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

Topic: “Pathological anatomy: content, tasks, objects and research methods. Disorders of metabolism in cells and tissues. Pathology of accumulation (dystrophy). Disorders of lipid metabolism"

1. The purpose of the lesson. To study the issues of etiology, pathogenesis, morphology, complications and outcomes of fat 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 fat (lipid) parenchymal and stromal-vascular dystrophies (fatty changes).

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

4. Characteristic changes in internal organs in fat (lipid) parenchymal and stromal-vascular dystrophies.

Theoretical aspects.

Methodological foundations of pathological anatomy

The objects studied by the pathologist can be divided into three groups: 1) cadaveric material; 2) substrates obtained from patients during their lifetime (organs, tissues and their parts, cells and their parts, secretion products, liquids) and 3) experimental material.

Cadaveric material. The main goal of autopsy is to establish the final diagnosis and cause of death of the patient. The correctness or erroneousness of the clinical diagnosis and the effectiveness of treatment are also evaluated. The importance of the sectional work of a pathologist consists not only in monitoring the quality of the therapeutic and diagnostic activities of clinicians, but also in the accumulation of statistical and scientific and practical data on diseases and pathological processes.

Material taken during the patient's life. Much more volume in the work of the pathologist is occupied by microscopic examination of the material obtained for diagnostic purposes during the patient's life. Most often, such objects are examined histologically or cytologically.

Histological examination. Operating and biopsy materials are subjected to this study. When the surgical material is received by the pathologist, the clinical diagnosis, as a rule, has already been established. Only histological confirmation (clarification) of the diagnosis is required. However, in the case of a biopsy, both the operation itself and the taking of the material (biopsy) are performed in order to establish a diagnosis.

For routine diagnostics, a universal histological examination of sections with hematoxylin and eosin is widely used. Tinctorial, i.e., dyeing, properties of hemato-silin appear in a slightly alkaline medium, and structures stained with this dye blue or dark blue are usually called basophilic. These include cell nuclei, calcium salt deposits, and bacterial colonies. Some types of mucus can show weak basophilia. Eosin, on the other hand, at pH less than 7.0 stains the so-called oxyphilic components pink-red or red. These include the cytoplasm of cells, fibers, erythrocytes, protein masses, and most types of mucus. Very often they change the color of picrofuchsino.m according to van Gieson. In this case, collagen fibers of the connective tissue are colored selectively, that is, selectively, in red, while other structures become yellow or greenish-yellow.

Cytological examination is carried out on smears made from the contents of hollow or tubular organs, as well as on preparations-imprints, punctates and aspirates (aspirating punctures sucked out with a syringe). Smears are often made from washes from the walls of organs, which allows you to capture cells that are in the process of natural or pathological desquamation (desquamation, exfoliation), for example, from the cervix. A more active intervention is scraping from the walls of organs. If the material of the nipple is abundant, then it is processed using histological techniques. In particular, this is done with diagnostic scrapings of the endometrium. With scanty scrapings, the material goes for cytological processing. Often, drugs are prepared from sputum, mucus, tissue trains and sediments in liquids. Sediments can be obtained after centrifuging the suspensions.

Cytological material is usually fixed on a slide, often during staining. The most popular stains are azure-eosin (its tinctorial properties are close to hematoxylin and eosin) or papanicolaou bismarck-brown.

Immunohistochemical study. In some pathological conditions (especially tumors) it is difficult and even impossible to determine the type of tissue or its origin (histogenesis) with the help of histological or cytological stains. Meanwhile, such verification is important for diagnostics and prognosis. Therefore, various additional methodological approaches are used. One of them is the immunohistochemical method: solutions with antibodies to the desired antigens: tumor, viral, microbial, autoantigens, etc. are applied to histological or cytological preparations. Antigens are not visible in normal histological stains of tissues. Antibodies in sera carry a label: either a fluorochrome, that is, a dye that glows in a dark field (in other words, giving fluorescence), or a dye enzyme. If the desired antigen is in the tissues or cells under investigation, then the resulting antigen-antibody complex plus the marker will accurately indicate its localization, quantity, and help to study some properties.

Molecular biology methods. In well-equipped pathological departments and research institutes, methods of molecular biology are used for intravital diagnostics: flow cytometry and in situ hybridization techniques. Flow cytometry is essential for quantitative analysis of DNA content in tumor cells and other pathological substrates. In situ combining (usually in the form of polymerase chain reaction) makes it possible to determine the composition of nucleic acids and complex proteins in the material under study.

