Materials
for students for practical training in pathological anatomy
at the Department of Pathological Anatomy

II year Faculty of Dentistry

Topic: "Inflammation. Part 2. Chronic (productive) inflammation. Granulomatous inflammation. Regeneration and Reparation ".

1. The purpose of the lesson. To study the issues of etiology, pathogenesis, morphology, complications and outcomes of productive and chronic inflammation.

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

1. Definition of chronic inflammation.

2. Definition of productive inflammation.

3. Etiology, pathogenesis, morphological characteristics of chronic inflammation.

4. Etiology, pathogenesis, morphological characteristics of productive interstitial burning.

5. Etiology, pathogenesis, morphological characteristics, outcomes of granulomatous inflammation.

6. Etiology and pathogenesis of specific granulomatosis.

Theoretical aspects.

Overview of Chronic Inflammation

Chronic inflammation can be defined as a long-term (over weeks and months) inflammatory process, in which there are simultaneously signs of active inflammation, tissue damage, and damage repair.

In contrast to acute inflammation, which manifests itself in noticeable alteration, vascular reactions, exudation, edema and severe neutrophil infiltration, in chronic inflammation, alteration is less pronounced. The process is characterized by a productive tissue reaction with infiltration of mononuclear cells (macrophages, lymphocytes and plasma cells), with foci of necrosis formed as a result of the activity of cells of the inflammatory infiltrate, as well as inadequate repair, angiogenesis and tissue sclerosis.

Chronic inflammation can develop as a result of acute inflammation. However, it often has a chronic character from the very beginning and a latent asymptomatic course for a long time.

Many chronic human diseases are characterized by the development of chronic progressive inflammation in target organs and tissues. For example, chronic glomerulonephritis or certain forms of idiopathic fibrosing alveolitis from the very beginning proceed as chronic inflammatory diseases.

Etiology and pathogenesis of chronic inflammation. The chronization of inflammation depends both on the characteristics of the cause that caused it, and on the individual characteristics of the reaction of the organism in which it develops.

Chronic inflammation can be caused by a variety of agents. It occurs in bacterial, viral, fungal infectious diseases (tuberculosis, syphilis, sepsis, diphtheria, typhus, chronic viral hepatitis, etc.), as well as in chronic exogenous and endogenous intoxications (dusty and interstitial lung diseases, interstitial nephritis) ... However, in many chronic diseases with immune pathogenesis (idiopathic fibrosing alveolitis, Abramov-Fiedler's myocarditis), the etiology of chronic inflammation remains unclear.

The pathogenesis of chronic inflammation can be understood from the standpoint of analyzing the causes that prevent the inflammatory response from completing reparation.

The causes of chronic inflammation include the following:

1) continued exposure to the cause of chronic inflammation that began as acute inflammation;

2) failure of the reparation processes in chronic inflammation, which began as an acute inflammation;

3) repeated episodes of acute inflammation;

4) chronic course from the very beginning (the most common variant) due to:

• persistence of an infection associated with certain microbes, such as tuberculosis bacilli, treponema pale (the causative agent of syphilis) and some fungi. These microorganisms have low toxicity and cause the development of delayed-type hypersensitivity (HRT) reactions. The inflammatory response is productive in the form of a granulomatous reaction;

• long-term exposure to potentially toxic exogenous and endogenous substances. This is observed when non-degradable inorganic substances enter the body, for example, with prolonged inhalation of silicon particles, an inflammatory lung disease occurs - silicosis;

• immunopathological processes, especially autoimmune reactions. In some diseases, protective reactions occur against the body's own tissues, which leads to the development of autoimmune diseases. In these diseases, autoantigens induce a spontaneous immune response that causes some generalized chronic inflammatory diseases, such as multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus.

The morphology of chronic inflammation. Morphological changes in chronic inflammation reflect its main feature - a long course with varying degrees of activity. In this regard, there are 5 main signs of chronic inflammation:

• the predominance of a productive tissue reaction;

• the presence of secondary tissue damage caused by the cells of the very focus of chronic inflammation;

• features and weak severity of exudative tissue reaction, incomplete phagocytosis;

• mononuclear tissue infiltration, diffuse or focal, up to the formation of granulomas;

• sclerosis and persistent destruction of connective tissue.

Productive tissue reaction. Its predominance is not accidental, since inflammation becomes chronic when, for various reasons, there is no effective cell proliferation in the focus of inflammation, which ends with tissue repair. At the same time, it should be remembered that a productive tissue reaction in chronic inflammation is combined with alteration, exudation and sclerosis.

Secondary tissue damage (alteration) caused by cells of the very focus of chronic inflammation. Alteration in the form of necrosis and histolysis in chronic inflammation is induced by inflammatory mediators of plasma and cellular origin, accumulating in the focus of chronic inflammation. An example is the appearance of caseous necrosis in a tuberculous granuloma, induced not only by factors secreted by mycobacterium tuberculosis, but also by cytokines produced by macrophage elements of the granuloma itself (primarily TNF□).

