Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

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METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Inflammation”

Duration: 3 hours

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EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To study the morphology of inflammation, its varieties, and pathogenesis. To draw attention to the fact that inflammation is a complex reaction of the organism in response to harmful stimuli. To emphasize that the reactivity of the organism, which can be altered by various conditions, is of decisive importance for the onset, nature, and outcome of the inflammatory process. To indicate the evolutionary-adaptive nature of the inflammatory reaction, its harmful and beneficial features for the organism. The main components of inflammation (alteration, exudation, proliferation) should be analyzed in detail. To note that manifestations of alteration (dystrophic and necrobiotic processes) occur not only in cells but also in the intercellular substance. To indicate that upon cell damage, biologically active substances are released that promote the development of vascular-exudative and proliferative processes. To explain the essence of exudation. To compare the composition of exudate and transudate. To provide an understanding of proliferative changes in inflammation. To list the clinical signs of inflammation. To define the concept of exudative inflammation and analyze its types depending on the nature of the exudate. To indicate the causes, most frequent localization, and outcomes of these types of inflammation, providing examples. To be able to identify macroscopic and microscopic signs of inflammation, explain their causes and mechanisms of development, evaluate their likely outcome, and determine their significance for the organism.
- To study the morphology of productive and specific inflammation. To indicate that productive inflammation is characterized by a predominance of proliferation, as evidenced by the reproduction of connective tissue cells and vascular proliferation, and that these changes are localized primarily in the stroma of organs. To analyze the variants of productive inflammation. To note that the course of productive inflammation is more often chronic and, as a rule, ends in organ sclerosis and functional impairment. To draw attention to the fact that specific inflammation is a clinical-morphological concept and is characterized by a combination of clinical and anatomical manifestations specific to a given disease. To demonstrate that specific inflammation, like any other, represents a combination of interrelated and interdependent phenomena of alteration, exudation, and proliferation. Its peculiarity is manifested in a specific sequence of tissue reactions, reflecting changes in the immune status of the organism. The granulomas formed during these inflammations are highly specific and are an indicator of high organism resistance. To examine the morphological manifestations of inflammation in tuberculosis, syphilis, leprosy, scleroma, and glanders. To thoroughly discuss the structure and cellular composition of granulomas in these diseases, noting the similarities and differences between them.

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

***Know*:**

- The definition of inflammation, explain its etiology and mechanism of development, and assess the significance of each phase of inflammation;
- The forms of inflammation according to classification;
- The definition of exudative inflammation and name its types;
- The macroscopic and microscopic characteristics of various types of exudative inflammation;
- The functional significance and outcomes of various types of exudative inflammation;
- The definition of productive inflammation and name its types;
- The etiology and mechanism of development of each type of productive inflammation;
- The types of productive inflammation based on their macroscopic and microscopic appearance;
- The outcomes, complications, and significance of productive inflammation;
- The definition of specific inflammation and name its differences from banal (nonspecific) inflammation;
- The etiology and mechanism of development of specific inflammation;
- The characteristic features of specific inflammation caused by the pathogens of tuberculosis, syphilis, leprosy, glanders, and rhinoscleroma based on their macroscopic and microscopic appearance;
- The outcomes, complications, and significance of specific inflammation.

Be able to:

- Identify major general pathological processes and diseases using histological specimens under light microscopy;
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body.

Master:

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;

- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Inflammation (inflammatio) is a complex, local vascular-mesenchymal reaction to tissue damage caused by various agents. Inflammation is a reaction developed during phylogenesis and has a protective-adaptive nature. It is aimed at eliminating the agent that caused the damage and restoring the damaged tissue. In human general pathology, inflammation is considered the most important "key" general pathological and, at the same time, biological process. Knowledge of this topic is essential for a deep understanding of the essence of most human diseases.

Mastering the materials of this topic is a necessary prerequisite for understanding the patterns of morphological reactions and their clinical manifestations in the development of a number of pathological processes and diseases that are based on productive inflammation. Furthermore, given the rise of socially significant diseases such as tuberculosis and syphilis, in which specific inflammation develops, knowledge of the morphological manifestations of these diseases will be necessary in the future professional activity of a physician for clinical diagnosis and treatment, as well as for analyzing the sources of diagnostic errors in clinical practice.