Study of chromosomes. With the help of chromosome analysis, abnormalities in the genetic apparatus (genome) of cells that have an innate or acquired character are detected. This analysis is especially important in the recognition and study of tumors, various variants of which are accompanied by quite specific marker rearrangements or chromosome aberrations.

Electron microscopy can be transmission (in a transmitted beam, similar to light-optical microscopy) and scanning (removing the surface relief). The first is used more often, especially for studying the details of the structure of cells in ultrathin tissue sections, detecting microbes, viruses, deposits of immune and other complexes, etc.

Experimental material. An experiment with a sufficient number of laboratory animals makes it possible to model and study diseases and pathological processes at any stage of their development.

Damage (alteration)

Causes of cell damage:

1. Hypoxia.

2. Physical agents (mechanical injury, fluctuations in ambient temperature, fluctuations in atmospheric pressure, radiation, electric current).

3. Chemical agents and drugs.

4. Infectious agents.

5. Immune reactions.

6. Genetic disorders.

7. Nutritional imbalance.

Cell damage mechanisms:

1. With insufficient supply of oxygen to the tissues, its free radicals are formed, causing free radical lipid peroxidation, which has a destructive effect on cells.

2. Disturbance of calcium homeostasis plays a special role in cell damage.

3. Loss of pyridine nucleotides by mitochondria and subsequent ATP deficiency, as well as a decrease in ATP synthesis, are characteristic of both ischemic and toxic cell damage.

4. Early loss of selective permeability by the plasma membrane.

The main forms of cell damage:

1. Ischemic and hypoxic damage.

2. Damage caused by free radicals, including

activated oxygen

3. Toxic damage.

All pathological and many physiological processes in the body are based on damage to its structures.

Damage is classified according to various principles:

1) by causative factors - exogenous (biological, including caused by bacteria, viruses, mycoplasmas, protozoa; physical, chemical) and endogenous (hypoxia, intoxication, immune damage);

2) the nature of the impact of the damaging factor - direct and indirect;

3) by the severity of the process - reversible and irreversible;

4) by value for the body - pathological and physiological;

5) in terms of prevalence - the number and volume of damaged structures.

Any damage manifests itself at various levels:

1) molecular (damage to cellular receptors, enzyme molecules, nucleic acids up to their disintegration);

2) subcellular - ultrastructural (damage to mitochondria, reticulum, membranes and other ultrastructures up to their destruction);

3) cellular (various dystrophies due to a violation of different types of metabolism with the possible development of necrosis like rexis or cell lysis);

4) tissue and organ (dystrophic changes in most cells and stroma with the possible development of necrosis (like a heart attack, sequestration, etc.);

5) organismic (a disease with a possible fatal outcome). Sometimes the level of tissue complexes or histions is additionally distinguished, which include the vessels of the microvasculature (arteriole, capillaries, venules) and the cells fed by them, parenchyma, connective tissue and terminal nerve endings.

Most of the damage at the subcellular (ultrastructural) level observed during electron microscopic study is of a nonspecific nature and does not depend on the type of damaging factors.

So, for example, in the myocardium during acute ischemia, toxic effects of catecholamines, morphine poisoning, diffuse purulent peritonitis, irradiation, similar changes in damaged cells are observed: 1) swelling of mitochondria and destruction of their membranes; 2) vacuolization of the endoplasmic reticulum; 3) focal destruction of myofibrils; 4) the appearance of an excessive amount of lipid inclusions.

The property of ultrastructures to undergo identical changes under the influence of various factors is called stereotypism.

With the same effect on the entire organ of any damaging factor, the entire spectrum of possible states of the cell is usually observed, from practically normal and even intensively functioning to death. This phenomenon is called mosaicism or discrete functions. For example, uneven lesions of hepatocytes in chronic venous stasis or ethanol poisoning.

The close functional relationship of all cellular ultrastructures leads, in the case of a sufficiently long and strong effect of a damaging factor, to significant damage to all components of the cell, regardless of the localization of the initial changes. This pattern is called complexity.

