outcomes so it can be mild "without inflammatory process" and could be associated with inflammation then it's called steatohepatits "more severe and can be associated with fibrosis,damage to the hepatocytes and may progress into cirrhosis"

The most common condition that is associated with the development of non alcoholic fatty liver disease is type 2 diabetes "because there's a connection between carbohydrates and fat metabolism"

Obesity itself is associated with increased free fatty acids in the circulation and deposition, so, very obese individuals with dyslipidaemia (increase in the free fatty acids in the blood, which are triglycerides and low density lipoproteins) are associated with fatty deposition in the liver.

when the fat depose in the liver it can interfere with different functions , it can cause impairment of oxidation of fatty acids, or increase the uptake of free fatty acids, or decrease the secretion of the mobilizers of fatty acids from the liver into circulation. Which in turn can cause fatty infiltration.

Fatty infiltration can stimulate response similar to inflammation, releasing of chemical mediators that can produce damage.

Usually patients are asymptomatic and most of the time abnormality is discovered by routine tests.
And if the symptoms is present usually they are non specific “fatigue, malaise, abdominal discomfort” sometimes if its severe and progressed we might have severe symptoms

Nowadays, fatty infiltration is believed to be a contributor in cryptogenic cirrhosis.

Hemochromatosis

The most common type of metabolic disorders in the liver

definition of Hemochsomatosis “accumalation of iron deposition in the liver and other organs such as pancreas

Can be primary “inherited” or secondary “acquired”

Usually we use the term “Hemochromatosis” for the inherited one

Secondary “acquired” Hemochromatosis is usually called hemosiderosis

Most common cause of secondary hemosiderosis is hemolytic anemia “such as thalassemia” as patients require constant blood transfusion, so as they get blood they are also getting extra iron to there body. The other thing is when the RBCs rupture it releases hemoglobin with contain iron that will accumulate in the organs particularly in the liver.

Ineffective erythropoiesis “type of hemolytic anemia” is when synthesized RBC can’t be released into the circulation and die within the bone marrow.

Another cause of secondary hemosiderosis is “Bantu siderosis” that’s common in African countries where people prepare their food with irony tool so they increase the uptake of iron

chronic liver disease also associated with increase the iron in the liver “not a significant increase like others” because in chronic liver disease iron can’t be released to be metabolised, so it accumulate in the reticuloendothelial system “ the liver is part of it”

Features

- cirrhosis

-Involvement of other organs such as “pancreas” and cause the destruction of beta-cells ”insulin release” so the patient will suffer from diabetes

-Liver enlargement
-pigmentation of the skin “iron deposited in the skin”
-cardiac problems and arthritis “iron deposited in joints and heart”

When you see these clinical symtoms together you should think of hemochromatosis, as these symptoms are very rare to appear together.

epidemiology

Patients are in their 5th – 6 th decades for females, for males in their 40ths

Males’ incidence is earlier than females because females loose blood monthly which delay the deposition of iron

There is genetic mutation contributes to this disease such as mutation in the HFE gene on chr.6, this gene is responsible to regulate the amount of iron entering our bodies.

Pathogenesis

The only way to control iron in our bodies is by controlling the absorption, and there is no regulation in the excretion. Absorption and secretion should be balanced, and increment in the absorption will end up depositing iron

Note: the accumulation to occur it needs time, so patients at old ages show the symptoms.

Normally body iron is about 2-6 gm in the body with 0.5mg in the liver however in patients with Hemochromatosis it increases to 50 gm with 1\3 in the liver.

Normally we need to compensate the loss of iron, that's a result of desquamated cells in skin and GI "minimal loss"

The source of iron in our body is through diet "absorption"

Absorption of iron in intestines is controlled through hormone known as "hepcidin" that synthesized by the liver

Hepcidin acts by inactivating channels located on the enterocytes for iron transport from the gut lumen into the enterocytes. So when there is a need for iron, the hepcidin level drops allowing the iron to inter from the lumen to the enterocytes, and there in the enterocytes some of the

iron are stored and some are transported to the liver to be deposited and utilized.

When there a mutation in hepcidin gene its level decrease causing increase in iron absorption which lead to deposition that lead to Hemochromatosis

Mutation that affect HFE gene is :
1-Mutation at 845 nucleotide → substitution of cysteine by tyrosine at AA 282 (C282 Y)

2-Substitution of histidine by aspartate at AA 63 (H63D)

Patients may have the first gene only or the second one only or both of them

Carrier rate of the c282y is 1\70 which isn't rare

Homozygous of the gene develop the diseases

complications

-Iron deposition may affect the lipids which will cause **Lipid peroxidation** (that's why these patients may have fatty change)

-Iron stimulate fibrous tissue that will cause **fibrosis** which can progress into cirrhosis

-Iron can react with the DNA and cause **DNA damage** which will cause loss of cells