QUESTIONS

1. Exudative inflammation. Definition. Classification. Pathophysiology.
2. Serous inflammation. Definition. Classification. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
3. Fibrinous inflammation. Definition. Classification. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
4. Purulent (suppurative) inflammation. Definition. Classification. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
5. Catarrhal inflammation. Definition. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
6. Putrid, hemorrhagic and mixed inflammation. Definition. Pathophysiology. Serous inflammation. Etiology. Morphology. Clinical examples. Outcomes.
7. Productive (proliferative) inflammation. Definition. Classification. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
8. Interstitial inflammation. Definition. Classification. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
9. Granulomatous inflammation. Definition. Classification. Pathophysiology. Etiology. Morphology. Clinical examples. Outcomes.
10. Specific granulomas in tuberculosis, syphilis, leprosy, scleroma, sarcoidosis. Morphology. Outcomes.

COURSE OF THE SESSION

Inflammation is the immune system's **response to harmful stimuli** such as pathogens, damaged cells, toxins, or radiation. Its primary role is to eliminate the harmful agents and initiate tissue healing.

Inflammation is vital for maintaining health. During acute inflammation, a series of cellular and molecular events work to **minimize injury or infection**. This process helps restore tissue balance, or homeostasis, and resolves the inflammation.

While acute inflammation is usually beneficial, if uncontrolled, it can become chronic, leading to various chronic inflammatory diseases.

Key Characteristics of Inflammation

1) **Redness**
2) **Swelling**
3) **Heat**
4) **Pain**
5) **Loss of Function**

During the inflammatory process, important events occur at the microcirculatory level:

1) **Changes in Vascular Permeability**: Allows immune cells and proteins to move into the affected tissue.

2) **Leukocyte Recruitment and Accumulation**: White blood cells are drawn to the site of infection or injury.

3) **Release of Inflammatory Mediators**: These chemicals drive the inflammatory response and help coordinate immune defense.

Inflammation can result from various causes like infection, tissue injury, or necrosis, all of which induce tissue damage. The etiology of inflammation is either infectious or non-infectious.

1) **Non-Infectious Causes**:

- *Physical factors* include burns, frostbite, physical injury, foreign bodies, trauma, and ionizing radiation.
- *Chemical factors* include glucose, fatty acids, toxins, alcohol, and chemical irritants like fluoride and nickel.
- *Biological factors* involve damaged cells.
- *Psychological factors* like excitement may also play a role.

2) **Infectious Causes**: bacteria, viruses, and other microorganisms.

In response to tissue injury, the body initiates a chemical signaling cascade to heal the affected area. These signals activate leukocyte chemotaxis, drawing white blood cells to the site of damage. The activated leukocytes produce cytokines, which further promote and sustain the inflammatory response.

Pathophysiology

Inflammation is a protective and adaptive reaction that serves three main purposes:

1) Delimiting the area of damage.

2) Destroying the agents causing inflammation.

3) Restoring damaged tissues.

The inflammatory response involves the coordinated activation of signaling pathways that regulate the levels of inflammatory mediators in resident tissue cells and inflammatory cells recruited from the bloodstream.

While the processes of the inflammatory response can vary based on the initial stimulus and its location in the body, they generally follow a common sequence:

1) **Recognition**: Cell surface pattern receptors identify detrimental stimuli.

2) **Activation**: Inflammatory pathways are activated in response.

3) **Release**: Inflammatory markers are released into the affected area.

4) **Recruitment**: Inflammatory cells are drawn to the site of injury or infection.

Phases of the inflammatory reaction

The first phase is alteration, which involves direct damage to cells and tissues due to harmful stimuli such as pathogens, toxins, or physical injuries. This cellular injury can lead to necrosis or apoptosis, releasing intracellular components that serve as danger signals to the immune system.

In the second phase, the release of inflammatory mediators occurs. After cell damage, various mediators, including cytokines, chemokines, and histamines, are released. These mediators trigger a series of reactions in the microvasculature, leading to vasodilation and increased blood flow to the affected area. This phase also includes changes in the rheological properties of the blood, facilitating the delivery of immune cells to the site of injury.