Sometimes alteration in chronic inflammation in severity can prevail over a productive tissue reaction, for example, in destructive forms of hematogenous and secondary tuberculosis (cavernous pulmonary tuberculosis, caseous pneumonia) or in chronic abscess.

Features and weak severity of exudative tissue reaction. In chronic inflammation, exudative changes are, as a rule, insignificant and are represented mainly by the emigration of cellular elements and phagocytosis, which is often incomplete (for example, in granulomatous inflammation). Without the process of exudation, it is impossible to imagine the formation of cellular inflammatory infiltrates in the foci of chronic inflammation and granulomas, since most of the cells of these infiltrates are of hematogenous origin. In certain types of chronic inflammation, exudation is pronounced, as, for example, in chronic catarrhal inflammation, chronic abscess, as well as in the infiltrative form of secondary pulmonary tuberculosis.

Mononuclear tissue infiltration, diffuse or focal up to the formation of granulomas. The main cells of mononuclear infiltration are cells of monocytic origin and lymphocytes. The traditional histological concept of "mononuclear cells, mononuclear cells" covers all mononuclear cells originating from a hematopoietic stem cell, except for erythrocytes and segmented leukocytes.

Macrophage is the main cell of chronic inflammation. Blood monocytes live for about 1 day, while tissue macrophages live for several months. Macrophages are part of the monocytic-macrophage system and are represented in various organs and tissues. It is believed that all macrophages are of bone marrow monocytic origin. In the focus of inflammation, the monocyte is transformed into a tissue macrophage. Macrophages secrete inflammatory mediators under the influence of cytokines produced by T cells. Macrophages are involved in a variety of processes related to both inflammatory and immune responses. The main function of macrophages is phagocytosis. They carry out phagocytosis not only of damaging agents (for example, microbes), but also of tissue detritus, thereby preparing the "soil" for reparative processes. In immune

reactions, the macrophage takes part in the stage of processing and presentation of the antigen associated with the main histocompatibility complex to T cells.

Other types of mononuclear cells are found in chronic inflammation: lymphocytes, plasma cells, eosinophils, and mast cells.

Lymphocytes are the main component of HRT reactions - a tissue response to viral infections, as well as in non-immune inflammation. Lymphocytes of different types (T-, B-lymphocytes) or in different states (native, activated) secrete different adhesive molecules and chemical mediators. In chronic inflammation, they have a reciprocal relationship with macrophages. Activated lymphocytes produce lymphokines, with IFNy being the main stimulator of monocytes and macrophages. Cytokines from activated macrophages (monokines), on the contrary, activate lymphocytes, which themselves also produce inflammatory mediators. This ensures the duration of the inflammatory response.

Plasma cells produce antibodies directed against a persistent antigen at the site of inflammation or against components of destroyed tissue.

Eosinophils are characteristic of immune responses associated with allergic reactions and parasitic infections. Clusters of eosinophils are observed in the respiratory tract in allergen-associated bronchial asthma and in tissues infected with multicellular parasites, in particular helminths. Like neutrophils, they use adhesive molecules and chemotactic agents formed by mast cells, lymphocytes and macrophages to escape from the bloodstream. Their granules contain a major protein, as well as a cationic protein that is toxic to parasites and causes lysis of mammalian epithelial cells.

Although neutrophils play a major role in acute inflammation, many forms of chronic inflammation lasting months are also accompanied by the accumulation of large amounts of neutrophils. This is due to the persistence of bacteria or the release of mediators by macrophages or necrotic cells. In chronic bacterial inflammation of the bones (osteomyelitis), neutrophilic exudate can be detected for several months. Neutrophils are important in chronic lung damage associated, for example, with smoking or other causes.

Mononuclear infiltration usually occurs in interstitial tissue; it is formed by diapedesis and proliferation of cellular elements released from the bloodstream, as well as proliferation of connective tissue cells of local (histiogenic) origin. Cells of hematogenous origin enter the infiltrate as a result of exudation processes and are represented by monocytes, macrophages, lymphocytes, plasma cells, single neutrophils, eosinophils and mast cells. Plasma cells of the infiltrate can turn into hyaline balls or fuchsinophilic bodies (Roussel's bodies). Cells of histiogenic origin in the tissue infiltrate are represented by histiocytes, fibroblasts, myofibroblasts, and elements of the vascular wall. As you can see, most of the listed cells are differentiated and lose their ability to proliferate. It is believed that the ability to divide is preserved in monocytes, lymphoid elements when leaving the vessel, as well as in fibroblasts, myofibroblasts and cells of the vascular wall.

Sclerosis and persistent destruction of connective tissue. The most important sign of chronic inflammation is also the development of sclerotic changes with persistent destruction of connective tissue, which is a manifestation of a violation of the repair processes. Therefore, the

restoration of destroyed tissues occurs by replacing damaged parenchymal cells with connective tissue, as a result of which fibrosis or scarring develops. This process is similar to wound healing, but due to the fact that the damage continues, and the inflammatory reaction subsides and then resumes, the events become less predictable.

