VOLGOGRAD STATE
MEDICAL UNIVERSITY
Department of Pathological Anatomy

Pathological anatomy: content, tasks, objects and research methods. Morphology of reversible and irreversible damage to cells and tissues: morphology of lipid metabolism disorders (lipid dystrophies).

Volgograd

1. **Purpose**: to consider the content and goals of pathological anatomy as a science, its importance for the theory and practice of medicine. Outline the main stages in the development of pathological anatomy, the role of domestic scientists in the development of science. Outline the basic principles of modern pathological anatomy (dialectical principle, evolutionary, relationship between structure and function, theory and practice, historical principle). Consider the morphological signs of reversible damage to cells and tissues, the morphology of lipid metabolism disorders.
2. **Requirements** for the level of the student for mastering the discipline - pathological anatomy.

Theoretical aspects.

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).
3) experimental material.

1). **Cadaveric material**. The main purpose 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 medical and diagnostic activities of clinicians, but also in the accumulation of statistical and scientific and practical data on diseases and pathological processes.
2). Material taken during the patient's life. A much greater volume in the work of a pathologist is occupied by microscopic examination of 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 admitted to the pathologist, the clinical diagnosis is usually already 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 material are performed in order to establish a diagnosis.

For routine diagnostics, universal histological staining of sections with hematoxylin and eosin is widely used. Tinctorial, i.e., coloring, properties of hematoxylin are manifested in a slightly alkaline medium, and structures colored 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 staining with picrofuchsin according to van Gieson is used. 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-prints, punctates and aspirates (aspiration punctures sucked out with a syringe). Smears are often made from the material of washes from the walls of organs, which makes it possible 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 scraping material 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 or impossible to determine the type of tissue or its origin using histo- and 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 histo - or cytological preparations. Antigens are not

visible in general 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 coloring enzyme. If the desired antigen is in the tissues or cells under study, then the resulting antigen-antibody complex plus the marker will accurately indicate its localization, quantity, and help to study the properties.
Molecular biology methods. In well-equipped pathological departments and research institutes, molecular biology methods are used for intravital diagnostics: flow cytometry and hybridization techniques. Flow cytometry is necessary for the quantitative analysis of DNA content in tumor cells, pathological substrates. Hybridization (usually in the form of a polymerase chain reaction) allows you to determine the composition of nucleic acids, 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.
3). 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.
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; H) pigments. All of them can accumulate transiently (temporarily) or permanently, be harmless or toxic, localized in the cytoplasm (more often in lysosomes) or in the nucleus.
Inclusions (intracellular clusters).
There are three types of inclusions (intracellular clusters). First, these are accumulations of natural endogenous metabolites, i.e. endogenous inclusions that are formed in a normal or accelerated rhythm, and the rate of their removal is insufficient (with fatty changes in the liver). Secondly, these are the accumulations of endogenous substances that cannot be metabolized and also belong to the group of endogenous inclusions. A common cause of such clusters
a genetic defect, as a result, metabolic products are not used, but are deposited inside the cell, accumulation diseases develop. Thirdly, the accumulation of abnormal exogenous substances, exogenous inclusions that the cell can neither destroy with the help of enzymes, nor transport to another place (coal particles).

I. Morphology of lipid metabolism disorders.

Lipids. Different lipids can accumulate in cells (intracellularly): triglycerides, cholesterol esters and phospholipids. The accumulation of lipids (triglycerides) in parenchymal cells is usually reversible and is called steatosis, or fatty degeneration. Fat 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, fatty changes are found in the liver, which is an organ involved in fat metabolism, in the heart, muscles, and kidneys.
Most often, hepatic steatosis is observed with alcoholism, obesity, diabetes mellitus, hypoxia, toxic effects, malnutrition (lack of protein or excess 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 mild accumulation does not affect liver function, and a significant accumulation of lipids can disrupt cell function, 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 features 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 to synthesize cell membranes, but in some pathological processes, cholesterol can accumulate in cells.
In atherosclerosis, cholesterol and its esters are found in smooth muscle cells and macrophages (intracellularly) 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 during the preparation of the drug give the cytoplasm a foamy appearance, they are also called xanthomal, since they contain lipids. Some of these cells rupture and lipids are released into the extracellular space (extracellular clumps). 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 at the sites of cell damage in the foci of inflammation, 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, in chronic cholecystitis, give the mucous membrane of the gallbladder a variegated appearance due to yellow stripes and small spots (cholesterosis of the gallbladder).

