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

Topic 3 (part 2): "Disorders of blood circulation: thrombosis, embolism, ischemia, stasis".

1. The purpose of the lesson. To study the causes, mechanisms of development, types, clinical and morphological manifestations, values and consequences of thrombosis, embolism, disseminated intravascular coagulation, ischemia, stasis.

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

1. Definition of hemostasis, its constituent components.

2. The concept of coagulation systems, fibrinolysis.

3. The value of endothelium in coagulation and fibrinolysis.

4. Platelets in the coagulation system.

5. Definition of thrombosis, its significance, characteristics of the causes and stages of its development.

6. Characteristics of blood clots in terms of structure, relation to the lumen of the vessel, conditions of occurrence.

7. Outcomes of a thrombus.

8. Differences between thrombus and thromboembolism, postmortem blood clot.

9. Concept, causes, mechanisms of development, stages and types of ICE-syndrome.

10. Morphological and functional changes developing in tissues and organs during disseminated intravascular coagulation.

11. Definition of embolism, its significance, types, causes and mechanisms of development.

12. The mechanism of disorders and death in thromboembolism of the pulmonary artery and its branches.

13. Etiology, mechanisms of development, morphological manifestations, outcomes and significance of ischemia and stasis.

Theoretical aspects.

Thrombosis

Normal blood circulation and the rheological properties of blood are maintained by a regulatory system that ensures a fluid state of the blood, affects the permeability of the vascular wall and prevents the release of plasma elements into the interstitium.

Violation of the regulation of hemostasis, that is, the balanced interaction of its 4 systems - coagulation, fibrinolysis, endothelial structure and platelets - leads to intravital pathological coagulation of blood in the lumen of the bloodstream - thrombosis (from the Greek thrombosis - coagulation).

The reasons leading to the development of blood clots in the arterial and venous bloodstream are quite diverse.

German pathologist Rudolf Virchow identified three **main causes of thrombus formation**.

1. ***Disturbance of the integrity of the vascular wall endothelium***. In normal undamaged vessels, the endothelium has atrombogenic properties, i.e. platelets do not adhere to it. In addition, the endothelium acts as a mechanical barrier between blood and the thrombogenic subendothelial lining. The endothelium produces a number of antithrombogenic factors, the main of which is the surface protein thrombomodulin, which binds thrombin. The latter is inactivated by plasma protein C. By isolating an inhibitor of adenosine diphosphate (ADP) and prostacyclin, the endothelium inhibits platelet aggregation, and also enhances fibrinolysis due to the production of plasmin activators. All this ensures the sliding of blood along the endothelium, which covers the basement membrane of blood vessels. At the same time, various substances are synthesized in the endothelium that enhance the adhesion and aggregation of platelets - the so-called prothrombotic substances. These include von Willebrand factor and platelet activating factor, as well as fibronectin, which provides adhesion. On the surface of normal endothelium, anticoagulation mechanisms predominate, and prothrombotic activity is minimal. That is why when the endothelium is damaged, the balance between thrombogenic and antithrombogenic factors is disturbed, which leads to the formation of a thrombus. Blood clots especially often occur when the endothelium is damaged in the area of atherosclerotic plaque, with allergic and infectious damage to the endothelium (vasculitis), with alteration of the valve cusps in endocarditis, with transmural myocardial infarction, when necrosis captures all layers of the heart.

2. ***Disturbance of blood flow*** - slowing down or changing the direction (vortex) of blood flow. A slowdown in blood flow, especially in chronic venous stasis, often leads to venous thrombosis, in which the blood flow rate is normally lower than in the arteries. In this case, blood clots appear in the veins of the pelvic tissue, the lower extremities. The increased viscosity of the blood causes stasis and, as a consequence, thrombosis of small vessels. During the formation of vortices, turbulent flows, while mixing the layers of the blood flow, platelets, moving from the center (where they are normal), come into contact with the damaged VASCULAR wall. This contributes to the concentration of thrombogenic factors and the violation of their clearance by the liver.