The outcomes of chronic inflammation are rarely favorable and are associated with the replacement of the inflammation focus with connective tissue.

In most cases, there are various complications (secondary amyloidosis, cachexia, arrosive bleeding), sclerotic changes leading to organ failure, as well as malignant tumors.

The relationship between chronic inflammation and tumor growth is proved by the development of stomach cancer in patients with chronic gastritis, lung cancer in patients with chronic inflammatory lung diseases with diffuse and focal pneumosclerosis (the concept of "cancer in the rumen").

Chronic inflammation can be represented by various morphological variants of productive and exudative inflammation. Chronic productive inflammation has three main types. When the mononuclear infiltrate is localized in the interstitial tissue of the parenchymal organs, they speak of interstitial (interstitial) inflammation, and in the case of the formation of granulomas in the tissues, granulomatous chronic inflammation. The development of chronic inflammation on the mucous membranes is often accompanied by the proliferation of epithelial cells, which leads to the appearance of inflammatory polyps and genital warts. Chronic exudative inflammation is represented by chronic purulent (chronic abscess) and chronic catarrhal inflammation.

Interstitial (interstitial) inflammation

Interstitial inflammation develops in the stroma of parenchymal organs - the myocardium, liver, kidneys and lungs. It can be not only chronic, but also acute. With inter-uterine inflammation, a combination of productive and exudative tissue reactions with sclerotic changes is characteristic.

The etiology of interstitial inflammation is diverse. It occurs in bacterial and viral infections with a severe course (sepsis, diphtheria, typhus, acute and chronic viral hepatitis, etc.), chronic exogenous and endogenous intoxications (interstitial lung disease, interstitial nephritis) and diseases of unknown etiology with immune pathogenesis (idiopathic fibrosing alveolitis, Abramov-Fiedler's myocarditis).

On a macroscopic examination, the organs are slightly changed. It is possible to note a slight increase in their size, uneven blood vessels and flabby consistency.

Microscopically, focal or diffuse inflammatory cellular infiltration in the stroma of the myocardium, liver, kidneys and lungs can be detected. In the parenchyma of organs, pronounced dystrophic and sometimes necrobiotic changes are found. Similar changes are observed, for example, in pneumocytes of the 1st and 2nd orders in interstitial lung diseases, cardiomyocytes in Ab-Ramov-Fiedler's myocarditis, in hepatocytes in viral hepatitis.

Sclerosis as a result of interstitial inflammation is caused by the activation of fibroblasts, which occurs as a result of initial damage, secondary damage due to inflammatory mediators, production of growth factors by infiltrate cells, primarily macrophages, endothelial cells.

Outcomes of chronic interstitial inflammation. In the end, connective tissue grows diffusely, which can lead to dysfunction of the organ. So, in the course of interstitial myocarditis, diffuse small-focal cardiosclerosis often develops, which is the basis of chronic heart failure. Interstitial lung diseases often lead to interstitial fibrosis with the formation of the so-called cellular lung and progressive pulmonary heart disease.

Granulomatous inflammation

Granulomatous inflammation is a form of chronic inflammatory reaction in which nodules and diffuse tissue infiltrates are formed. The predominant type of cells in infiltrates are cells of monocytic-macrophage origin: macrophages, epithelioid cells, giant multinucleated cells of foreign bodies and Pirogov-Langhans cells.

The etiology of granulomatous inflammation is diverse. Granulomatous inflammation of the established etiology is caused by both endogenous and exogenous factors, which in turn can be infectious and non-infectious in nature. Exogenous factors that cause the formation of granulomas include biological (bacteria, fungi, protozoa, helminths), organic and inorganic substances (dust, smoke, etc.), drugs (granulomatous hepatitis). Endogenous factors include sparingly soluble products of damaged tissues, especially adipose tissue (soap), as well as products of impaired metabolism, such as urates.

Among the infectious agents that cause granulomatous inflammation, banal and specific (tuberculous mycobacterium, treponema pallidum, leprosy mycobacterium, rhinoscleroma bacillus) are distinguished.

However, in some cases, the etiology of granulomatous inflammation remains unclear. Granulomas of unknown etiology include granulomas in sarcoidosis, Crohn's disease, primary biliary cirrhosis, etc.

The pathogenesis is due to the persistence of the damaging factor due to incompleteness or impossibility of phagocytosis, which is typical for other types of chronic inflammation. There are three hypotheses explaining the formation of accumulations of monocytes in tissues: the hypothesis of permanent diapedesis of monocytes, immortalization of monocytes, proliferation of monocytes and transformed granuloma cells.

