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ALGORITHM OF MORPHOLOGICAL SIGNS OF PNEUMONIA WITH COVID-19

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RESUME

The entire world is suffering from the pandemic of the coronavirus infection, and it has been found that the SARS-CoV-2 virus infects the respiratory tract and lungs in most cases. Active replication of the virus in the epithelium of the respiratory tract leads to acute respiratory syndrome (OO'RS) and SARS, viremia, immune disorders, hypoxia, and clinical severity in the 2nd week after infection. In order to study the pathomorphological changes that develop in the lungs, 8 people who died from coronavirus were autopsied. Under the influence of the virus, the covering epithelium of the bronchi and alveoli, blood vessels and interstitial connective tissue are damaged and destroyed, and the alveoli are affected by pathological atelectasis, dystelectasis and distress syndrome. Another feature of lung tissue damage caused by coronavirus is the proliferation of fibroblasts, which are part of the connective tissue around the bronchi, vessels and between the alveoli, resulting in interstitial fibroplastic alveolitis.

Keywords: virus, coronavirus, respiratory system, lung, alveolocyte, pneumonia, pneumonitis, distress syndrome.

THE URGENCY OF THE PROBLEM

On March 11, 2020, the World Health Organization (WHO) declared a pandemic of the coronavirus infection, and it was considered the 11th pandemic of the XX-XXI centuries by SARS-CoV-2. SARS-CoV-2 is a single-stranded RNA virus belonging to the Coronaviridae family. The S-protein of SARS-CoV-2 is similar to angiotensin-converting enzyme 2 (APF2) and its affinity is 10 times stronger than that of the previous virus SARS-CoV, which ensures a high level of infectivity[3, 5]

APF2 receptor expression is detected in respiratory epithelium, alveolocytes, alveolar monocytes, vascular endothelium, gastrointestinal epithelium, urinary tract epithelium, macrophages and even other cells. SARS-CoV-2 is characterized by active replication in the epithelium of the upper respiratory tract. Therefore, the course and outbreak of COVID-19 causes severe acute respiratory syndrome (SARS) and SARS, whose strong replication causes viremia, immune disorders, hypoxia, and damages a number of organs, namely the heart, kidney, gastrointestinal tract and other organs, the receptor for APF2-enzyme is expressed in the cells of these organs and causes clinical severity in the 2nd week after infection [1, 2].

At the same time, the main and fundamental essence of this disease is the development of microangiopathy in the form of destructive-productive thrombovasculitis and hypercoagulable syndrome and damage to the immune system.

In severe and critical development of COVID-19, vascular inflammation affects the body's coagulation, including IL-6 as an important trigger, activates the blood coagulation system and slows down the fibrinolytic system. The direct effect of the virus on the vascular endothelium

provokes hypercoagulation and causes an aggressive immune response, as a result of which the appearance of antiphospholipid antibodies increases the coagulopathy. The severe and rapid course of COVID-19 is due to a sharp decrease in the number of lymphocytes and an increase in neutrophils in the patient's body [3, 4, 5]. But the reasons for the development of lymphopenia in COVID-19 remain unknown. Based on some data, lymphopenia can be attributed to the death of lymphocytes by apoptosis or pyroptosis, as well as pathological mitosis of macrophages.

In response to SARS-CoV-2, hyperergic immune reaction in the patient's body causes a strong systemic inflammatory syndrome, severe alteration of lung alveolar tissue and other organs leads to the development of septic shock. In addition to the above, many aspects of the pathogenesis and morphogenesis of COVID-19 are still unclear and undefined, including the temporary loss of smell in the respiratory tract (anosmia).

APF2 enzyme is present in respiratory epithelium, alveolocytes, alveolar monocytes, vascular endothelium, gastrointestinal epithelium, urinary tract epithelium, macrophages and even other cells. The outer shell of the virus and the membrane of the human cell adhere to each other. SARS-CoV-2 virus enters the cell cytoplasm through S-protein and cellular APF2-enzyme. Inside the cell, the coronavirus loses its outer shell, that is, it "undresses". This is how coronaviruses activate their parasitism. It has a cytopathogenic effect on cells, disrupts protein exchange in the cytoplasm, creates virus particles from cellular RNA. One virus particle reproduces 1000 times in one cycle, and 10,000,000 times after 3 cycles.

