

Diseases of Liver, Gallbladder and Pancreas

Subject Actuality

pathology of hepatobiliary organs is quite common.

Most of all one has to do with liver diseases.

The liver is remarkable for a great variety of its functions.

No other organ has such a wide range of influence on the body's homeostasis.

The liver's main functions are: metabolic, disintoxicational, biligenetic and that of biliary excretion. Besides, it is involved in digestion, blood coagulation, thermal regulation, hemodynamics, phagocytosis and other processes.

Diseases of Liver

•Liver lesion is caused by various factors. Among them are biologic agents (hepatitis virus, tubercle bacillus, spirochete, lamblias, amoebas, actinomycete, echinococci, ascarids); hepatotropic poisons, including medicines (tetracycline, PAS(A), sulfanilamides, steroid hormones), industrial chemicals (carbon tetrachloride, chloroform, arsenic), vegetal toxins (aflatoxin, muscarine); vaccines and serums. The following disorders are etiologically important blood circulation disorders in hepatic vessels (thrombosis, embolism), tumours, endocrine and metabolic diseases (pancreatic diabetes, thyrotoxicosis, obesity), hereditary fermentopathies.

Diseases of Liver

•The pathogenesis of the diseases manifests itself in two mechanisms:

•1) direct lesion of hepatocytes in the form of dystrophy and necrosis;

•2) immune lesion of hepatocytes by auto-antibodies.

•Besides, physicians often have to do with diseases of gallbladder, bile duct and pancreas. All this arouses the necessity of knowing the structural bases of the given pathology.

Hepatosi

•Massive hepatic necrosis (acute hepatosis) is characterized by the progressive necrosis of liver parenchyma. It is usually caused by exogenous (mushroom poison, chemical compounds) and endogenous (pregnancy, thyrotoxicosis) factors. In the progression of massive hepatic necrosis one singles out the stages of yellow atrophy, red atrophy and recovery. The duration of the disease is about three weeks.

Hepatosi

•During the first days one can observe fatty degeneration of hepatocytes in the centre of the particle. It is quite soon followed by necrosis and autolytic destruction. The liver becomes smaller, flaccid and turns yellow. That's why it is called **yellow atrophy**.

Fatty hepatosis

– Fatty liver and liver cirrhosis.

•The detritus yields to resorption by macrophages. The stroma becomes "uncovered" and sinusoids, finding no resistance of hepatocytes, become overfilled with blood. The liver turns yellow with red specks (the stage of red atrophy). At this stage hepatic failure often develops.

•Hepatic failure has general clinical representations of tissue turgor decline, xeroderma, skin icteritiousness and sclera, vessel "stars" and skin haemorrhages, enlargement or diminution of liver, there often occurs splenomegaly, ascites, edemas. The pathologic process progression provokes a complex of hepatic, mental and neurologic disorders. The affected person has fetor hepaticus, the liver aches at palpation and he/she suffers from fever and leucocytosis.

•The gravity of hepatic failure is usually estimated according to how deep nervous and mental disorders go. Three stages of hepatic failure are singled out. The stage of psycho-emotional disorders is characterized by emotional instability: swift change of humour, depression or euphoria, insomnia at night and sleepiness in daytime, headache, giddiness, memory weakening. The stage of neurologic disorders and impairment of consciousness manifests itself in sudden excitation which is followed by inhibition, tremor of hands, lips and eyelids. Progressive hepatic failure ends with coma (the third stage).

fatty change

- This liver is slightly enlarged and has a pale yellow appearance, seen both on the capsule and cut surface. This uniform change is consistent with fatty metamorphosis

hepatic fatty change

- The lipid accumulates in the hepatocytes as vacuoles. These vacuoles have a clear appearance with H&E staining. The most common cause of fatty change in developed nations is alcoholism. In developing nations, kwashiorkor in children is another cause. Diabetes mellitus, obesity, and severe gastrointestinal malabsorption are additional causes.

fatty change

- Here are lipid vacuoles within hepatocytes in a case of macrovesicular steatosis. The lipid accumulates when lipoprotein transport is disrupted and/or when fatty acids accumulate. Alcohol, the most common cause, is a hepatotoxin that interferes with mitochondrial and microsomal function in hepatocytes, leading to an accumulation of lipid.

Hepatitis

- Hepatitis is an acute or chronic liver disease characterized by dystrophic and necrobiotic changes of parenchyma combined with the inflammatory stroma infiltration. Hepatitis may be a separate nosologic unit (primary) or a manifestation of other diseases (secondary).

Primary hepatitis

- develops under the influence of hepatotropic viruses (viral hepatitis), alcohol (alcoholic hepatitis), medicines (medicamentous hepatitis), cholestasis (cholestatic hepatitis). Viral and alcoholic hepatitis are the most common forms of hepatitis.