The third phase involves impaired vascular permeability, characterized by increased permeability of blood vessels. This allows plasma proteins and immune cells to exit the bloodstream and enter the affected tissue, resulting in exudation. The accumulation of fluid, proteins, and leukocytes in the interstitial space manifests as redness, swelling, heat, and pain, which are hallmark signs of inflammation.

The final phase is proliferation, which focuses on tissue repair and regeneration. This phase includes the proliferation of fibroblasts, endothelial cells, and other cell types essential for healing. New blood vessels form through angiogenesis, and extracellular matrix components are synthesized to restore tissue integrity. Depending on the severity of the injury, this phase may lead to scar formation if healing is prolonged.

Morphological types of inflammation

Inflammation can be categorized into three main morphological types, reflecting the predominant changes occurring during the inflammatory response.

1) Alterative inflammation is characterized by cellular injury and necrosis. Histologically, this type often shows necrotic tissue without significant cellular inflammatory infiltration.

2) Exudative inflammation is marked by increased vascular permeability and the presence of exudates containing fluid, proteins, and cells. This type can be further classified into serous, fibrinous, purulent (which includes pus), and hemorrhagic

exudates, each indicative of different underlying processes and severities of inflammation.

3) Proliferative inflammation focuses on tissue repair and regeneration. It involves the proliferation of fibroblasts and angiogenesis, resulting in granulation tissue that temporarily replaces damaged tissue during the healing process. Histologically, this type shows numerous blood vessels, fibroblasts, and inflammatory cells, emphasizing the active healing phase.

Alteration

The alteration phase is primarily characterized by tissue damage resulting from necrosis, rather than inflammation. This phase often reflects the initial response to harmful stimuli that can lead to cell death without the typical signs of inflammation.

In the context of diseases like HIV/AIDS, the alteration phase can be exemplified by:

1) **Direct Viral Damage**: As HIV progresses to AIDS, it leads to the destruction of immune cells, particularly CD4+ T lymphocytes.

2) **Lack of Inflammation**: In this advanced stage, necrosis can occur in lymphoid tissues and other organs with minimal inflammatory response. This is partly due to the immune system's dysfunction, which fails to mount an effective inflammatory reaction against the necrotic tissue. As a result, the necrotic cells may not trigger the typical inflammatory mediators that would promote healing or clear debris.

Stages of exudation

1) **Microvascular Reaction**: Initially, the microvasculature reacts, resulting in changes to the rheological properties of the blood that impact blood flow dynamics.

2) **Increased Permeability**: Following this, there is an increase in the permeability of the microvasculature, allowing substances to pass more freely through the walls of blood vessels.

3) **Plasma Leakage**: Plasma then exits the bloodstream and enters the affected tissues, contributing to localized swelling.

4) **Cell Emigration**: Concurrently, leukocytes (immune cells) migrate from the bloodstream into the tissue to address the site of injury or infection.

5) **Phagocytosis**: Once at the site, these immune cells engage in phagocytosis, where they engulf and digest cellular debris, pathogens, and other harmful substances. This process is crucial for clearing the area of potentially damaging agents.

6) **Formation of Exudate**: Finally, these processes culminate in the formation of exudate, a fluid rich in proteins and immune cells, along with an infiltrate of inflammatory cells. This exudate is a key feature of inflammation, facilitating the healing process by providing necessary components for tissue repair and defending against infection.

Exudation

Exudation is a complex process that leads to the formation of inflammatory exudate, with sources including blood, lymph, and local tissue cells where the

inflammatory process occurs. The primary components of the inflammatory effusion are typically of hematogenous origin. The formation of this exudate results from both microcirculatory and cellular reactions.

Exudate consists of two main parts:

1) The **liquid** part, which includes water, plasma proteins (albumins, globulins), fibrinogen, mineral salts

2) The **cellular** part, which includes both cells of hematogenous origin (neutrophils, lymphocytes, monocytes, histiocytes, erythrocytes), and mesenchymal cells (macrophages, epithelial, mesothelial cells, etc.).

The balance between the liquid and cellular components, as well as the predominance of specific cell types, varies depending on the type of inflammation present.

Microcirculatory changes in exudation

Vasodilation and stasis: the first change in microcirculation is a transient and slight vasoconstriction, which is then replaced by a pronounced dilatation of arterioles, capillaries and venules. Vasodilation causes an initial increase in blood flow to the inflamed area (**hyperemia**). Then stasis develops, which is characterized by a sharp decrease in blood flow.