A feature of granulomatous inflammation is the presence of cellular transformation of a monocyte into a macrophage - an epithelioid cell - a multinucleated giant cell. After leaving the bloodstream, the monocyte divides only 1-2 times, and then transforms into a macrophage. 7 days after the emergence and reproduction, the macrophage turns into an epithelioid cell, so named because of its external resemblance to an epithelial cell.

The most important reason for the transformation of a macrophage into an epithelioid cell is incomplete phagocytosis. With incomplete phagocytosis, a kind of macrophage-bacterium symbiosis, called endocytobiosis, can occur. Endocytobiosis is a form of symbiosis in which the microbe remains viable in the cell.

The reasons for incomplete phagocytosis can be:

• inability to digest the damaging agent (foreign bodies);

• damage to the macrophage (SiO_2 crystals in silicosis);

• inhibition of macrophage activity by bacterial products (cord factor and hetero-polysaccharide LAM of mycobacterium tuberculosis) or T-cells;

• penetration of the pathogen into the macrophage by interacting with C3-receptors without induction of a respiratory burst (tuberculosis);

• secretion of urease by the causative agent, which prevents the acidification of the environment by lysosomes (tuberculosis).

The epithelioid cell has a large, pale oval nucleus and a pale pink granular cytoplasm. Epithelioid cells usually do not form secondary lysosomes, which indicates a low phagocytic activity. At the same time, a rough endoplasmic reticulum is developed in these cells and a variety of cytokines (FGF, TGF, IPFR-1; fibronectin, IL-1) are synthesized, stimulating the processes of sclerosis in tissues.

At the 2nd week, epithelioid cells are transformed into giant multinucleated cells of Pirogov-Langhans, and after 2-3 weeks - into giant cells of foreign bodies. Most authors associate the appearance of multinucleated cells with the fusion of epithelioid cells into a multinucleated symplast, in which the cytoskeleton is ordered over time, the nuclei are located under the cytolemma. However, another mechanism for the formation of giant multinucleated cells is not excluded - by dividing the nuclei of epithelioid cells without cell division. The morphological features of the Pirogov-Langhans giant cells are large size (up to 40-50 microns), the presence of a large (up to 20) number of nuclei, which are located eccentrically on one side in the shape of a horseshoe. In a giant cell of foreign bodies, up to 30 nuclei are found (describe cells containing up to 100 nuclei), which are located chaotically, mainly in the center of the cell. Both types of giant cells are distinguished by the absence of lysosomes, therefore, capturing various pathogenic factors, giant cells are not able to digest them, that is, phagocytosis in them is incomplete and is "replaced" by endocytobiosis. The question of the cytokine activity of multinucleated giant cells remains open.

In many infectious immune granulomas, secondary tissue damage develops in the form of caseous necrosis in the center of the inflammatory focus. The development of caseous necrosis is associated with the production of a large number of mediators (TNFa, reactive oxygen species, proteases) by the activated macrophages granulomas, which have an indiscriminate damaging effect.

Granuloma morphogenesis consists of 4 stages:

1) accumulation of monocytes in the focus of tissue damage;

2) the maturation of these cells into macrophages and the formation of macrophage granulomas;

3) transformation of macrophages into epithelioid cells and the formation of epithelioid cell granulomas;

4) transformation of epithelioid cells into giant cells (Pirogov-Langhansa and / or foreign bodies) and the formation of giant cell granulomas.

Thus, given the cellular composition of granulomas, 3 types of granulomas are distinguished by morphological features: macrophage (simple or phagocytoma); epithelioid cell and giant cell.

The classification of granulomatous inflammation takes into account its etiology, pathogenesis, course and morphological features. The following types of granulomatous inflammation are distinguished:

By etiology:

• unknown etiology;

• established etiology:

1) non-infectious,

2) infectious (commonplace and specific). By pathogenesis:

• immune;

• non-immune.

By morphology:

• tuberculoid type (with the formation of granulomas, classified by cell composition and type of necrosis);

• diffuse type (with the formation of granulomatous infiltrate).

Morphology. Granulomatous inflammation can be represented by granulomas. This type of granulomatous inflammation is usually called tuberculoid. However, in a number of diseases (tertiary syphilis, leprosy), the second type of granulomatous inflammation develops - diffuse granulomatous infiltration. The structure of granulomas is largely stereotyped, which is determined by their pathogenesis.

Immune granulomas are a morphological expression of type III and IV hypersensitivity reactions and are characterized by cell cooperation macrophage - lymphocyte - fibroblast. Immune granulomas are most often built according to the type of epithelioid-cell, although depending on the stage of development they can be built from macrophages and contain giant Pirogov-Langhans cells. They always contain an admixture of a fairly large number of lymphocytes and plasma cells, and at later stages and fibroblasts. Immune granulomas develop when the damaging agent is an antigen (for example, tuberculosis, leprosy, syphilis, rhinoscleroma). Sometimes the products of tissue damage become a source of antigenic irritation. In these cases, the autoimmune mechanisms of granuloma formation are turned on.