It should be said that the "removed" shell of the coronaviruses is now filled by the proteins of the host cells. As a result, the damaged cells do not recognize it and completely lose their ability to resist. Viruses then leave the dead cells and enter other healthy cells and repeat the same process in them. That is why the disease has its own characteristics in the population of each country, and the degree of damage is also different.

MATERIAL AND METHODS

As a research material, 32 people who died of pneumonia caused by the coronavirus in August-September of the pandemic period were dissected and examined by the autopsy method at the Uz SSV Republican Pathological Anatomy Center. During the autopsy, samples were taken from all internal organs, including the lungs, for histological examination. The sections were processed in the usual way and paraffin blocks were prepared. Histological sections were taken from it and stained with hematoxylin-eosin. It was studied under a light microscope and the necessary areas were photographed. For the preparation of this article, histological sections from the lungs were studied in 10, 20, 40 objects of a light microscope, and microphotographs were taken that show the most significant pathomorphological changes that develop in lung tissue under the influence of coronavirus. From respiratory tract, terminal bronchioles and alveolar tissue were studied.

It is known that the covering epithelium of lung alveoli, i.e. alveolocytes, consists of 3 types of cells: type 1 flat or respiratory epithelium; Type 2 large or granular epithelium; 3-ciliated epithelium. I-type flat or respiratory epithelium covers 95-97% of the surface of the alveoli, carries out aerogematic, that is, gas exchange. It is an epithelium with a thin cytoplasm of 0.2 µm, few organelles, many pinocytosis vesicles. Type II - large granular cells cover 2-5% of the area. It is round or cube-shaped, protrudes from the surface of the alveolus, and is rich in

microvilli. Cytoplasm contains many mitochondria and endoplasmic reticulum and osmiophilic bodies, and they consist of phospholipids. A surfactant film 0.05 µm thick forms on the surface of the alveoli. Type III- peripheral cells perform chemoreception and neurosecretory functions.

RESULTS AND THEIR DISCUSSION

The results of the investigation showed that the SARS-CoV-2 virus primarily damages type II and III alveolocytes. At the same time, the lower part of the respiratory tract, i.e. the bronchioles and respiratory bronchioles, develops a number of pathological changes, damaging the mucosa covering epithelium. Microscopically, due to dystrophic changes in both cytoplasm and nucleus, the covering epithelium swells, changes its shape, the nucleus is irregularly located, escapes from the basement membrane, some of them become desquamated and migrate from their place. Others adhere to each other and form hyperchromic cushions, others take on a multi-line form, and others become flattened and turn into a thin eosinophilic membrane, in which the nuclei also become smaller and flattened. In this case, the bronchiole cavity is filled with a large number of desquamated epithelium, erythrocytes, lymphoid cells, macrophages and other tissue fragments. It is observed that the basal membrane of the wall of the bronchiole is severely swollen, myxmatous, and it is determined that there are disorganized fibrous structures in its composition. It is determined that activated macrophages, lymphoid cells, erythrocytes and necrobiotic detritus are present in it.

Therefore, due to the damage and destruction of the covering epithelium and basal membrane of the bronchiole wall, the virus and its toxins spread to the lung tissue around the bronchioles and cause inflammation.

Microscopic examinations showed that SARS-CoV-2 mainly damages type II alveolocytes. In the micrograph, it can be seen that both the cytoplasm and the nucleus of type II alveolocytes in all alveoli are greatly enlarged due to the effect of the virus. In particular, it is observed that the cytoplasm has increased in size and entered into an uncertain shape, it is stained with eosin in a chaotic manner, it is desquamated, and it falls into the alveolar cavity. In some places, it is determined that they are connected to each other, forming large multinucleated cells. It can be specially noted that the alveolar tissue damaged by the virus has lost its normal histotopography, the tissue structures are chaotically located. Due to the displacement of the covering epithelium, the walls of the alveoli are broken and destroyed by blood vessels and connective tissue. Strong swelling, myxomatosis and infiltration of lymphoid cells are detected in them. In other areas of lung alveolar tissue, it is observed that discirculatory changes, i.e., diffuse hemorrhages predominate. In these areas, the alveolar space and interstitial tissue are diffusely filled with erythrocytes. In these areas as well, it is determined that alveolocytes have undergone dystrophy and destruction, large multinucleated giant cells have appeared.