Based on the results of histochemical study, the stages in the development of cell damage have been established. So, with hypoxia at the initial stage, there is a decrease in the production of ATP in the mitochondria. At the second stage, a compensatory increase in anaerobic glycolysis is observed, manifested in an increase in the activity of lactate dehydrogenase (LDH), simultaneously with a decrease in the glycogen content. The result of this stage is an increase in the content of lactic acid in the cells, which leads to an increase in the acidity of the cellular environment. The third stage is characterized by cellular acidosis, under conditions of which the activity of hydrolytic lysosomal enzymes increases, primarily acid phosphatase, which enhance intracellular autolytic processes.

Damage at the cellular level can sometimes be specific. **Specific changes** are caused by intracellular replication of the virus (with the appearance in the nucleus or cytoplasm of inclusions, which are either accumulations of viral particles, or reactive changes in the cellular substance in response to their replication), tumor metamorphosis and congenital or acquired fermentopathies, leading to the accumulation of normal metabolites in the cell in excess or abnormal - in the form of inclusions.

Cells and their constituent parts can undergo various structural changes. At the initial stages of exposure, they are reversible and indicate only the functional tension of the cells. In the future, there is a gradual increase in their manifestations; they take on the character of damage, initially reversible, and then irreversible.

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 accumulations.

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).

Lipids. Various lipids can accumulate in cells: triglycerides, cholesterol esters, and phospholipids. The accumulation of lipids (three glycerides) in parenchymal cells is usually reversible and is called steatosis, or fatty degeneration.

Fatty inclusions can be detected using a number of stains, the most often used is Sudan III, which stains lipids in a yellow-red color. Most often, such fatty changes occur in the liver, which is the main organ involved in fat metabolism, as well as in the heart, muscles and kidneys.

Most often, ***hepatic steatosis*** is observed with alcoholism, obesity, diabetes mellitus, hypoxia, toxic effects, in case of malnutrition (lack of protein or excess of lipids in food). Lipids enter the liver from adipose tissue or food mainly in the form of free fatty acids, and in the liver cells are converted into triglycerides. For the transport of lipids from the hepatic cell, apoprotein is required; when intracellular triglycerides are combined with its molecules, lipoproteins are formed. The accumulation of triglycerides in the liver can result from defects in the conversion of fatty acids to lipoproteins. Alcohol, which damages the functions of mitochondria and microsomes, contributes to these defects. Some toxins reduce apoprotein synthesis. Hypoxia inhibits fatty acid oxidation. Fasting increases the mobilization of lipids from adipose tissue and accelerates the synthesis of triglycerides, protein starvation disrupts the synthesis of apoprotein.

The significance of steatosis is due to the cause and severity of lipid accumulation. A weak accumulation does not affect the liver function, and a significant accumulation of lipids can disrupt cell function and irreversibly damage intracellular processes.

Fatty degeneration of the myocardium develops, as a rule, due to hypoxia (with blood diseases, cardiovascular insufficiency) and intoxication (with alcoholism, infectious diseases, poisoning with phosphorus, arsenic, etc.).

The mechanism for the development of such dystrophy is associated with a decrease in lipid oxidation due to the destruction of mitochondria under the influence of hypoxia or toxin. The peculiarities of fatty degeneration of the myocardium are the focal nature of the lesion mainly along the venous knee of capillaries and small veins, as well as the accumulation of lipids in the cytoplasm in the form of small drops (dust-like obesity). The contractility of the myocardium in fatty degeneration decreases.

Cholesterol and its esters. Most cells use cholesterol for the synthesis of cell membranes, however, in some pathological processes, cholesterol can accumulate in cells.

In atherosclerosis, cholesterol and its esters are found in smooth muscle cells and macrophages in atherosclerotic plaques located in the intima of the aorta and large arteries. Such cells are called foamy, since when stained with hematoxylin and eosin, the vacuoles in place of the lipids dissolved in the preparation of the drug give the cytoplasm a foamy appearance, they are also called xanthoma, since they contain lipids. Some of these cells rupture and lipids are released into the extracellular space. Extracellular cholesterol can crystallize into long needles (crystals).

In congenital hyperlipidemic conditions, accumulations of foam cells containing cholesterol are found in the superficial dermis and tendons. They form tumor-like clusters (xanthomas). Foamy macrophages are often found in places of cell damage in inflammation foci, where they are formed due to phagocytosis of cholesterol from the membranes of destroyed cells. Multiple small-focal deposits of cholesterol esters contained in macrophages, with chronic cholecystitis, give the mucous membrane of the gallbladder a variegated appearance due to yellow stripes and small spots (cholesterosis of the gallbladder).