Finally, immune granulomas are formed as a result of patient contact with organic and inorganic particles of dust and aerosols (for example, beryllium oxide is a compound that causes the appearance of immune granulomas of the sarcoid type).

Non-immune granulomas include most of the granulomas that develop around foreign bodies, consisting primarily of particles of inorganic dust, suture material, and parasites. Most often they are built like a phagocytoma or a giant cell granuloma, consisting of macrophages and giant multinucleated cells of foreign bodies. When comparing these granulomas with immune ones, fewer lymphocytes and plasma cells are noted.

Some granulomas of infectious etiology have a relative morphological specificity. Identification of the causative agent is required to confirm the diagnosis.

Specific are those granulomas, the formation of which is associated with specific pathogens:

• mycobacterium tuberculosis;

• mycobacterium leprosy;

• pale treponema;

• a rhinoscleroma stick.

Specific granulomas are characterized by relatively specific morphological manifestations (only for these pathogens and not for any others), and the cellular composition, and sometimes the location of cells inside the granulomas (for example, in tuberculosis) is also quite specific.

Granulomas of all 4 types occur in diseases that have a chronic wave-like course, that is, with periods of exacerbation and remission. As a rule, with all these diseases, a special type of secondary tissue damage develops in the center of the granulomas - caseous necrosis.

Outcomes of granulomatous inflammation. The following outcomes are possible:

• resorption of cellular infiltrate;

• development of sclerosis;

• necrosis of granulomas;

• suppuration of granulomas.

With many infections (glanders, yersiniosis, tularemia) and fungal lesions at the first stages, many neutrophils appear, but only in the case of a mycotic lesion, they cannot cope with the pathogen, die, and the products of their death, being chemoattractants, attract leukocytes. So there are a kind of granulomas with an abscess in the center.

Tuberculous granuloma.

Macroscopic examination of organs containing tuberculous granulomas reveals small, the size of a grain of millet (from Latin milium - millet) tubercles (tuberculum), which are accumulations

of several granules. This was the basis for the name of the disease tuberculosis, or tuberculosis, and this form of tuberculosis - miliary tuberculosis. Tuberculous granulomas are so small (their diameter does not exceed 1-2 mm) that in other forms of tuberculosis they are most often detected only microscopically.

Microscopically, the granuloma is built of epithelioid cells, giant cells of Pirogov-Langhans and lymphocytes, which reflects its pathogenesis (it is a granuloma with immune pathogenesis). In the center of the granuloma, a focus of caseous necrosis is found, behind which there is a shaft of radially located (elongated along the length from the center to the periphery) epithelioid cells; behind it there are single giant multinucleated cells of Pirogov-Langhans and, finally, on the periphery of the granuloma there is a shaft of lymphoid cells. In addition to the listed typical cells, the granuloma may contain an admixture of a small number of plasma cells and macrophages. When impregnated with silver salts, a thin network of argyrophilic (reticular) fibers is found among the granuloma cells. Blood vessels in a tuberculous granuloma usually do not occur. When staining according to Ziehl-Nielsen, acid-resistant mycobacterium tuberculosis is detected in giant cells.

With a favorable course of granulomas, sclerosis is ruled and hyalinized, and the zone of caseous necrosis is subjected to petrification. With an unfavorable course, an increase in exudative and necrotic changes occurs, infiltrative and destructive forms of tuberculosis develop, leading to pulmonary or respiratory failure and fatal arrosive bleeding. Often, the disease is complicated by the development of cachexia and secondary amyloid dose.

Syphilitic granuloma is called **gum** (from Latin gummi - gum).

Gumma is characteristic of the tertiary period of syphilis, which usually develops several years (4-5 and later) after infection and lasts for decades. In tertiary syphilis, in addition to gum, a diffuse variant of granulomatous inflammation may occur - gummy infiltration.

In addition to granulomatous inflammation, the causative agent of syphilis, pale treponema, causes the development of obliterating endarteritis and productive vasculitis with perivascular mononuclear infiltrates. Vasculitis appears secondarily in response to fixation of treponema in vascular endothelial cells. The binding of treponema to the endothelium is provided by fibronectin molecules that coat the microbe. Then, immune inflammation occurs in the walls of blood vessels and adjacent tissues (hypersensitivity reactions of types III and IV).

Macroscopically, gum can be localized in different organs and tissues: bones, skin, liver, brain, etc. It looks like a solitary (from Latin solitarius - prone to loneliness) node with a size of 0.3-1.0 cm (on skin) to the size of a chicken egg (in the internal organs). On the cut from these nodes, a jelly-like mass of yellow color, reminiscent of gum arabic glue (gum arabic), is released, hence the name of syphilic granuloma - "gum".