Therefore, it is observed that the alveoli suffer from pathological atelectasis, dystelectasis and distress syndrome due to the severe damage and destruction of the epithelium covering the alveolar wall, blood vessels and interstitial connective tissue under the influence of the virus.

As a result of severe dystrophy and destruction of type II alveolocytes, pathological protein substances are synthesized from them instead of the standard surfactant. As a result, fibrous structures, which are initially randomly located in the alveolar cavity, form a unique network and fill the alveolar cavity. In this case, alveolar wall structures were completely destroyed and

diffusely infiltrated with lymphoid cells. As a result of the movement of lung tissue and air entering the alveoli, coarse protein substances formed in the alveolar cavity accumulate at the edge of the alveolar cavity, that is, on the inner surface of the alveolar wall, and form hyaline membranes. As a result, oxygen exchange on the surface of the alveolar wall becomes difficult and hypoxia develops. Therefore, in most cases, damage to type II alveolocytes, production of coarse fibrillar protein instead of surfactant, and formation of hyaline membranes are confirmed under the influence of coronavirus.

It is known that the enzyme ASE2 of cells is an integral part of the renin-angiotensin system (RAS) and its function controls the homeostasis of the cardiovascular system, controls systolic blood pressure, osmotic and electrolyte balance. Under the influence of coronavirus, the activity of this enzyme increases, and this mechanism is strengthened, the bronchial wall shrinks smooth muscle tissue, lung fibroblasts proliferate, alveolar epithelium undergoes apoptosis, vascular wall permeability increases and leads to acute respiratory distress syndrome. If ASE2 acts through the Mas receptor, it causes vasodilation and lowers blood pressure. Based on these mechanisms, if we shed light on the microscopic changes of blood vessels in lung tissue damaged by SARS-CoV-2, the following can be said. All the vessels of the lung tissue are vasodilated, widened and full. In particular, the venous vessels are sharply dilated, filled with blood, the permeability of their walls increases, and blood is poured around them by the diapedesis method. Arteries are also relatively widened, plump, but all layers of their walls are thickened due to edema, myxomatosis and inflammatory infiltrate. Countless capillaries in the alveolar interstitial tissue are also diffusely dilated and filled, and the surrounding tissue and alveolar space are perfused by diapedesis.

It is known from the above-mentioned mechanisms that under the influence of SARS-CoV-2, the endothelium of blood vessels is also damaged. As a result, strong dystrophy and destruction processes develop in endothelial cells, their cytoplasm swells, desquamates, and moves out of place. Damage to the endothelium of blood vessels is the main local cause of the thrombosis process, which leads to the coagulation of blood cells and fibrinogen in the vessel cavity. As shown in the microphotograph below, it is confirmed that fibrin protein and white blood cells have accumulated in the space of postcapillary venules, in other words, microthrombi have appeared. In this disease, it is observed that fibrin thrombi appear not only in small blood vessels, but also in the cavity of large veins.

It is known that the cellular immune network of the immune system responds to viral diseases. In SARS-CoV-2 viral infection, inflammation in the form of diffuse lymphocytic infiltration is observed in the lung tissue. In this case, it is determined that the blood vessels of the lungs, the wall and the periphery of the bronchi, and the interalveolar tissue are diffusely filled with activated lymphoid cells at different levels. Therefore, it was observed that under the influence of the SARS-CoV-2 virus, the endothelium of blood vessels is also damaged, often leading to fibrin thrombosis.

Under the influence of the C protein of SARS-CoV-2 virus, the activity of ASE2 enzyme in not only the respiratory epithelium, but also the endothelium and smooth muscle cells of the blood vessel wall increases, as a result, the smooth muscle tissue of the bronchial wall shrinks, the fibroblasts of the interstitial tissue of the lung proliferate and increase, the permeability of the vascular wall increases, and the vessels the wall and surrounding tissue structures undergo

swelling, protein absorption, and destruction. In response to it, an inflammatory reaction and cell proliferation are triggered. If ASE2 acts through the Mas receptor, it causes vasodilation and lowers blood pressure.