Increased permeability: the permeability of capillaries and venules depends on the state of intercellular junctions between vascular endothelial cells. Normally, only small molecules can pass through the pores, and pinocytosis selectively transports large molecules through the capillary into the interstitial tissues. In a normal capillary, fluid exits the microvasculature into tissues under the influence of capillary hydrostatic pressure and returns back under the influence of the osmotic pressure of plasma colloids.

In acute inflammation active contraction of actin filaments in endothelial cells leads to the expansion of these intercellular pores. Direct damage to endothelial cells by toxic agents can lead to the same result.

Impaired permeability leads to local **inflammatory edema**.

Cellular reactions in exudation

Types of cells involved: Acute inflammation is characterized by the infiltration of inflammatory cells from the blood in the site of injury. Neutrophils dominate in the early stage (in the first 24 hours). After the first 24-48 hours, phagocytic cells of the macrophage system and immunologically active cells such as lymphocytes and plasma cells appear in the focus of inflammation. However, **neutrophils remain the predominant cell type** for several days.

In a normal blood vessel, cells are located in the central part of the vessel, separated from the endothelial surface by a zone of plasma fluid. This separation occurs under the influence of physical laws, the influence of which leads to the accumulation of the heaviest cellular particles in the center of the vessel. Since the blood flow velocity in the dilated vessels during acute inflammation is reduced, the distribution of cellular elements is violated.

Leukocytes move to the periphery and come into contact with the endothelium, on which many of them adhere. This occurs as a result of an increase

in the expression of various cell adhesion molecules (CAM, cell adhesion molecules) on leukocytes and endothelial cells.

Exudation

Emigration of neutrophils: adherent neutrophils actively leave the blood vessels through the intercellular pores and pass through the basement membrane, entering the interstitial space.

Penetration through the vessel wall lasts 2-10 minutes; in the interstitial tissue neutrophils move at a speed of up to 20 microns/min.

Red blood cells enter the inflamed area passively, in contrast to the active process of leukocyte emigration. They are pushed out of the vessels by hydrostatic pressure through the expanded intercellular pores following the migrating leukocytes (diapedesis).

In severe injuries associated with impaired microcirculation, a large number of erythrocytes can enter the focus of inflammation (hemorrhagic inflammation).

Proliferation

Proliferation is the final phase of inflammation, which is characterized by the multiplication of cells capable of proliferation in the field of inflammation, followed by their differentiation and transformation. In the focus of inflammation, there is a proliferation of different types of cells: cambial cells of the connective tissue, B-lymphocytes and T-lymphocytes, monocytes, mesothelial, epithelial cells, etc.

Then, we can observe cellular differentiation and transformation: B-lymphocytes transform to plasma cells, monocytes – to histiocytes and macrophages. Macrophages can be a source of formation of epithelioid giant cells. Cambial connective tissue cells can further differentiate into fibroblasts that produce collagen protein and glycosaminoglycans.

As a result, **fibrous connective tissue** often grows as a result of inflammation.

Classification of inflammation

According to the predominance of one or another **component of inflammation**:

- exudative inflammation
- proliferative inflammation

According to the **speed** of development:

- acute
- subacute
- chronic

According to **localization** in the organ:

- parenchymal
- interstitial (interstitial)
- mixed

According to the type of **tissue reaction**:

- specific
- non-specific

Depending on the nature of the **exudate**:

- *serous*

- *fibrinous*
- *purulent*
- *putrid*
- *hemorrhagic*
- *catarrhal*
- *mixed*

Serous inflammation

Serous inflammation is characterized by the formation of exudate containing 1.7-2.0 g/l of protein and a relatively low number of cells.

Etiology: The causes include thermal and chemical factors, such as **burns** in the bullous stage, viral infections like **herpes**, and allergens from plants and animals.

Localization: This type of inflammation most commonly occurs in **serous membranes** (pleura, peritoneum, and pericardium), **mucous membranes** (respiratory and gastrointestinal tracts), and the **skin**, particularly in blistering conditions. It can also affect internal organs, with exudate accumulating in perisinusoidal spaces of the liver, between muscle fibers in the myocardium, and in the lumen of the glomerular capsule in the kidneys.