Microscopically, the center of the gum is represented by a focus of caseous necrosis, much larger in size than in tuberculosis. On the periphery of the necrosis focus, there are many lymphocytes, plasma cells and fibroblasts. These three types of cells predominate, but epithelioid cells, macrophages and single giant cells of the Pirogov-Langhans type can be found in a small amount

in the gum. Syphilitic granuloma is characterized by rapid, due to the proliferation of fibroblasts and their synthesis of procollagen,

overgrowth of massive dense connective tissue, which forms a kind of capsule. From the inside of this capsule, among the cells of the infiltrate, numerous small vessels are visible, and outside - larger vessels with the phenomena of productive endovasculitis. It is extremely rare among the cells of the infiltrate with the help of silver plating it is possible to reveal pale treponema.

In addition to gum, in the tertiary period of syphilis, diffuse granulomatous inflammation can develop - ***gummy infiltration***. Gummy infiltrate is usually represented by the same cells that dominate in the gum, that is, lymphocytes, plasmocytes and fibroblasts. At the same time, a tendency to sclerosis appears very quickly - granulation tissue grows. Infiltration cells are located in the middle and outer membranes of the aorta along the vasa vasorum - small capillary type of vessels: productive vasculitis is also found in these vessels.

Gummy infiltration most often occurs in the ascending part and the arch of the thoracic aorta and is called syphilitic mesaortitis. Gummy infiltrate destroys the elastic frame of the aorta. The destruction of elasticity is associated with the production of elastase infiltrate cells and under conditions of high blood pressure in the aorta can lead to the development of an aneurysm of the ascending part or thoracic aorta. When stained with fuchselin, lysis of elastic fibers is found at the site of the former infiltrate. Connective tissue grows in place of elastic fibers.

At the same time, the intima of the aorta is not affected by gummy infiltration, but it becomes uneven and wrinkled due to the multitude of cicatricial retractions and bulges and resembles "shagreen skin". Gummy infiltration can spread to the aortic valve, which results in the formation of aortic heart disease.

Diffuse gummy infiltration in the liver leads to the development of a lobular liver.

Outcomes of syphilitic granulomatous inflammation are usually unfavorable. Gums in organs cause destruction and development of cirrhotic changes. Syphilitic mesaorthitis is complicated by aortic aneurysm, heart defect, and the patient dies from rupture of the aortic aneurysm and fatal arterial bleeding, or from progressive chronic heart failure.

Leprosy granuloma (leproma) has a polymorphic cellular composition: a large number of macrophages, epithelioid cells, as well as giant, plasma cells, fibroblasts.

Mycobacteria of Hansen-Neisser are found in huge quantities in macrophages (it has been established that 1 g of leproma contains up to 5 x 109 lepromatous mycobacteria). The latter, overflowing with pathogens, increase, as it were, swell, fatty inclusions appear in their cytoplasm. In such macrophages (Virchow's leprosy cells), mycobacteria are arranged in strictly ordered rows, resembling cigarettes in a pack, which is especially clearly seen when stained according to Ziehl-Nielsen. Subsequently, mycobacteria, sticking together, form leprosy balls. The macrophage is destroyed over time, the leprosy balls that have fallen out are phagocytosed by giant cells of foreign bodies. The presence of a huge amount of mycobacterium in leprosy is due to incomplete phagocytosis in macrophages with leprosy.

Tissue reactions in leprosy are closely related to the reactivity of the body, as well as the relationship between the macro- and microorganism, which determines the whole variety of clinical manifestations of the disease. There are several variants of the course of leprosy, including a form with a high host resistance - tuberculoid and with a low host resistance - lepromatous.

The tuberculoid form of leprosy is clinically benign, sometimes with self-healing against the background of pronounced cellular immunity. Skin lesions are diffuse, with many spots, plaques and papules, followed by depigmentation of the affected areas. Morphologically, epithelioid-cellular granulomas are found, and mycobacteria are detected in rare cases, which confirms the development of leproma by the HRT mechanism. Damage to the nerves is characterized by diffuse infiltration of their epithelioid cells, which is manifested by early sensory disturbances. Changes in the internal organs for this form are uncharacteristic.

The lepromacosis form of leprosy is characterized by the development of diffuse granulomas of atotic inflammation. Skin lesions often have a diffuse nature, the process involves, and then completely destroyed, the appendages of the skin - sweat and sebaceous glands, the vessels are damaged. Macrophages, giant cells and many mycobacteria are found in leprosy. Diffuse infiltration of the skin of the face sometimes leads to complete disfigurement of the appearance ("lion's face"). Leprosy neuritis is of an ascending nature, diffuse infiltration of all elements of the sensory nerves by macrophages develops, with gradual replacement of the nerve fiber with connective tissue. Granulomas from macrophages with a large amount of mycobacteria are found in the liver, spleen, bone marrow, lymph nodes, the mucous membrane of the upper respiratory tract, and in the endocrine organs. All of the above may indicate a significant inhibition of cellular reactions of immunity in the lepromatous form of leprosy, while a pronounced dysfunction of the humoral link is noted.