3***. Changes in blood composition leading to hypercoagulability***. The process of blood coagulation occurs sequentially, starting with the activation of enzymes called coagulation factors, and ending with the formation of thrombin, which transforms soluble fibrinogen into insoluble protein fibrin. Each stage of the reaction is carried out with the participation of an enzyme (activated substrate coagulation factor - proenzyme) and a system of cofactors (accelerates). The cofactor systems include phospholipid globules of platelets, on the surface of which all reactions take place, as well as calcium ions.

Inhibition of blood coagulation occurs with the participation of the following mechanisms:

• a decrease in the concentration of clotting factors;

• cessation of the flow of clotting factors to the site of thrombosis due to closure of the vessel, as well as due to an increase in the concentration of factors of the anticoagulation system in the blood - protease inhibitors.

Antithrombin III in the presence of heparin is the main inhibitor of thrombin, and protein C inhibits factors VI and VIII, therefore their deficiency predisposes to the development of blood clots.

A change in blood composition can occur with the following diseases:

• nephrotic syndrome (antithrombin III is excreted in the urine);

• congenital deficiency of antithrombin III and protein;

• severe injury, burns;

• common malignant tumors (hypercoagulability, hyperfibrinogenemia);

• in late pregnancy and childbirth.

In structure and color, thrombus can be white, red, hyaline and mixed.

White thromboses are more common in arteries and consist of platelets, fibrin, leukocytes. Macroscopically, these thrombi are dense, fragile, grayish-white masses. If they are parietal, then they have a rough corrugated surface, which reflects the rhythmic prolapse and adhesion of platelets and fibrin in conditions of blood flow.

Red thrombus. In addition to platelets and fibrin, they are represented by a large number of erythrocytes. Macroscopically, such blood clots are soft, gelatinous, dark red in color, their surface is uneven and dull. More often, red blood clots are found in veins in conditions of slowing blood flow.

Mixed thrombus is characterized by alternating areas of white and red, located in layers. Often these blood clots have a characteristic structure: a head attached to the endothelial lining of blood vessels and having the structure of a white blood clot; a body freely lying in the lumen and including zones of white and red; tail, structure corresponding to a red blood clot. Mixed blood clots often form in the veins, in the cavity of the aortic and heart aneurysms.

Hyaline thrombus is formed in small vessels. They are mainly composed of broken down red blood cells, platelets and precipitating plasma proteins, which makes them look like hyaline.

In relation to the lumen of the vessel or the cavities of the heart, thrombi are parietal, obturating and spherical.

Blood thrombus can form in arteries, veins, heart cavities, aneurysms of the heart and blood vessels.

The causes of thrombus formation in the veins are:

• progressive heart failure;

• immobility after complex operations;

• severe and prolonged course of tumors and infections (Maranth thrombi);

• inflammation of the veins (phlebitis);

• vein catheterization.

The causes of thrombus formation in the arteries are:

• ulceration of atherosclerotic plaques;

• arterial aneurysms;

• inflammation of the arteries (vasculitis).

Thrombus formation in the cardiac cavities occurs in the atria in the region of the ear, either in a chronic aneurysm, or on the valves of the left ventricular valves.

The causes of thrombosis in the heart cavities are:

• heart failure and expansion of heart cavities;

• myocardial infarction, spreading to the endocardium;

• damage to the valves (endocarditis) in rheumatic diseases and sepsis.

Blood clot outcomes include:

1. an increase in the size of a thrombus by layering thrombotic masses on the primary thrombus;
2. contraction (compression) of the thrombus tissue due to the reduction of the mass of fibrin in it;

3. lysis of a thrombus with the participation of plasmin and proteolytic enzymes of neutrophilic leukocytes;
4. organization and sewerage of a thrombus, ie, its replacement by connective tissue and the development of a network of capillaries;
5. the formation of fibrous tissue at the site of a thrombus and its calcification (petrification);
6. detachment of a thrombus and the development of thromboembolism;
7. purulent septic fusion of a thrombus.