Secondary hepatitis

- accompanies a wide range of diseases. They are infectious diseases (typhoid fever, dysentery, cytomegalia, yellow fever, malaria, tuberculosis, sepsis), thyrotoxicosis, rheumatic diseases, digestive tract pathology, intoxications.

Acute hepatitis

- can be exudative and productive. Exudative hepatitis is in its turn divided into serous and suppurative.

Chronic hepatitis

- is characterized by parenchyma destruction, cellular infiltration of stroma, sclerosis and changed regeneration. Three types of it are singled out – aggressive, where hepatocytes dystrophy and necrosis prevails, persistent, where cellular infiltration of portal areas and intraparticular stroma prevails, cholestatic characterized by cholestasis, cholangitis and cholangiolitis.

Viral hepatitis

- is caused by hepatotropic viruses. Liver cells are damaged either by the allergic reaction of cytolytic type or by the hypersensibility of delayed type. Autoimmunisation is connected with a specific liver lipoprotein that forms as a result of virus replication in hepatocytes and acts as an auto-antigen. After the recovery the disease leaves typospecific immunity that's why the person may be affected by a different type of viral hepatitis.

- The following clinicopathologic forms of viral hepatitis are singled out:

- acute cyclic (icteric), anicteric, necrotic (malignant), cholestatic, chronic.

- At its peak the *cyclic (icteric) form* is characterized by the ballooning degeneration, focal and coagulation necrosis of hepatocytes. Groups of hepatocytes that have undergone coagulation necrosis form round homogenous eosinophilic structures which are forced out into perisinusoid spaces – Councilman's corpuscles. Cholestasis and necrosis of hepatocytes results in hepatocellular jaundice. At the same time there occurs lympho- and macrophage infiltration of portal tracts and sinusoids. Macroscopically, the liver is larger in size, the capsule is tense, dense and red (*large red liver*).

Acute viral hepatitis- lympho- and macrophage infiltration of portal tracts.

Acute viral hepatitis.

Acute viral hepatitis - acute cyclic (icteric) form.

- In the course of recovery the liver returns to normal size, hyperaemia decreases. The capsule is somewhat thickened and dingy; adhesions appear between the capsule and the peritoneum. Reparative processes prevail over the destructive ones, lympho- and macrophage infiltration becomes focal. The process ends with liver sclerosis that may develop into cirrhosis.

- The ***anicteric form of viral hepatitis***, compared to the icteric one, is characterized by less evident morphologic changes although at laparoscopy one finds the picture of large red liver. Ballooning degeneration and Councilman's corpuscles are rarely found in this form. But one can clearly observe proliferation of reticuloendotheliocytes. Lympho- and macrophage infiltrations do not destroy the terminal plate, there is no cholestasis.

- The ***necrotic form*** is first and foremost marked by the progressive necrosis of parenchyma. The liver rapidly diminishes in volume, becomes contracted and grey-brown in section. Microscopically one can observe necroses of hepatocytes, the accumulation of reticuloendotheliocytes, Councilman's corpuscles, "uncovered" stroma as a result of resorption of necrotic masses, haemorrhages, cholestasis in capillaries. If the affected person does not die of hepatic coma, postnecrotic liver cirrhosis develops.

Acute viral hepatitis - necrotic (malignant) form.

- The ***cholestatic form*** manifests itself in prevailing cholestasis with the development of cholangitis and cholangiolitis on the basis of hepatocytes destruction, and lympho-, macrophage and neutrophil infiltration of stroma. One often finds Councilman's corpuscles.

The ***chronic form*** of viral hepatitis

- is represented by active or persistent hepatitis. Active hepatitis develops on the basis of sclerotic liver changes. It is characterized by ballooning degeneration, necrosis of hepatocytes and inflammatory stroma infiltration. Liver regeneration proves incomplete which leads to the development of cirrhosis. The persistent form is characterized by prevailing infiltration of sclerosed portal areas with lymphocytes, histiocytes and plasmatic cells. Dystrophic hepatocyte changes are low-grade.

- Chronic persistent hepatitis rarely develops into cirrhosis.

- In viral hepatitis death occurs due to acute or chronic hepatic failure.

Alcoholic hepatitis

- is an acute or chronic liver disease caused by alcoholic intoxication. Ethanol and acetaldehyde are hepatotropic poisons. Ethanol is neutralized by liver ferment - alcohol dehydrogenase. Its synthesis in liver is genetically predetermined and quantitatively specific for each individual. After a long period of alcohol abuse the alcohol dehydrogenase's protective effect is not sufficient to safeguard the liver from affection and at a certain alcohol concentration there occurs hepatocyte necrosis. The cytotoxic effect of alcohol, even in small doses, manifests itself in the liver which has been previously affected by such diseases as chronic hepatitis, fatty hepatosis and cirrhosis. Cessation of alcohol consumption leads the process into a benign course. But if alcohol consumption continues, chronic hepatitis progresses and ends with liver cirrhosis as ethanol drastically suppresses regenerative potential of the organ.