With effective treatment, a favorable outcome is possible up to a complete cure. Unfavorable outcomes are caused by tissue destruction with the formation of ulcers, necrosis of large areas of tissue up to self-amputation of body parts.

Rhinoscleral granuloma is characterized by the accumulation of macrophages, lymphocytes, a large number of plasma cells and their degradation products - Roussel's eosinophilic bodies. Very large mononuclear cells with vacuolated cytoplasm, Mikulich cells, are specific for scleroma granulomas. Macrophages intensively seize diplobacilli, however, phagocytosis in them is incomplete. Part of the macrophages is destroyed, and part, increasing, turns into Mikulich's cells, in which they find the causative agent of rhinoscleroma - Volkovich-Frisch's stick.

Rhinoscleral granuloma is usually located in the mucous membrane of the upper respiratory tract - the nose, larynx, trachea, less often - the bronchi.

The process ends with the formation of rough scar tissue in place of granulomas, as a result of which the mucous membrane is deformed, the airways are sharply narrowed and even sometimes completely closed, there is a danger of asphyxia.

Granulomatous diseases

This is a heterogeneous group of diseases (nosological forms) of various etiologies, the structural basis of which is granulomatous inflammation. These diseases have a number of symptoms:

• the presence of granulomatous inflammation;

• violation of immunological homeostasis;

• polymorphism of tissue reactions;

• tendency to chronic course with frequent relapses;

• frequent vascular damage in the form of vasculitis.

Classification of granulomatous diseases. It is based on the etiology of the disease.

Granulomatous diseases of established etiology.

1. Granulomatous diseases of infectious etiology: rabies, viral encephalitis, cat scratch disease, typhus, typhoid fever, paratyphoid fever, yersiniosis, brucellosis, tularemia, glanders, rheumatism, rhinosclerosis, tuberculosis, syphilis, leprosy, malaria, toxo plasmosis, leishmaniasis, actinomycosis, candidiasis, schistosomiasis, trichinosis, alveococcosis.

2. Granulomatous diseases of non-infectious etiology: silicosis, asbestosis, talcosis, anthracosis, aluminosis, beryllium, zirconia, bogassosis, byssinosis, amylosis.

3. Granulomatous drug diseases: granulomatous drug hepatitis, oleogranulomatous disease, gluteal granuloma of infants.

Granulomatous diseases of unknown etiology. These include sarcoidosis, Crohn's disease, Horton's disease, rheumatoid arthritis, primary biliary cirrhosis, Wegener's granulematosis, Weber-Christian panniculitis, xanthogranulomatous pyelonephritis.

Inflammation with the formation of polyps and genital warts

- Productive inflammation, in which there is a simultaneous proliferation of parenchymal elements and stroma; the stroma is diffusely infiltrated by mononuclear cells.
- Characterized by a chronic course;
- Typical localization is mucous membranes.
- Examples: polyps of the nasal cavity, maxillary sinuses, bronchi, gastric mucosa, intestines, uterus.
- Genital warts - formed at the junction of squamous and prismatic epithelium (anus, genitals); caused by papillomavirus (HPV); may be accompanied by dysplasia; are a risk factor for squamous cell carcinoma.

3. Lesson plan

Macropreparations

1. To study the productive inflammation around the animal parasite according to the macroscopic picture. Describe the macropreparation "**Alveococcosis of the liver**". - Pay attention to the size and consistency of the liver, especially its structure in the section.

2. To study miliary pulmonary tuberculosis by macroscopic picture. Describe the macropreparation "**Miliary pulmonary tuberculosis**". - Pay attention to the size and consistency of the lung, the number, location, size and color of tuberculous tubercles.

3. To study caseous pneumonia according to the macroscopic picture. Describe the macropreparation "**Caseous pneumonia**". - Pay attention to the area of the lesion, consistency, color of the lung tissue in these areas.

4. To study syphilitic mesaortitis on a macroscopic picture. Describe the macropreparation "**Syphilitic mesaortitis**". - Pay attention to the localization of the lesion in the aorta, the perimeter and thickness of the aortic wall in the damaged section, the nature of the intimal lesion.

Micropreparations

1. To study the interstitial (interstitial) inflammation according to the microscopic picture. Describe the micropreparation "**Interstitial (interstitial) myocarditis**" (staining with hematoxylin and eosin). - Pay attention to the cellular composition and localization of the inflammatory infiltrate, the number of connective tissue elements in the myocardium; assess the state of myocardiocytes in the area of inflammation.

4. To study the productive inflammation around the animal parasite by microscopic picture. Describe the micro-preparation "**Liver alveococcosis**" (staining with hematoxylin and eosin). - Pay attention to the localization of the parasite, the structure of its shell, the localization and cellular composition of the inflammatory infiltrate, the state of the liver tissue.