Embolism

Embolism is the transfer of material or particles by the blood stream that are absent in normal blood.

1. Direct (orthograde) embolism - in three directions:

1) from the venous system of the systemic circulation and the right heart -> into the vessels of the small circle of blood circulation,

2) from the pulmonary veins, the left half of the heart and the aorta -> into the arteries of the systemic circulation (heart, brain, kidneys, spleen, intestines, extremities),

3) from the branches of the portal system -> to the portal system.

2. Paradoxical embolism - with an open foramen ovale, the presence of a defect in the atrial or interventricular septum with a discharge of blood from the right heart to the left, paradoxical embolism of the systemic circulation can be observed, bypassing the pulmonary vessels.

3. Retrograde embolism - when the movement of the embolus obeys not the hemodynamic laws, but the gravity of the embolus.

Types of embolism, depending on the nature of the embolus:

1) ***thromboembolism*** (occurs when a blood clot or part of it breaks off, usually with venous thrombosis),

2) ***fat embolism*** (the source is fat droplets),

3) ***air embolism*** (air entering the bloodstream),

4***) gas embolism*** (develops with a rapid transition from high pressure to normal or from normal to low),

5) ***tissue embolism*** (with tissue destruction due to extensive trauma or tumor breakdown),

6) ***microbial embolism***,

7) ***embolism by foreign bodies***.

Embolism, Depending on localization:

1. embolism of the systemic circulation,
2. pulmonary embolism,
3. embolism of the portal vein system.

Thromboembolism is one of the most common adverse outcomes of thrombosis, when a thrombus or parts of it break off and begin to circulate through the blood stream (orthograde embolism). Much less often, thromboembolism, as a result of its severity, moves against the bloodstream (retro-hail embolism). Prognostically, the most unfavorable is thromboembolism of the pulmonary artery and its branches, which can be the cause of a sudden cessation of blood supply to the lungs or, which is more common, a sudden cardiac arrest due to the pulmonary coronary reflex. In this case, spasm of the bronchioles, branches of the pulmonary artery and coronary arteries occurs. Blockage of the branches of the pulmonary artery by parts of the embolus leads to the development of hemorrhagic pulmonary infarction, especially against the background of venous stasis. Also quite often there is a separation of blood clots in the presence of parietal blood clots at the site of ulcerated atherosclerotic plaques. From the ascending aorta, thromboemboli enter the carotid artery and cerebral vessels, causing ischemic infarction (gray softening of the brain); from the thoracic and abdominal aorta, getting into the mesenteric arteries, thromboemboli lead to the development of intestinal gangrene, in the renal arteries - to kidney infarction, in the arteries of the lower extremities - to foot gangrene.

The source of thromboembolism can be blood clots in the cavities of the heart or thrombotic overlays on the valve cusps. In addition to detached blood clots, tumor cells can enter the blood when a malignant tumor of the vessels grows. When they are engrafted (implanted), daughter nodes develop - metastases.

Microbial embolism is also possible (microbes circulating in the blood obturate the smallest vessels), fat embolism (fat particles enter the vessels, for example, with fracture of long tubular bones). Most often, fat particles enter the capillaries of the lungs, leading to acute pulmonary failure and cardiac arrest.

During thoracic operations (operations in the chest cavity), venous or arterial catheterization, during decompression, air embolism is possible, when air bubbles (if their volume in the blood is

more than 100 ml) cause blockage of the capillaries of the pulmonary circulation and lead to sudden cardiac death.