- At the time of acute alcoholic hepatitis the liver is larger in volume and dense, light brown areas alternate with brown-red ones. Microscopically one can observe necrosis of centrilobular hepatocytes. The so called alcoholic hyaline (Malori's corpuscles) can be found in their cytoplasm which is an important diagnostic sign. Peripheral hepatocytes are in the state of fatty degeneration. Necrosis areas and portal tracts are infiltrated with neutrophils.

Occasionally, especially in previously affected liver, massive hepatic necrosis occurs. In most cases after the cessation of alcohol consumption the liver structure regenerates.

non-alcoholic steatohepatitis (NASH)

- the appearance of fatty liver in patients without a history of alcoholism. NASH can be seen with diabetes mellitus. NASH can be reversible, but in some cases it proceeds to fibrosis and even cirrhosis. There is variable inflammation. This trichrome stain demonstrates blue-staining collagen extending from the centrilobular region at the right.

Liver cirrhosis

- is a chronic diseases characterized by sclerosis, structural change and the deformation of liver. The pathomorphology of cirrhosis includes the following liver changes: hepatocytes dystrophy and necrosis, deranged regeneration, diffuse sclerosis, structural change and deformation of the organ. At the time of cirrhosis the liver is dense and gibbous, its volume usually diminishes but in rare cases it may increase.

The cirrhosis

- development is based on hepatocytes dystrophy and necrosis. Their destruction leads to intense regeneration of preserved parenchyma. It results in the formation of nodular regenerates and false particles which are wrapped in connective tissue. The false particles are characterized by deranged angioarchitecture. They often lack the central vein or it is located in peripheral areas and connective tissue membrane develops in sinusoids. All this causes blood circulation disturbance in the liver. Increasing hypoxia leads to dystrophy and destruction of hepatocytes in nodular regenerates and to intense excrescence of connective tissue, which further disturbs the microcirculation. The process develops like a chain reaction with constant intensification of sclerotic changes.

The classification of sclerosis

- is based on etiologic, morphologic, morphogenetic and clinicofunctional criteria.

Postnecrotic cirrhosis

- develops after massive necrotic liver changes, for example after massive hepatic necrosis, viral or alcoholic hepatitis. The necrotized tissue resolves, the stroma and central veins collapse, triads are close to each other. Vast fields of connective tissue develop in these areas and from the organ's surface they look hollow. Big nodular regenerates appear. According to its morphology, it is usually a macronodular form of cirrhosis, more rarely – a mixed one.

Portal cirrhosis

- is a micronodular form. It develops as a result of the circulation deficiency, chronic alcoholic hepatitis, malnutrition and metabolic disorders. The connective tissue expands in the directions of portal tracts and penetrates into liver particles in the form of processes dividing the particles into smaller false ones. Moderate cellular infiltration of stroma remains as a manifestation of previous hepatitis.

Portal cirrhosis.

Biliary cirrhosis

- can be primary and secondary. *Primary cirrhosis* is the result of nonsuppurative destructive (necrotic) cholangitis and cholangiolitis. In response to destruction there occurs proliferation and cicatrisation of bile ducts, infiltration and sclerosis of the periportal areas, the destruction of peripheral hepatocytes and the formation of septa and false particles as in portal cirrhosis. The liver is enlarged, grey-green in section, and its surface is smooth or fine-grained.

– Biliary cirrhosis.

Liver in mechanical (obstructive) jaundice

Secondary biliary cirrhosis

- is caused by cholestasis (cholangiostatic cirrhosis) as a result of extrahepatic obstruction of bile duct (stone, tumour) or by bile duct infection with the development of bacterial, usually suppurative, cholangitis and cholangiolitis (cholangiolitic cirrhosis).

Secondary biliary cirrhosis

Morphologic symptoms of cirrhosis

- are dilatation and rupture of bile capillaries, which causes peripheral hepatocytes necrosis. Connective tissue expands according to the morphogenesis of portal cirrhosis. In secondary biliary cirrhosis the liver is enlarged, dense and green due to bile impregnation, in section one can see dilated ducts filled with bile.

Mixed cirrhosis

- appears as a result of portal one supplemented at a certain stage by necrotic liver changes.

Mixed cirrhosis

- Liver cirrhosis causes typical extrahepatic derangements: jaundice and haemorrhagic syndrome as a sign of hepatocellular deficiency, cholestasis and cholemia; exhaustion as a result of digestion disorders caused by stasis and atrophy of gastrointestinal tract in portal hypertension; splenomegalia as a result of reticuloendothelium hyperplasia and sclerosis. This leads to the development of extrahepatic portacaval shunts due to which some blood bypasses the liver and discharges the portal vein. Affected people have dilated veins in the esophagus, the hemorrhoidal plexus and in the stomach, dilated hypodermic veins in the thorax and the abdominal wall. The latter are called "Medusa heads". The varicosity of the above mentioned veins goes together with the thinning of their walls which is often the cause of profuse esophageal, gastric or hemorrhoidal haemorrhage.