3. Examine the tuberculous granuloma on a microscopic picture. Describe the micro-preparation "**Tuberculous granuloma in the lungs** (miliary tuberculosis)" (staining with hematoxylin and eosin). - Pay attention to the localization, cellular composition, the state of the central part of the tuberculous granuloma, changes in the surrounding lung tissue.

4. To study exudative tissue reaction in the lungs with tuberculosis. Describe the micro-preparation "**Exudative tissue reaction in the lungs in tuberculosis (caseous pneumonia**) (staining with hematoxylin and eosin). - Pay attention to the localization and composition of the exudate, morphological signs of caseous necrosis.

5. Examine the syphilitic granuloma (gum) by a microscopic picture. Describe the micropreparation "**Solitary gum of the liver**" (staining with hematoxylin and eosin). - Pay attention to the localization, cellular composition, state of the central part and vessels of the granuloma.

6. To study syphilitic mesaorthitis on a microscopic picture. Describe the micro-preparation "**Syphilitic mesaortitis**" (stains with hematoxylin and eosin, fuchselin). - Pay attention to the localization and cellular composition of the infiltrate, the state of elastic fibers in the aortic wall and lesions.

7. Examine leprosy granuloma in a microscopic picture. Examine the micropreparation "**Leprosy granuloma**" (staining with hematoxylin and eosin, according to Tsil-Nielsen). - Pay attention to the localization and cellular composition of the granuloma, the accumulation of the pathogen, detected by staining according to Tsil-Nielsen.

8. Examine the rhinoscleroma granuloma in the microscopic picture. Describe the micro-preparation "**Rhinoscleral granuloma**" (staining with hematoxylin and eosin). - Pay attention to the cellular composition of the granuloma.

Electronograms

1. To study the structure of the macrophage and giant cell of Pirogov-Langhans using electron microscopy. Describe the electron diffraction patterns "**Tissue infiltrate macrophage**" and "**Pirogov-Langhans' giant cell**". - Pay attention to the state of ultrastructures: the number of lysosomes and phagolysosomes, the presence and nature of inclusions in the tubules of the cytoplasmic reticulum in both cells.

Situation cases

Situation case 1

2 weeks after the flu, the patient K., 35 years old, consulted a doctor with complaints of severe weakness, shortness of breath, discomfort in the region of the heart (interruptions, palpitations). Objectively: pallor of the skin, pulse of weak filling, arrhythmic, 105 / min. BP 110/75 mm Hg. Art. With percussion - expansion of the boundaries of the heart, with a-scultation - deafness and systolic murmur at the apex, arrhythmia. X-ray: diffuse enlargement of the shadow of the heart in the absence of signs of hypertrophy. Sluggish pulsation of its contours with a reduced amplitude. On the ECG, ventricular extrasystonia. In the general analysis of blood, attention is drawn to leukocytosis 10.7 x 109 / l (normally 4-9 x 109 / l). Leukocyte formula without features; ESR 27 mm / h (normal 2-10 mm / h). Biochemical blood test: α-globulins 13.5% (normal 5.1-8.3%), γ-globulins 24.1% (normal 15-22%). Total lactate dehydrogenase - 39 mmol / (h l) (normally 13.0-30 mmol / h l); creatinine phosphokinase - 34 mmol / (h 'l) (normal 0.10-12 mmol / (h' l); iso enzyme MB-CPK - 21 mmol / (h 'l) (normal 0-1 mmol / (h 'l); C-reactive protein 10.1 mg / l (normally 0.07-8.2 mg / l).

Questions to the situation case 1

1. What is the pathological condition of the patient?

2. What indicates the presence of an inflammatory process?

3. What indicates the development of a pathological process in the heart muscle?

4. Why does the patient have low blood pressure and enlarged heart?

5. Name the morphological changes in the stroma of the myocardium.

6. Name the morphological manifestations of cardiomyocyte lesions.

Situation case 2

A patient with tuberculosis died of pulmonary heart failure. Autopsy revealed interstitial myocarditis, multiple foci the size of millet grain in the lungs, liver and spleen.

Questions to the situation case 2

1. Name the lesion of the lungs, liver and spleen.

2. What tissue reaction do these bumps reflect?

3. Describe the structure of the tuberculous granuloma.

4. Give the characteristic of tuberculous granuloma by pathogenesis and by the level of metabolism.

5. Name the stages of granuloma morphogenesis.

Situation case 3

A patient suffering from heart disease (insufficiency of the aortic valves) suddenly developed pallor of the skin, blood pressure dropped sharply, and death occurred. Autopsy revealed a ruptured aneurysm in the ascending aorta, intima of the ascending aorta with multiple tuberosities and retractions. Solitary gum was found in the liver.

Questions for situation case 3

1. What is the etiology of the process?

2. What pathological process is associated with the development of aortic aneurysm?

3. What is the cellular composition of the infiltrate in the aortic wall, and in what layers is it localized? '

4. How do elastic fibers in the aortic wall change?

5. What is gumma?

6. Indicate the structure of the gum.

Literature to the Topic 3

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