Parenchymal fatty degeneration (lipidosis).
Disorders of the metabolism of cytoplasmic lipids can manifest itself in an increase in their content in cells, where they are found in normal conditions, in the appearance of lipids where they are usually not found, and in the formation of fats of an unusual chemical composition. Usually neutral fats accumulate in cells.
Parenchymal fatty degeneration occurs most often in the same place as protein - in the myocardium, liver, kidneys.
Stromal-vascular fatty degeneration (lipidosis).
Stromal-vascular fatty degeneration occurs in metabolic disorders:
a) neutral fats,
b) cholesterol and its esters.

Disorders of neutral fat metabolism.
Disturbances in the metabolism of neutral fats are manifested in an increase in their reserves in adipose tissue, which can be general or local in nature.

Disorders of cholesterol and its ester metabolism.
Disorders of the metabolism of cholesterol and its esters underlie a serious illness - atherosclerosis. In this case, not only cholesterol and its esters accumulate in the intima of the arteries, but also β-low-density lipoproteins and blood plasma proteins, which is facilitated by an increase in vascular permeability. The accumulating high-molecular substances lead to the destruction of the intima, disintegrate and saponify. As a result, fat-protein detritus (athere - mushy mass) forms in the intima, connective tissue (sclerosis - compaction) grows and a fibrous plaque is formed, often narrowing the lumen of the vessel.

3. Lesson plan.

Macropreparations:

1. Macropreparations "Liver steatosis" (fatty liver). Pay attention to the size, surface, consistency, color and appearance of the liver in section.
2. Macropreparation "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 region of the trabeculae and papillary muscles.
3. Macropreparation "Aortic atherosclerosis". Pay attention to the color, shape, consistency of changes in the intima of the aorta.
4. Macropreparation “Cholesterosis of the gallbladder”. Pay attention to the wall thickness and condition of the mucous membrane of the gallbladder.
5. Macropreparation “Simple obesity of the myocardium”. Pay attention to the localization of changes, the size and color of the inclusions.

Micropreparations:

1. Micropreparation “Liver steatosis (fatty liver)” (staining with hematoxylin and zosin, Sudan III). When staining with hematoxylin and eosin, pay attention to changes in the ditoplasm and nuclei of hepatocytes; when staining with Sudan III, note the color of the drops in the cytoplasm of hepatocytes. Pay attention to the differences in the size of drops in the peripheral and central parts of the lobules.
2. Micropreparation “Aortic lipoidosis” (stained by Sudan III). Pay attention to the thickness of the intima, the presence of inclusions, characteristic cells and crystals.
3. Micropreparation “Fatty degeneration of the myocardium” (stained by Sudan III). Pay attention to the localization of changes, the size and color of the inclusions.
4. Microdrug “Simple obesity of the myocardium”. Pay attention to the localization of changes, the size and color of the inclusions.

Electronogram

1. Electronogram “Fatty degeneration of the myocardium”. Pay attention to the cytoplasm of cardiomyocytes, filled with small drops of fat.

4. QUESTIONS

Choose one correct answer

1. Biopsy material for histological examination is sent to the pathologist
a) in formalin,
b) in alcohol,
c) in isotonic solution,
d) frozen,
e) in glutaraldehyde.

2. Staining with picrofuchsin according to van Gieson selectively reveals:
a) mucus-secreting epithelium,
b) nerve fibers,
c) macrophages of connective tissue,
d) smooth muscle cells,
e) collagen fibers of connective tissue.

3. The popularity of the immunohistochemical method is determined by:
a) simplicity and availability,
b) high sensitivity,
c) the use of fluorochrome,
d) non-specific luminescence,
e) the use of dewaxed funds.

4. Electron microscopy is required to identify:
a) viruses in tissues,

b) lymphomas of B- and T-cell types,
c) bacteria in tissues,
d) immune complexes with pemphigoid,
e) immune complexes with glomerulonephritis.

5. Flow cytometry for DNA analysis determines:
a) the number of dividing cells,
b) the number of resting (stable) cells,
c) aneuploidy,
d) diploid,
e) the presence of pathogens.

6. The hybridization technique is applied
a) identification of viral DNA,
b) identification of cellular lymph
c) differentiation of breast cancer and ovarian cancer,
d) studying the genome in case of its congenital disorders.

