Materials
for students for practical classes in pathological anatomy
at the Department of Pathological Anatomy
II year Faculty of Dentistry

Topic: "**Disorders of metabolism in cells and tissues.** Pathology of accumulation (dystrophy). Disorders of protein and carbohydrate metabolism. Hyaline changes. Mucoid and fibrinoid swelling"

1. The purpose of the lesson. To study the issues of etiology, pathogenesis, morphology, complications and outcomes of violations of protein and carbohydrate metabolism on the examples of parenchymal and stromal-vascular dystrophies.

2. Requirements for the level of the student for mastering the discipline - pathological anatomy. The student should know:

1. Terms - pathological anatomy, autopsy, biopsy, injury, dystrophy, parenchymal dystrophies, stromal-vascular dystrophies, mixed dystrophies, decomposition, perverted synthesis, infiltration, transformation, "tiger heart".

2. Questions of etiology, pathogenesis, morphology of protein and fat parenchymal and stromal-vascular dystrophies, pathological calcification.

3. The essence and basic patterns of development of dystrophies.

4. Characteristic changes in internal organs in protein and carbohydrate parenchymal and stromal-vascular dystrophies.

5. Mechanisms of development, morphology and functional significance of hyaline changes and hyalinosis.

Theoretical aspects.

Damage can be represented by two pathological processes - dystrophy and necrosis, which are often sequential stages.

Non-lethal cell damage is called **dystrophy**. This damage can manifest itself as intracellular or extracellular accumulations (accumulation) of abnormal amounts of various substances: 1) water, lipids, proteins and carbohydrates; 2) abnormal substances, including exogenous ones, such as ions, products of disturbed metabolism; 3) pigments. All of them can accumulate transiently or

permanently, be harmless or toxic, localized in the cytoplasm (more often in lysosomes) or in the nucleus.

Intracellular accumulation. There are three types of intracellular accumulation.

Firstly, these are accumulations of natural endogenous metabolites, which are formed in a normal or accelerated rhythm, and the rate of their removal is insufficient (for example, with fatty changes in the liver).

Secondly, it is the accumulation of endogenous substances that cannot be metabolized. A common cause of such accumulations is a genetic defect, as a result, metabolic products are not used, but are deposited inside the cell, and accumulation diseases develop.

Thirdly, the accumulation of abnormal exogenous substances that the cell can neither destroy with the help of enzymes, nor transport to another place (for example, coal particles).

Proteins. With an excess of protein in the cytoplasm of cells, clusters are revealed that look like round eosinophilic drops, vacuoles or masses. Such changes are called protein dystrophy.

Parenchimatous protein dystrophy

Hyalin changes in the cells (hyaline-dropsical degeneration)

In renal diseases associated with the loss of protein in the urine (proteinuria), the protein passes through the glomerular filter into the proximal tubules, from where it is reabsorbed by epithelial cells using pinocytosis. In the case of an excess of protein in the primary urine, the process of reabsorption is disrupted and phagolysosomes are formed during the fusion of pinocytic vesicles with lysosomes, which form large eosinophilic drops in the cytoplasm of epithelial cells of the proximal tubules.

Roussel's bodies are an example of excess protein accumulation.

Eosinophilic inclusions in liver cells in alcoholic illness, especially characteristic of acute alcoholic hepatitis, are called Mallory bodies.

Disturbance of protein metabolism is often combined with damage to the Na +, K + -pump. Cells lose their ability to maintain ionic and fluid homeostasis, which leads to the accumulation of sodium ions and cell swelling or hydration. This pathological process is called **hydropic dystrophy.** Protein hydropic dystrophy can occur in the epithelium of the renal tubules in nephrotic syndrome as a result of damage to the systems responsible for the reabsorption of protein and water.

Hydropic degeneration of hepatocytes is characteristic of viral hepatitis B, which reflects the perversion of the protein-synthetic function of liver cells due to the reproduction of the virus. The most pronounced hydropic dystrophy bordering on colliquation cell necrosis is called balloon dystrophy.

Hyperkeratosis is a pathological process characterized by excessive keratinization of the stratified squamous keratinizing epithelium (skin).

Leukoplakia is a pathological process characterized by excessive keratinization of the stratified squamous non-keratinizing epithelium (mucous membranes of the oral cavity, pharynx, esophagus, cervix).

Stromal-vascular (mesenchymal) dystrophies develop as a result of metabolic disorders in the connective tissue and are detected in the stroma of organs and vascular walls.

Stromal vascular dysproteinosis.