Esophageal haemorrhage.

- As a result of portal hypertension and the lesion of liver parenchyma where the degradation of antidiuretic hormone occurs, the transudate infiltrates into the abdominal cavity, sometimes in the volume of 10 litres. This phenomenon is called ascites. The ascitic fluid, accumulated in the abdominal cavity, compresses blood vessels and internal organs deranging the blood flow. In kidneys one finds signs of acute renal insufficiency (tubular epithelium necrosis) and, occasionally, hepatic immune complex glomerulonephritis, which cause the development of hepatorenal syndrome. In most cases people affected by cirrhosis die of chronic hepatic failure. Besides, cirrhosis may be the basis for the development of liver cancer.

Cholecystitis

- Among the pathologic processes in the gallbladder acute and chronic inflammation (cholecystitis) and gallstones are the most common.

acute cholecystitis

- At the time of the inflammation can be catarrhal, fibrinous and suppurative (phlegmonous). It is caused by ascending and descending infection on the basis of biliary dyskinesia and cholestasis. Important to its development are gallstones which traumatize mucous tunic often causing pressure sores. Acute cholecystitis is complicated by the breaking of gallbladder wall with the development of bile peritonitis. In cases of gallbladder duct obstruction and pus accumulation in the cavity gallbladder empyema develops. The spreading of the suppurative process beyond the organ is complicated by suppurative cholangitis, cholangiolitis and pericholecystitis with the formation of adhesions.

Jaundice peritonitis

Chronic cholecystitis

- is the result of acute one. Morphologically it manifests itself in mucous tunic atrophy and sclerosis with lymphohistiocytic infiltration. Occasionally the petrification of the gallbladder wall and adenomatous excrescence of the mucous tunic occur.

- Gallstones are often the cause of calculous cholecystitis. Such cases manifest themselves in the chronic inflammation with periodic exacerbations. The gallbladder wall may be broken by the stone causing the development of bile peritonitis. When the stone comes down into the general bile duct and causes its occlusion, obstructive jaundice develops.

Calculous cholecystitis and biliary cirrhosis.

Liver Cancer

- Primary liver cancer is the eighth on the list of cancers of other localization.

- According to the macroscopic picture, one singles out nodular – one or several green nodes – and diffuse cancer, according to its growth pattern – infiltrating, expansive and mixed cancer. According to the histogenesis, one singles out hepatocellular and cholangiocellular cancer.

Hepatocellular cancer

- is the most common one. In 60-80% of cases it develops on the basis of liver cirrhosis. One often finds HbsAg in cancer cells.

- According to the macroscopic picture, liver cancer may have trabecular, solid or trabecular-solid construction with cellular atypism, invasion into venous vessels and subsequent hematogenic metastasis.

Cancer of liver.

Cholangiocellular cancer

- is more common among people older than 60. It grows out of bile duct epithelium and is not connected with cirrhosis. In the macroscopic picture it resembles a dense node of white colour. According to the microscopic structure, it is more often an adenocarcinoma, sometimes tumour cells secrete mucus. It usually spreads in a lymphogenous way.

- More often one can find secondary metastatic malignant tumours in the liver which metastasize from the gastrointestinal tract, lungs, kidneys or mammary gland.

- The malignant process in the liver may result in hepatic failure which is often the cause of death.

Pancreas diseases

- Pancreatitis*. One distinguishes between acute and chronic pancreatitis.

Acute pancreatitis

- is connected in 80 % of cases with cholelithiasis or with alcoholism. Important to the pathogenesis of the disease development is the ischemic lesion of the organ's parenchyma due to arterial thrombosis; medication damage, etc. With the disease progression there appear white or yellow-white areas of fat necrosis in the surrounding tissues (steatonecrosis). The gland is swollen, sometimes one can observe haemorrhagic imbibition of parenchyma. In such cases the tissue turns black-brown with the areas of necrosis.

Fat necrosis of pancreas

Chronic pancreatitis

- often occurs after a long period of alcohol consumption. Fibrosis, cicatricial narrowing of ducts, acinar tissue atrophy develops in the tissue. The gland is dense and grey; in some places one can find cysts with calcareous content.

Pancreas tumours

- are divided into benign (adenoma) and malignant (carcinoma). The head of pancreas is affected in 60% of cases, the body – in 20%, the tail – in 5%. Head carcinomas obstruct the outlet of general bile duct and cause obstructive jaundice.

thanks