DIC syndrome

Disseminated intravascular coagulation ¬

DIC syndrome - characterized by widespread blood coagulation in the vessels of the microvasculature, due to the progressive activation of coagulation. This condition is characterized by a combination of hypercoagulation in small vessels with the simultaneous development of hemorrhagic diathesis and, as a consequence, the occurrence of acute, often fatal bleeding. Hemorrhagic phenomena are caused by a pronounced consumption of blood coagulation factors and an excessive increase in fibrinolysis, which occurs in response to an increase in blood clotting.

DIC syndrome develops in severe conditions of the body:

• embolism by amniotic fluid;

• placental abruption;

• hypoxia of newborns;

• burns;

• acute pancreatitis;

• infectious and septic conditions;

• poisoning with hemocoagulating snake venom;

• malignant tumors of the lung, pancreas and prostate glands, colon, stomach;

• transfusion of incompatible blood;

• with almost all types of shock (very rarely with cardiogenic shock).

The factors triggering this syndrome are numerous and interrelated. So, in infections caused by gram-negative microbes, endotoxins released by microbes and damaging the endothelium can activate both the external and internal coagulation systems. Activation occurs due not only to damage to the endothelium, but also to the release of thromboplastin from the cells of the inflammatory exudate. In addition, endotoxins reduce the anticoagulant activity of protein C by inhibiting the expression of thrombomodulin. Also, endotoxins can directly activate factor XI 1.

In case of massive trauma and extensive burns, the leading mechanism for the formation of DIC is the autoinfusion of tissue thromboplastins. With obstetric pathology and even normal delivery, thromboplastins originating from the placenta or prenatally dead fetus or amniotic fluid can also enter the bloodstream.

Of the malignant tumors, acute promyelocytic leukemia, cancer of the lung, pancreas, colon and stomach are most often associated with DIC syndrome. In these tumors, various thromboplastic substances are secreted, in particular, tissue factors, proteolytic enzymes, mucins and other tumor products.

Thus, for the development of DIC syndrome, the generalized activation of the coagulation system, which occurs under the influence of various factors, is significant. This is the release of thromboplastin into the bloodstream, and a decrease in the synthesis of prostaglandin (PG) PGI2 and protein S, and activation of the coagulation system. The result of platelet aggregation with thrombin is a decrease in their number (thrombocytopenia). Aggregates with platelets are either deposited in damaged areas of the bloodstream, or removed by mononuclear phagocytes.

Plasminogen activators are released from the damaged endothelium, as well as from platelets and leukocytes, which convert it into plasmin, which in turn breaks down fibrin. Fibrin degradation products appear in the blood. The efficiency of the fibrinolytic process is determined by the amount of fibrin deposited in small vessels.

Microthrombi lead to impaired blood flow in the microvasculature and the development of dystrophy and necrosis in various organs, combined with multiple hemorrhages.

Thrombi formed in microvessels consist of fibrin with a small admixture of platelets, leukocytes and erythrocytes. They are round and cylindrical homogeneous formations, they are usually called hyaline, or fibrin, thrombi. Most often, blood clots are found in the vessels of the brain, heart, lungs, cells, adrenal glands, spleen and liver. In the kidneys, renal capillary thrombosis leads to microinfarctions and even bilateral cortical necrosis. Multiple fibrin clots in the capillaries of the lung can be combined with the formation of hyaline membranes of the respiratory alveoli. Fibrin clots in the capillaries of the adrenal cortex with extensive hemorrhages cause the development of acute adrenal insufficiency syndrome (Waterhouse-Friderichsen syndrome) or similar changes in the hypophysis - anterior pituitary insufficiency syndrome (Sheechen syndrome).

Ischemia (local anemia)

Ischemia (local anemia) is the condition of tissues with a decrease or insufficient blood supply. The causes of ischemia are occlusion, obstruction, or obstruction (ie, blockage) of the arteries with a thrombus, embolus, and prolonged vasospasm. Ischemia can occur when an artery is compressed by a tumor, ligature, or as a result of blood redistribution. So, for example, with the rapid exit of fluid from the abdominal cavity (laparocentesis with ascites), blood rushes into its vessels, and the brain tissue experiences little blood.