Morphology: Serous exudate appears as a **straw-yellow, opalescent liquid** primarily consisting of proteins like albumins and globulins, along with lymphocytes, a few neutrophils, and mesothelial or epithelial cells. Although serous exudate resembles transudate, they can be differentiated by the condition of the serous membranes; exudation shows signs of inflammation, while transudation reflects venous congestion.

Outcome: The prognosis for serous inflammation is **generally favorable**, as a significant volume of exudate is often reabsorbed by the body. However, chronic serous inflammation can lead to sclerosis in internal organs.

Fibrinous inflammation

Fibrinous inflammation is characterized by the formation of an **exudate rich in fibrinogen**, which converts to fibrin in the affected tissue. This transformation is facilitated by the release of a significant amount of thromboplastin in the zone of necrosis. Fibrinous inflammation is typically acute, although it can be chronic in certain cases, such as tuberculosis.

Etiology: Fibrinous inflammation can be caused by various pathogens and substances, including:

1) **Bacterial Pathogens**: Diphtheria and dysentery pathogens, as well as streptococci and staphylococci.

2) **Mycobacterium tuberculosis**: Known for causing chronic fibrinous inflammation.

3) **Influenza Viruses**: These can also lead to fibrinous reactions.

4) **Endotoxins**: Such as those encountered in uremia.

5) **Exotoxins**: For example, mercury chloride poisoning.

Types pf fibrinous inflammation

1) **Croupous Inflammation**: This occurs with superficial necrosis in mucous membranes covered with prismatic epithelium, where the connection between the epithelium and the underlying tissue is loose. This allows fibrinous plaques to easily detach without effort. Macroscopically, the mucous membrane appears thickened, swollen, and dull, resembling a surface sprinkled with sawdust. If the plaque is separated, it results in a surface defect. Fibrinous pericarditis is also known as "hairy heart." In croupous inflammation, the resulting defects are superficial, and complete regeneration is possible.

2) **Diphtheritic Inflammation**: This develops with deep tissue necrosis, where necrotic masses become impregnated with fibrin on thick mucous membranes. The fibrinous plaque in diphtheritic inflammation is tightly soldered to the underlying tissue. Defects resulting from diphtheritic inflammation are deep, resembling ulcers, and heal through scarring. In serous membranes, fibrin masses can undergo organization, leading to the formation of adhesions between the visceral and parietal layers of the pleura, peritoneum, and pericardium.

Purulent inflammation

Purulent inflammation is characterized by a **predominance of neutrophils in the exudate**, which, along with the liquid component, forms pus. The composition of pus includes mostly neutrophils and necrotic cells from the affected tissue. Macroscopically, pus appears as a turbid, creamy liquid with a yellowish-greenish color.

Purulent inflammation can be caused by various pathogens, including:

1) **Bacteria**: Such as staphylococci and streptococci.

2) **Fungi**: Certain fungal infections can also lead to purulent inflammation.

3) **Chemicals**: Aseptic purulent inflammation can occur when certain chemicals damage the tissues.

It is important to note that lysosomal enzymes released during the inflammatory response can exert destructive effects not only on the pathogens but also on the surrounding tissues, leading to histolysis. The degree of cell death varies across different forms of purulent inflammation, which can occur in any organ or tissue.

Types of purulent inflammation

1) An **abscess** is a focal purulent inflammation resulting in tissue melting and the formation of a cavity filled with pus. Abscesses can be acute or chronic. In acute abscesses, the wall consists of the tissue from the organ where it develops. Over time, the abscess becomes surrounded by a shaft of granulation tissue, rich in capillaries, facilitating the increased emigration of neutrophils. Eventually, it becomes encased in fibrous connective tissue, at which point it is classified as a chronic abscess. The membrane that produces pus in an abscess is known as the pyogenic membrane.

2) **Empyema** refers to purulent inflammation with pus accumulation in anatomical cavities, such as the pleural, pericardial, abdominal, maxillary, frontal cavities, gallbladder, appendix, or fallopian tubes.