Among stromal-vascular dysproteinosis, mucoid swelling, fibrinoid swelling, hyalinosis and amyloidosis are distinguished.

Mucoid swelling, fibrinoid swelling and hyalinosis can be successive stages in the disorganization of connective tissue (for example, in rheumatic diseases).

A. Mucoid swelling.

* Superficial and reversible disorganization of the detachable tissue.

* It is characterized by the accumulation of glycosaminoglycans (mainly hyaluronic acid) in the paraplastic substance (in the main substance of the connective tissue), which leads to an increase in vascular tissue permeability and the release of finely dispersed plasma proteins - albumin.

The development mechanism is infiltration.

Mucoid swelling is more common in the walls of arterioles and arteries, heart valves, parietal endocardium.

Macroscopic picture: an organ or tissue is usually not changed.

Microscopic picture: the phenomenon of metachromasia is revealed, especially with toluidine blue: in the foci of mucoid swelling, the accumulation of glycoaminoglycans is visible, giving metachromatic (lilac) staining.

Electron microscopic picture: enlarged interfibrillar spaces containing granular protein masses are revealed; collagen fibers are preserved, only in places some of their razvlecheniya comes to light.

Is mucoid swelling a reversible process? however, it often turns into an irreversible process of deep disorganization of the connective tissue - fibrinoid swelling.

b. Fibrinoid swelling.

* It is based on the destruction of the basic substance and fibers of connective tissue, accompanied by a sharp increase in vascular permeability and the release of coarse plasma proteins, primarily fibrinogen, followed by conversion into fibrin.

* Characteristic is the formation of a substance - a fibrinoid, in the formation of which, in addition to the destruction of collagen fibers, an important role is played by the state of the basic substance, primarily its glycosaminoclycans, which can be precipitated by alkaline proteins

released when the fibrous and cellular structures of the connective tissue are damaged. In addition, plasma proteins, primarily fibrinogen, with subsequent conversion into fibrin, take part in the construction of fibrionid.

The development mechanism is infiltration and decomposition.

Electron microscopic picture: in the area of fibrinoid changes, destruction of collagen fibers and fibrin is revealed. The process is irreversible, ends with fibrinoid necrosis, hyalinosis, sclerosis.

Hyalinosis.

* It is characterized by the accumulation in the tissues of translucent dense masses resembling hyaline cartilage.

* Occurs as a result of fibrinoid swelling, plasmorrhage, sclerosis, necrosis.

* Hyaline is a complex fibrillar protein.

* The mechanism of formation of hyaline consists of the destruction of fibrous structures and their impregnation with fibrin and other plasma components (globulins, beta-lipoproteins, immune complexes, etc.).

Allocate: hyalinosis of the connective tissue proper and vascular hyalinosis; both of these types of hyalinosis can be common and local.

An example of local hyalinosis of the connective tissue itself, which developed as a result of mucoid swelling and fibrinoid changes, is hyalinosis of the valves of the heart valves in rheumatism (rheumatic heart disease).

Macroscopic picture: the heart is enlarged, the cavities of the ventricles are enlarged. The leaflets of the mitral valve are dense, whitish in color, adhered to each other and sharply deformed. The atrioventricular opening is narrowed. Chordal filaments are thickened and shortened.

There are 3 types of vascular hyaline:

a) simple hyaline - arises as a result of plasmorrhage of unchanged plasma components (more often found in hypertension, atherosclerosis);

b) lipogyalin - contains lipids and beta-lipoproteins (most typical for diabetes mellitus);

c) complex hyaline - is built from immune complexes, fibrin and decaying structures (typical for diseases with immunopathological disorders, for example, for rheumatic diseases).

* Widespread hyalinosis of arterioles occurs in hypertension and diabetes mellitus as an outcome of plasmorrhage.

* In hypertensive disease due to hyalinosis of arterioles arteriolosclerotic nephrosclerosis develops, or primary-shriveled kidneys: small, dense kidneys with a fine-grained surface and a sharply thinned cortical layer.

* Widespread hyalinosis of small vessels (mainly arterioles) underlies diabetic microangiopathy.

I. Morphology of carbohydrate metabolism disorders.

Carbohydrates detected in cells and tissues using histochemical methods are subdivided into polysaccharides (glycogen), glycosaminoglycans (mucopolysaccharides) and glycoproteids.