The hemodynamic mechanism of ischemia is distinguished, which may be based on the "steal phenomenon", systolic and diastolic effects in the myocardium, as well as the "reflow" phenomenon. With stenosis of the subclavian artery, subclavian steal syndrome occurs, and the blood from the vertebral artery through the anastomoses passes into the subclavian artery, reducing the blood supply to the brain. With the syndrome of intracerebral robbery, the

appearance of arterial hyperemia around the ischemic zone leads to an even greater decrease in blood flow in this area (Robin Hood syndrome).

The ref1ow phenomenon occurs when blood flow is restored after short-term ischemia, however, due to hypoxia, pronounced edema of endothelial cells occurs, the lumen of the capillaries is sharply narrowed and blood flow is not restored.

Changes in tissues with ischemia are due to the duration of the resulting hypoxia, the accumulation of metabolites, a decrease in the drainage function and the degree of tissue sensitivity to it.

Ischemia can be acute, and if it is complete, a heart attack develops, and if it is partial, then parenchymal dystrophy. Chronic ischemia is also distinguished, in which parenchyma atrophy and stromal sclerosis occur. The area of ischemia differs from normal tissues by pallor due to a decrease in arterial blood flow.

3. Lesson plan

Macropreparations

1. To study the mixed parietal thrombus in the aorta in atherosclerosis according to the macroscopic picture. Describe the macro-preparation "***Aortic atherosclerosis with parietal thrombus***". Pay attention to the color, the surface of the thrombus, its relation to the intima and the lumen of the vessel. Note the changes in the aortic intima that contributed to thrombus formation.

2. Examine the obstructing red thrombus in the vessel according to the macroscopic picture. Describe the macro-preparation "***Thrombus in the deep veins of the lower extremities***". Pay attention to the type and color of thrombotic masses, to their relation to the intima and lumen of the vessel.

3. To study pulmonary thromboembolism according to the macroscopic picture. Describe the macro-preparation "***Pulmonary embolism***". Pay attention to the localization of the thromboembolus, describe its color, shape, surface condition, attitude to the intima of the vessel.

4. To study the microbial embolism according to the macroscopic picture. Describe the macropreparation "***Embolic purulent nephritis***". Pay attention to the number, shape, size, color, localization of foci of purulent inflammation.

5. To study the cell embolism in the macroscopic picture. Describe the macropreparation "***Metastases of gastric cancer to the liver***". Pay attention to the number, shape, size, color, localization of tumor nodes in the liver tissue.

6. To study the different types of heart attacks on the macroscopic picture. Describe macro-preparations: "***Ischemic spleen infarction***". Pay attention to the shape, color, consistency of the necrotic area, changes in the pericardium, pleura and spleen capsule in the infarction zone.

7. To study different types of infarction on a macroscopic picture. Describe macro-preparations: "***Ischemic myocardial infarction with hemorrhagic corolla***." Pay attention to the shape, color, consistency of the necrotic area, changes in the pericardium, pleura and spleen capsule in the infarction zone.

8. To study different types of infarction on a macroscopic picture. Describe macro-preparations: "***Hemorrhagic pulmonary infarction***." Pay attention to the shape, color, consistency of the necrotic area, changes in the pericardium, pleura and spleen capsule in the infarction zone.

Micropreparations

1. To study the fatty embolism of the lung on the microscopic picture. Describe the micro-preparation "***Fat embolism of the lung***" (stained by Sudan III). Pay attention to the localization and color of fat drops in the lung tissue.

2. Examine the mixed thrombus in the vessel according to the microscopic picture. Describe the microdrug "***Mixed thrombus in a vessel***" (staining with hematoxylin and eosin). Pay attention to the state of the lumen and wall of the vessel, localization and structure of the thrombus.

3. To study the process of organizing a blood clot in a microscopic picture. Describe the micro-preparation "***Organizing thrombus***" (staining with hematoxylin and eosin). Pay attention to the appearance of connective tissue in the thrombus and its localization.