- *Pleural Empyema*: This condition can arise as a complication of pneumonia, lung cancer, pulmonary tuberculosis, bronchiectasis, or septic pulmonary infarction.
- *Abdominal Empyema*: Often seen as an extreme manifestation of purulent peritonitis, it can occur as a complication of various diseases.

Phlegmon

Phlegmon: A diffuse purulent inflammation of the tissue or the walls of a hollow organ.

Mediastinitis: An acute purulent inflammation of the mediastinal tissue, which can be classified into anterior and posterior types. Anterior mediastinitis often complicates inflammatory processes in the anterior mediastinum, pleura, or neck. Posterior mediastinitis is frequently caused by esophageal issues, such as traumatic injuries from foreign bodies, esophageal cancer, or purulent-necrotic esophagitis.

Paranephritis: Purulent inflammation of the perirenal tissue, commonly a complication of purulent nephritis, septic kidney infarction, or kidney tumors.

Parametritis: Purulent inflammation of the parauterine tissue, which may occur due to septic abortions, infected childbirth, or malignant tumors of the uterus.

Paraproctitis: Inflammation of the tissue surrounding the rectum, which can be caused by dysentery ulcers, ulcerative colitis, anal fissures, hemorrhoids, or tumors.

Hemorrhagic inflammation

Hemorrhagic inflammation is characterized by the formation of exudate, represented mainly by **erythrocytes**.

The mechanism of its development is associated with a sharp increase in the permeability of microvessels, pronounced erythrodiapedesis and reduced leukodiapedesis due to negative chemotaxis in relation to neutrophils. Sometimes the quantity of erythrocytes is so high that the exudate resembles a hemorrhage, for example, with anthrax meningoencephalitis.

Causes: severe infectious diseases (influenza, plague, anthrax), sometimes hemorrhagic inflammation can join other types of inflammation.

Localization. Hemorrhagic inflammation occurs in the skin, in the mucosa of the upper respiratory tract, gastrointestinal tract, lungs, and lymph nodes.

Other types of inflammation

Catarrhal inflammation develops on the **mucous membranes** and is characterized by an abundant accumulation of mucous exudate on their surface due to **hypersecretion of the mucous glands**.

Catarrhal inflammation develops with **viral, bacterial infections**, under the influence of physical and chemical agents, it can be of an infectious-allergic nature, the result of autointoxication (uremic catarrhal gastritis, colitis).

Putrid inflammation is usually associated with Clostridial infection in combination with pyogenic microorganisms. Extensive foci of necrosis are characteristic.

Mixed inflammation is very common, since in most cases more than one type of exudate can be observed.

Proliferative (productive) inflammation

Proliferative (productive) inflammation is characterized by a predominance of **cell proliferation**. Alterative and exudative changes recede into the background.

The course of proliferative inflammation can be **acute**, but in most cases it is **chronic**.

Acute proliferative inflammation is observed in a number of infectious (typhus, tularemia, brucellosis), infectious-allergic diseases (acute rheumatism, acute glomerulonephritis).

Chronic proliferative inflammation is characteristic of most interstitial productive processes (proliferative myocarditis, hepatitis, nephritis with an outcome in sclerosis), most types of granulomatous inflammation.

Productive inflammation classification

1. Type:

- acute;
- chronic.

2. By morphology:

- interstitial;
- granulomatous;
- sclerotic or polypoid.

3. By prevalence:

- diffuse;
- focal (granuloma).

Interstitial inflammation

Interstitial proliferative inflammation is characterized by the formation of a **cellular infiltrate in the stroma** of the myocardium, liver, kidneys, and lungs.

The composition of the infiltrate may include: sensitized lymphocytes (activated by antigen), plasma cells, macrophages, tissue basophils, single neutrophils and eosinophils.

These cells are diffusely scattered in the tissue and **do not form granulomas**.

It is also called **chronic non-granulomatous inflammation**. Non-granulomatous chronic inflammation is a combination of several different types of immune response to different antigenic agents. As a result, sclerosis develops more often.

Granulomatous inflammation

Chronic granulomatous inflammation is characterized by the formation of **epithelioid cell granulomas**.

A granuloma is a **collection of macrophages**.

There are two types of granulomas:

- epithelioid cell granuloma, which occurs as a result of an immune response, and macrophages are activated by lymphokines of specific T-cells;
- granuloma around foreign bodies, in which non-immune phagocytosis of foreign non-antigenic material by macrophages is carried out.