Disorders of glycogen metabolism - one of the examples of disorders of carbohydrate metabolism - is most often observed in diabetes mellitus and in hereditary carbohydrate dystrophies - glycogenosis. The depot of glycogen in the body is the liver and skeletal muscles, the glycogen of these organs is called "labile glycogen", as it is consumed depending on the needs of the body. Another type of glycogen is glycogen of nerve cells, the conducting system of the heart, aorta, endothelium, epithelial tissues, cartilage, leukocytes - "stable glycogen", the content of which does not undergo noticeable fluctuations and which is a necessary component of cells. It is possible to detect glycogen in cells and tissues by means of histochemical staining with Best carmine. Intracellular accumulation of glycogen is observed with disorders of glucose or glycogen metabolism. In diabetes mellitus, there are: 1) intracellular accumulation of glycogen in the epithelial cells of the distal convoluted tubule: the epithelium becomes high, with a light, foamy cytoplasm, glycogen grains are also found in the lumen of the tubules; 2) the inclusion of a glyco-gene in the nuclei of hepatocytes, which become light ("perforated", "empty" nuclei).

Impaired metabolism of glycoproteins in cells or in the intercellular substance is characterized by the accumulation of mucins and mucoids (the so-called mucous or mucoid substances).

Glycoproteins in cells and tissues can be detected by histochemical staining with toluidine blue or methylene blue. Obturation of the excretory ducts of the glands with mucus leads to the development of cysts; obturation of the lumen of the bronchi with mucus can lead to the development of atelectasis and foci of pneumonia.

Hereditary disorders of glycogen metabolism are called glycogenosis. Established 11 types of glycogenosis, each of which is caused by a deficiency of one of the enzymes involved in the metabolism of glycogen: type I - Gierke's disease, type II - Pompe disease, type III - measles disease, type IY - Andersen's disease, type Y - Mark-Ardl's syndrome, YI type - Hers disease, YII type - Thomson's disease, YIII type - Tarui disease, IX type - Haga disease, X and XI types. Along with this, there are mixed types of glycogenoses, as well as glycogenoses with an unidentified enzyme defect. Depending on whether the sludge is affected by enzymatic defects in the liver, muscles, or at the same time many organs, hepatic, muscular and generalized forms of glycogenosis are distinguished. The most important sign of pathological accumulation of glycogen in tissues during glycogenosis is the absence of postmortem glycolysis (while the absorbed glycogen can be easily extracted with an aqueous solution of formalin, which at the same time becomes cloudy, grayish-white milky species; when alcohol is exposed to this solution, it falls out jelly-like masses, giving a pronounced brown color with iodine).

Brief description of the five **main types of glycogenosis**

Type I glycogenosis - Gierke's disease - hepatic form - occurs due to deficiency of glucose-6-phosphatase. The disease manifests itself in infancy; characteristic: lagging of the increase in body weight, vomiting, anorexia, hypoglycemia, periodically - ketonemic crises. In the future - proportionally small growth in the pituitary type, the "doll-type" face, hepatomegaly. Causes of

death are acidotic coma or infections. Macroscopic picture: the liver is enlarged by 3-4 times, its surface is smooth, on the cut the tissue is pale red with an emphasized pattern of lobules; kidneys - enlarged, swollen, pale, yellowish-red in color with a wide cortical zone; the spleen is not enlarged. Microscopic picture: hepatocytes are sharply enlarged with "watery" cytoplasm, well-defined boundaries and a nucleus located in the center. Staining for glycogen is sharply positive even after fixing the material in formalin.

Type II glycogenosis - Pompe disease - generalized form - arises due to a deficiency of the lysosomal enzyme acid maltase, which leads to the accumulation of glycogen primarily inside the lysosomes of cells of striated and smooth muscles, liver, lungs, spleen, vascular walls, and brain , skin. The course of the disease is unfavorable, death occurs in the 1st year of life from heart or respiratory failure, often from aspiration pneumonia. Macroscopic picture: cardiomegaly, macroglossia, damage to the muscles of the esophagus and pylorus. Microscopic picture: myocardial fibers are swollen, light, sharply contoured, similar to plant cells; in the neuromuscular variant - the accumulation of glycogen in the ganglionic and glial cells of the anterior horns of the spinal cord, spinal and autonomic peripheral nodes, damage to skeletal muscles and especially smooth muscles; the amount of glycogen in the liver and skin increases. Electron microscopic picture: lysosomal and cytoplasmic inclusions associated with cell membranes, containing multiple □-particles of glycogen, the size of inclusions 0.2-1.5 microns.

Glycogenosis of the III type, limitdextrinosis (measles disease) occurs due to the absence of amylo-1,6-glcosidase, which leads to a violation of the breakdown of glycogen - glycogen molecules with short external chains are formed. The disease is characterized by the accumulation of abnormal glycogen (limitdextrin) mainly in the liver, as well as in skeletal muscles and myocardium. The clinical and morphological picture is similar to that in type I glycogenosis, but less pronounced.