4. To study ischemic infarction by microscopic picture. Describe the micropreparation "***Myocardial infarction***" (staining with hematoxylin and eosin). Pay attention to changes in the areas of necrosis, demarcation inflammation and intact tissue.

5. To study the hemorrhagic infarction on a microscopic picture. Describe micro-preparations "***Hemorrhagic pulmonary infarction***" (staining with hematoxylin and eosin) Pay attention to changes in the zones of necrosis, demarcation inflammation and intact tissue.

6. Examine the stasis on a microscopic picture. Describe the micropreparation "***Stasis in the capillaries of the brain***." Pay attention to the state of the lumen and walls of blood vessels, to the contents of the lumen of the capillaries.

Electronograms

1. To study the second stage of thrombus formation using electron microscopy. Describe the electronogram "***The second stage of thrombus formation***". Pay attention to the state of the endothelium, platelets and the conversion of fibrinogen in the damaged areas.

Situation cases.

Situation case 1

An autopsy of the deceased patient A., 72 years old, in the abdominal aorta from the side of the intima revealed multiple yellowish-whitish plaques, ulcerated in places, with gray-red crumbling masses attached to these areas, with a dull rough surface, practically not narrowing the vessel lumen. In the lumen of the pulmonary artery, free-lying red masses with a shiny smooth surface, elastic consistency, filling the entire lumen of the vessel were revealed.

Questions to the situation case 1

1. What formations are found on the surface of the aorta?

2. How are these formations characterized in appearance, in relation to the lumen of the vessel?

3. What changes in the vessel contributed to their occurrence?

4. What mass is found in the lumen of the pulmonary artery?

5. What are the characteristics of the formation in the aorta and pulmonary artery?

Situation case 2

Patient B., 62 years old, who suffered from severe atherosclerosis of the coronary arteries of the heart, underwent an operation of their prosthetics. Microscopic examination of the artery revealed a pronounced narrowing of its lumen by an atherosclerotic plaque, on the surface of which a dense formation was found, consisting of fibrin and hemolyzed erythrocytes and leukocytes, which is replaced by connective tissue from the side of the intima in places with the formation of cracks lined with endothelial cells.

Questions to the situation case 2

1. What is the name of the formation found on the surface of an atherosclerotic plaque?

2. What kind of this formation has been identified by its microscopic structure?

H. What is the name of this formation in relation to the lumen of the vessel?

4. What changes (outcomes) of this formation are determined by microscopic examination?

5. What other outcomes of this education are possible?

6. What change in the myocardium could develop during obturation of the lumen of the coronary artery?

Situation case 3

Patient V., 68 years old, who suffered from decompensated heart disease with pronounced edema of the lower extremities, underwent an operation to remove the appendix of the cecum for appendicitis. In the postoperative period, on the 4th day, chest pain suddenly developed during breathing, hemoptysis, and on the 6th day, when trying to get up from the bed, the patient suddenly lost consciousness, her face turned blue and, despite attempts to resuscitate, came death. An autopsy revealed red crumbling masses that filled the lumen of the deep veins of the legs, attached to the vascular wall. In the lumen of the trunk of the pulmonary artery, red, crumbling, free-lying masses were found. In the lungs, a dense, dark red triangular lesion was found, covered from the side of the pleura with fibrin overlays.

Questions for situation case 3

1. What is the name of the formations identified in the deep veins of the lower leg?

2. What factor contributed to their formation in the veins?

3. What kind of this formation in appearance and in relation to the lumen of the vessel was revealed?

4. What changes, found at autopsy, developed in the patient on the 4th day after the operation, their reason?

5. What is the name of the formation in the lumen of the pulmonary artery?

6. What other possible sources of this education can be?

7. What is the mechanism of death?

Literature to the Topic 3

Basic literature:

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Additional literature:

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