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 lipidoses

Stromal-vascular lipidoses include a violation of the metabolism of fat, adipose tissue and fat depots and a violation of the metabolism of fat (cholesterol and its esters) in the walls of large arteries in atherosclerosis.

An increase in fat in adipose tissue is called **obesity**.

Depending on the mechanism of development, the following types of obesity are distinguished:

1) alimentary;

2) cerebral (with trauma, brain tumor);

3) endocrine (with Frohlich's and Itsenko-Cushing's syndrome, adiposogenital dystrophy, hypothyroidism, etc.);

4) hereditary.

By external manifestations, they are distinguished:

1) symmetrical type (even distribution of fat);

2) upper (face, back of the head, neck, upper shoulder girdle);

3) medium (in the abdomen in the form of an apron);

4) lower (in the area of the thighs and legs).

Depending on the percentage of excess body weight:

I degree - 20-29%;

II degree - 30-49%;

III degree - 50-59%;

IY degree - more than 100%.

Depending on the number of adiposites and their sizes:

1) hypertrophic variant of general obesity:

- the number of adiposites is not changed;

- adiposites are enlarged and contain several times more triglycerides;

- malignant course;

2) hyperplastic obesity:

- the number of adiposites is increased;

- the function of adiposites is not impaired;

- the course is benign.

Heart obesity develops with general obesity of any genesis. Macroscopic picture: the size of the heart increases, a large amount of fat accumulates under the epicardium, fatty tissue grows into the stroma of the myocardium, cardiomyocytes atrophy; accompanied by the development of heart failure; possible rupture of the right ventricle, in which obesity is more pronounced.

3. Lesson plan.

Macropreparations

1. **Liver steatosis** - pay attention to the size, surface, texture, color and appearance of the liver in section.

2. **Fatty degeneration of the myocardium** ("tiger heart") - pay attention to the size of the heart, the size of its chambers, consistency, color, the presence of yellow-white striation under the endocardium of the left ventricle in the area of trabeculae and papillary muscles.

3. **Atherosclerosis of the aorta** - pay attention to the color, shape, consistency of changes (atherosclerotic plaques and their condition) in the intima of the aorta.

4. **Cholesterosis of the gall bladder** - pay attention to the wall thickness and the state of the mucous membrane of the gallbladder.

5. **Simple obesity of the heart** - pay attention to the localization of fatty tissue deposits (under the epicardium, mainly in the right ventricle), the state of the heart cavities, the size of the heart.

Micropreparations

1**. Liver steatosis** (staining with hematoxylin and eosin, Sudan III). When staining with hematoxylin and eosin, pay attention to changes in the cytoplasm and nuclei of hepatocytes; when staining with Sudan III, note the color of drops in the cytoplasm of hepatocytes. Pay attention to the differences in the size of drops in the peripheral and central sections of the lobules.

2. **Fatty degeneration of the myocardium** (staining by Sudan III) - pay attention to the localization of changes, the size and color of inclusions.

3. **Lipoidosis of the aorta** (staining with Sudan III) - pay attention to the thickness of the intima, the presence of inclusions, characteristic cells and crystals.

6. **Simple obesity of the heart** - pay attention to the localization of lipocytes, the state of cardiomyocytes

Situational case 1

Situation case 1

Patient K., 47 years old, who has been abusing alcohol for a long time, was admitted to the hospital with complaints of severity and pain in the right hypochondrium. On examination and on ultrasound, the liver was enlarged. A liver biopsy was performed. Microscopic examination of a histological specimen of liver tissue stained with hematoxylin and eosin revealed colorless vacuoles of various sizes (from very small to large) in hepatocytes; in some areas, the liver tissue resembles adipose tissue.

Questions to the situation case 1

1. Describe the possible macroscopic changes in the liver.

2. Name the pathological process.

3. Name the stains that should be used to clarify the diagnosis.

4. Specify the mechanism of formation of the detected inclusions.

5. Classify the process according to the type of impaired exchange.

Situation case 2

Patient A., 70 years old, suffering from decompensated diabetes mellitus, died from ischemic cerebral infarction. 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 for situation case 2

1. Name the disease, which is characterized by an increase in body weight by 45% of the norm.

2. Describe the possible macro- and microscopic changes in the liver in this disease.

3. Describe the macro- and microscopic changes in the heart that can be found on autopsy.

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

Reference to the Topic

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