Type IY glycogenosis, amylopectinosis (Andersen's disease) is a rare type of glycogenosis, characterized by impaired glycogen synthesis, arising from a defect in the branching enzyme, which normally catalyzes the stepwise synthesis of glycogen branches. The disease manifests itself in late infancy or early childhood in the form of liver cirrhosis, hepato- and splenomegaly, ascites, jaundice, bleeding. Cirrhosis of the liver is small-nodular, with the accumulation of poorly soluble abnormal glycogen in hepatocytes, which is perceived by the body as a foreign body and causes the development of cirrhosis. Glycogen is also accumulated in the histiocytes of the spleen, lymph nodes, in the Kupffer's cells of the liver.

Type Y glycogenosis (McArdle disease) is a classic muscle glycogenosis associated with the absence of muscle phosphorylase; characterized by myalgias that arise after muscle tension, stiffness in the joints of the limbs and muscle weakness gradually develop, dark urine (due to myoglobin). The disease develops in childhood (after 10 years). Under the sarcolemma of skeletal muscles, sharply CHIK-positive vacuoles are found, individual muscle fibers are hyalinized.

3. Lesson plan.

Macropreparations

1. **Hyalinosis of the spleen capsula** - pay attention to the size, surface, texture, color and appearance of the spleen, and pay attention to white thickened area of hyalinosis.

Micropreparations

1. **Hydropic degeneration of the liver** (staining with hematoxylin and eosin) - pay attention to the size, shape, color, number of protein inclusions in the cytoplasm of the epithelium, the state of the nuclei and the size of epithelial cells, the lumen of the tubules.

1. **Hydropic degeneration of the epithelium of the proximal convoluted tubules of the kidney** (staining with hematoxylin and eosin) - pay attention to the number and size of vacuoles in the cytoplasm, the state of the nuclei and the size of epithelial cells, the lumen of the tubules.

2 **Fibrinoid swelling in the derma (skin).** H&E - pay attention to the color of the upper part of derma.

3. **Hyperkeratosis (papiloma of the skin). H&E** (staining with hematoxylin and eosin) - pay attention to the thickened eosinophilic (pink) masses on surface of the papilloma (benign tumor of the skin) .

4**. Hyalonosis of the spleen capsule . H&E.** – pay attention to the thickened eosinophilic (pink) masses on surface of the capsula of the spleen.

Situational casess

Situational case 1

Patient A., 70 years old, suffering from decompensated diabetes mellitus, died from ischemic cerebral infarction. According to clinical data, hyperglycemia and glucosuria were periodically noted, manifestations of cardiovascular insufficiency were increasing. Body weight exceeded by 45%. An autopsy revealed a cerebral infarction in the background of atherosclerosis of the cerebral arteries, atherosclerosis with damage to the aorta and all its branches. Atherosclerotic plaques on the cut are white, stony density. Found changes in the heart, liver, kidneys.

Questions to the situation case 1

1. Describe the macroscopic changes in the liver that can be detected at autopsy, name the pathological process.

2. Describe the microscopic changes in the liver, the color that should be used to clarify the diagnosis.

3. Describe the gross changes in the heart that can be found on autopsy. Name the pathological processes that can lead to impaired contractility of the myocardium.

4. Describe the microscopic changes in the myocardium in heart failure. Name the color that you need to use to clarify the diagnosis, the cause of this pathological process.

5. Indicate the metabolic disorder of which substances is the basis of atherosclerosis.

6. What microscopic changes in the renal tubules can be detected in connection with glucosuria?

7. Name the pathological process that led to the hardening of atherosclerotic plaques.

Situation case 2

Patient B., 40 years old, suffered from subacute glomerulonephritis for 5 months. The clinic revealed edema, a complex of symptoms (nephrotic syndrome), including massive proteinuria (more than 50 mg / kg per day), hypoalbuminemia (less than 25 g / l), hyperlipidemia (cholesterol more than 6.5 mmol / l). Died of pulmonary edema. On external examination, pronounced edema. Autopsy revealed shrunken kidneys, dropsy of serous cavities, pulmonary edema, and cerebral edema.

Questions to the situation case 2

1. Explain the mechanism of development of individual symptoms.

2. List the changes in the kidney tubules that can be detected by microscopic examination.

3. Which parts of the tubules change? Explain the cause and mechanisms of development of damage to the renal tubules, describe the changes.

4. What additional stains should be used to confirm the histological diagnosis?

Reference to the Topic 2

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