If we study the pathomorphological changes that develop as a result of these mechanisms microscopically, the following results are obtained. After the endothelium on the inner surface of the blood vessel wall is damaged by the virus, it undergoes dystrophy and destruction, moves out of place and undergoes necrobiosis. As a result, the basement membrane becomes swollen, swollen, loses its histotopography, disintegrates and fragments. These changes cause thrombosis, which adheres to the vessel wall. Among the morphological changes that develop under the influence of the virus, the following are noteworthy, that is, fibroblasts around the basal membrane, which are in fact very few in number, proliferate, spread and infiltrate the basal membrane and muscle layers. At the same time, connective tissue cells in the adventitia tissue outside the vessel wall, including fibroblasts, increase dramatically and proliferate, causing the vessel wall to thicken and form a sheath-like wrap around it.

If we study the changes in the wall of another arteriole microscopically, there are almost no endothelial cells on the inner surface of the vessel wall, only fragments of cells and nuclei of various sizes are preserved adhering to the basement membrane. It is determined that the basal membrane is sharply thickened due to strong fibrinoid swelling and fibrinoid necrosis. The appearance of fibrin threads and rough protein material adjacent to the basement membrane at one end of the vascular space indicates that a fibrin thrombus is forming in the damaged vessel. In the adventitial layer around the arteriole, it is observed that lymphoid cells and fibroblasts proliferate and infiltrate the surrounding tissue.

Another characteristic of the pathomorphological changes that develop in the lung tissue damaged by the SARS-CoV-2 virus is the proliferation of connective tissue cells in the lung tissue. This is because the ASE2 enzyme, activated by the S protein of the virus, causes fibroblasts to proliferate. As seen in this photomicrograph, fibroblasts have proliferated in almost all areas of the lung tissue, i.e. in the bronchi, around the vessels, and in the interstitial tissue of the alveoli. While only a bunch of fibroblasts appeared around the bronchi and vessels, proliferative infiltrates along with lymphoid cells appeared in the alveolar interstitial tissue.

When individual fibroblastic infiltrates were studied under a microscope lens, it was found that the center of the infiltrate was occupied by young, hyperchromic fibroblasts. In the peripheral parts of the infiltrate, there are sparsely located, comparatively elongated fibrocytes, with fibrous structures appearing between them. Lymphoid cell infiltration is observed in some areas of the periphery.

The peculiarity of the fibroblastic infiltrate that appeared in the perivascular area is that the vessel wall is densely mixed and united with the tissue structures. In this case, both the nucleus and cytoplasm of the vessel endothelium are enlarged and hyperchromasic state is confirmed. It is determined that the basement membrane is sharply thickened due to fibrinoid swelling and fibrinoid necrosis. It is observed that the composition of the infiltrate mainly consists of fibroblasts, among which there are lymphoid cells, plasma cells and even eosinophils (Fig. 7). It is determined that in the central part of the infiltrate, that is, adjacent to the vessel wall, there are few lymphoid cells, and there are many in the peripheral part and they are scattered in the surrounding tissue.

Proliferation of fibroblasts developed in lung tissue under the influence of coronavirus is actually a morphological change characteristic of chronic inflammation, resulting in the growth of connective tissue. The micrograph below shows the alveolar tissue of the lung, where it is observed that the fibroblasts that have been proliferated under the influence of the coronavirus improved, differentiated, turned into well-developed fibrocytes, and produced fibrous structures by themselves (Fig. 8). As a result, it is confirmed that the interalveolar tissue of the lung has thickened and become denser and has turned into fibrous tissue. This process is called fibrosing interstitial alveolitis disease. So, it can be concluded that while the coronavirus infection is an acute disease, in the lung tissue pathomorphologically, proliferative inflammation, which continues with the increase of fibroblasts, and as a result, the development of interstitial fibroplastic alveolitis is observed. As a result, fibrocytic proliferative infiltrates appear in almost all areas of the lung tissue.

SUMMARY

It was observed that under the influence of coronavirus, type II and III alveolocytes were damaged, both their nucleus and cytoplasm were deformed and took different forms, polymorphic and giant cells appeared, desquamated and filled the alveolar space.

- Pathomorphological changes specific to COVID-19 occurred in the pulmonary blood vessels, the endothelium suffered dystrophy, destruction and desquamation, the basement membrane was severely swollen and disorganized, as a result of which plasma fluid and proteins poured into the wall and cavity of the alveoli, hemorrhagic exudate and foci of hemorrhage appeared. is determined.

- Due to the effect of coronavirus, fibroblasts have proliferated in the tissues of the bronchi, vascular atrophy, and alveolar spaces, a specific productive infiltrate has appeared, and finally, alveolitis with interstitial fibromatosis has developed in the lungs.

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