Epithelioid cell granuloma

Epithelioid cell granuloma is a collection of activated macrophages. Epithelioid cells (activated macrophages) appear microscopically as **large cells with pale, foamy cytoplasm**; they are called epithelioid because of their distant resemblance to epithelial cells.

Epithelioid cells have an increased ability to secrete lysozyme and various enzymes, but have a **reduced phagocytic potential**. Granulomas are usually surrounded by lymphocytes, plasma cells, fibroblasts, and collagen.

A typical feature of epithelioid cell granulomas is the formation of Langerhans giant cells, which are formed by the fusion of macrophages and are characterized by the presence of up to 50 nuclei at the cell periphery.

Granulomatous inflammation

Specific granuloma is a type of granulomatous inflammation in which, by its morphology, it is **possible to determine the nature of the pathogen** that caused this inflammation.

Specific granulomas include granulomas in **tuberculosis, syphilis, leprosy,** and **rhinoscleroma**.

Non-infectious granulomas are found in **dust diseases** (silicosis, talcosis, asbestosis, etc.), drug exposure (oleogranulomas), around foreign bodies.

Granulomas of unknown origin include granulomas in **sarcoidosis, Crohn's disease, Wegener's granulomatosis** and others.

The tuberculous granuloma is characterized by a specific cellular composition and the nature of the location of these cells. Three types of cells are part of the granuloma – lymphocytes, epithelioid and **Langerhans giant multinucleated cells**. In the central part of the granuloma we can find **caseous necrosis**.

Syphilis

In its development, a number of **subsequent stages** occur:

1) Primary (productive tissue reaction prevails – hard chancre).

2) Secondary (exudative reaction – syphilides).

3) In tertiary syphilis, there is a development in the organs and systems of syphilitic productive-necrotic inflammation in the form of syphilitic granuloma. The edges of the syphilitic granuloma are composed of large fibroblasts, resembling epithelioid cells in tuberculosis. Giant cells are very rare.

Most often syphilitic granuloma are found in the **skin and mucous membranes, in the liver, bones and testicles**.

Cardiovascular syphilis is characterized by damage to arteries of various calibers with the development of proliferative arteritis with an outcome in arteriosclerosis and chronic interstitial myocarditis with an outcome in diffuse cardiosclerosis. **Aortic involvement** is typical.

Leprosy granulomas are formed by well vascularized granulation tissue, forming confluent nodules, consisting mainly of **macrophages** with a small amount of plasma cells and **histiocytes**.

In leproma, a large number of **mycobacteria are detected inside macrophages**, which gradually increase in size.

After a while, these cells become very large and foamy, since they contain **partially disintegrated bacilli**.

Such cells are called **Virchow's cells**.

Rhinoscleroma

Rhinoscleroma is manifested by the formation of granulomas consisting of lymphocytes, plasma cells with Russell bodies (eosinophilic hyaline balls) and macrophages. The appearance of large macrophages with a light cytoplasm, called **Mikulicz cells**, is very characteristic.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

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3. Robbins Basic pathology / [ed. by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. - 9th ed. - [Philadelphia] : Elsevier ; Saunders. - 910 p. : ill., scheme, tab.

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3. Sobotta. Atlas of human anatomy. [V. 3]. Head, neck, and neuroanatomy / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 370 p. : ill., col. ill.

4. Weir & Abrahams' imaging atlas of human anatomy / ed.: J. D. Spratt [and oth.] ; consultant eds.: J. Weir, P. H. Abrahams. – 5th ed. - [S.l.] : Elsevier, 2017. - xvi, 263 p. : ill.

NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

Access mode: http://patan.by/menyu/administrativnyie-proczeduryi.html - The date fccess: 20.03.2022.

ELECTRONIC DATABASES

1. Physician's consultant. Electronic Medical Library = Consultant of the doctor. Electronic medical library [Electronic resource] / Publishing group

"GEOTAR-Media", LLC "IPUZ". – Access mode: http://www.rosmedlib.ru/ . – Access date: 03/15/2022.

2. Springer Link [Electronic resource] / Springer International Publishing AG. – Access mode: https:link.springer.com. – Date of access: 03/15/2022.