7. The accumulation of metabolites in the cell leads to:
a) accelerated formation of substances,
b) insufficient excretion of substances,
c) genetic defect,
d) violation of innervation,
e) circulatory disorders.

Choose one correct answer
8. The accumulation of lipids in parenchymal cells is called:
a) apoptosis,
b) steatosis,
c) hyalinosis,
d) sclerosis,
e) melanosis.

Select all correct answers
9. Liver steatosis is observed when:
a) alcoholic illness,
b) obesity,
c) diabetes mellitus,
d) anemia,
e) atherosclerosis.

Choose one correct answer
10. It will help to reliably determine lipids in a micropreparation:
a) Congo red,
b) hematoxylin and eosin,
c) Sudan III,
d) toluidine blue,
e) picrofuchsin.

11. With protein starvation, steatosis develops in:
a) liver,
b) kidneys,
in the heart,
d) adrenal glands,
e) spleen.

12. The figurative name of the liver when
a) "goose"
b) "glaze",
c) "brindle",
d) "sago".

13 The main reason for the development of fatty degeneration of the myocardium:
a) hypoproteinemia,
b) hypocalcemia,
c) hypoglycemia,
d) hypercholesterolemia,
e) hypoxia.

14. The figurative name of the heart with fatty degeneration:
a) "hairy"
b) "drip",
c) "bullish"
d) "goose",
e) "playing".

15. Cells containing cholesterol are called:
a) cricoid,
b) foamy,
c) lipocytes,
d) lipofibroblasts,
e) coniophages.
16. A plasma cell with an excessive accumulation of protein is called a body:
a) Kaunsilmen,
b) Mallory,
in Roussel,
d) Heinz,
e) Pappenheim.

5. List of recommended literature:

Basic literature:

1. “Basic pathology” Vinay Kumar, Ramzi S. Cotran, Stanley L. Robbins, 1997.

Additional literature:

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2. “Textbook of Pathology ” Harsh Mohan, 2002.
3. “General and Systemic Pathology” Joseph Hunter, 2002.
4. “General and Systematic Pathology ” Ed. J.C.E. Underwood – Edinburgh: Churchill Livingstone, 1996 (2^{th}).
5. “Histology for Pathologist” Ed. S.S.Sternberg – Philadelphia: Lippincott Raven Publ, 1997 (2^{th}).
6. “Histopathology. A Color Atlas and Textbook” Damjanov I., McCue P.A. – Baltimore, Philadelphia, London, Paris etc.: Williams and Wilkins, A Waverly Co., 1996.
7. “Muir’s Textbook of Pathology” Eds. R.N.M. MacSween, K. Whaley London: ELBS, 1994 (14^{th}).
8. “Pathology” Eds. Rubin, J.L. Farber – Philadelphia: Lippincott Raven Publ, 1998 (3^{th}).
9. “Pathology Illustrated” Govan A.D.T., Macfarlane P.S., Callander R. – Edinburgh: Churchill Livingstone, 1995 (4^{th}).
10. “Robbins Pathologic Basic of Disease” Eds. R.S.Cotran, V.Kumar, T.Collins – Philadelphia, London, Toronto, Montreal, Sydney, Tokyo: W.B.Saunders Co., 1998 (6^{th}).
11. “Wheater’s Basic Histopathology. A Color Atlas and Text” Burkitt H.G., Stevens A.J.S.L., Young B. – Edinburgh: Churchill Livingstone, 1996 (3^{th}).
12. “Color Atlas of Anatomical Pathology” Cooke R.A., Steward B. – Edinburgh: Churchill Livingstone, 1995 (10^{th}).
13. “General Pathology ” Walter J.B., Talbot I.C. – Edinburgh: Churchill Livingstone, 1996 (7^{th}).
14. “Concise Pathology” Parakrama Chandrasoma, Glive R. Taylor.
15. “Pathology” Virginia A. LiVolsi, Maria J. Merino, John S. J. Brooks, Scott H. Saul, John E. Tomaszewski, 1994.
16. “Short lectures on pathology” Zagoroulko A., 2002
17. “Robbins pathologic basis of diseases” Cotran R., Kumar V., Collins T.
18. “General pathology” Dr. Fatma Hafez, 1979.
19. “Anderson’s Pathology ” Damjanov I., Linder J. – St. Louis: Mosby Inc., 1995 (10^{th}).

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