PATHOGENETIC MECHANISMS OF DISORDERS IN THE HEMOSTASIS SYSTEM OBSERVED IN PATIENTS INFECTED WITH COVID-19

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ANNOTATION

Coronaviruses are a large family of viruses that are known to cause illnesses ranging from the common cold to more severe diseases such as Acute Respiratory Distress Syndrome (ARDS) and thromboembolic complications with fatal consequences. Disturbances in the blood coagulation system due to endotheliopathy in the disease increase the risk of developing thromboembolic complications.

Keywords: COVID-19, SARS-CoV-2, Microthrombosis, Immune response, Alveolar epithelial cells, Willebrand factor, Protein C

It is no secret that the COVID-19 pandemic, recognized as the largest pandemic observed in the history of mankind after the last 100 years, has taken the lives of many people, regardless of the level of development of medicine and the pharmaceutical industry in the countries of the world. Undoubtedly, the reduction of morbidity rates and lethal consequences is due to the tireless research of representatives of the medical field from all over the world, the introduction of effective treatment methods, the introduction of mass vaccinations, and effective preventive measures against the virus. However, today, infections caused by many mutated strains of coronavirus are recorded as seasonal epidemics in different countries of the world. If we focus on the statistics, according to the WHO data, from January 1, 2020, to December 31, 2021, 14.9 million deaths related to the COVID-19 pandemic were recorded.

Susceptibility to the pathogen is high in all population groups. The risk groups for a severe course of the disease and the risk of death include people over 60 years of age, and patients with chronic diseases (diseases of the respiratory system, cardiovascular system, diabetes mellitus, oncological diseases). Mortality varies from 2 to 4%. The SARS-CoV-2 virus is characterized by low resistance in the environment. Dies under the influence of UV radiation, and disinfectants, when heated to 40 ° C for 1 hour, to 56 ° C - in 30 minutes. On the surface of objects at 18-25°C it remains viable from 2 to 48 hours.

COVID-19 is an epidemic-threatening infectious disease caused by infection with the single-stranded RNA virus SARS-CoV-2.

The main target cells for coronaviruses are alveolar epithelial cells, in the cytoplasm of which the virus replicates. After the assembly of virions, they pass into cytoplasmic vacuoles, which migrate to the cell membrane and exit into the extracellular space by exocytosis. Expression of virus antigens on the cell surface does not occur before the release of virions from the cell; therefore, antibody production and interferon synthesis are stimulated relatively late. The formation of syncytium under the influence of the virus makes it possible for the latter to rapidly spread into the tissues. The action of the virus causes an increase in the permeability of cell membranes and increased transport of fluid rich in albumin into the interstitial tissue of the lung and the lumen of the alveoli. At the same time, the surfactant is destroyed, which leads to the collapse of the alveoli, as a result of a sharp violation of gas exchange, acute respiratory distress syndrome (ARDS) develops. The immunosuppressive state of the patient contributes to the development of opportunistic bacterial and mycotic infections of the respiratory tract. In patients infected with COVID-19, damage to all organs and systems is characteristic, in particular,

hypercoagulation and thrombus formation caused a severe course of the disease, generalized vasculopathies, and thromboses and thromboembolic complications with a fatal outcome.

Diffuse damage to the alveoli is accompanied by microthrombosis of the lungs. Diffuse microthrombosis of the lungs was identified by Swiss scientists S. Lax et al. when conducting 11 autopsies of patients who died from COVID-19 [4].

There is evidence of the development of COVID-19 and arterial thrombosis, strokes, and heart attacks. At the same time, it was cerebrovascular thrombosis that was most often noted [7]. In addition, atypical venous and arterial thromboses are described in the literature: thrombosis of venous sinuses [8], mesenteric arterial and venous thrombosis [9], thrombosis of aortic grafts

Coagulopathies in the form of hypercoagulability are caused by oxidative stress and severe inflammation that damage the mitochondria of cells. Cell damage leads to its death, the accumulation of a large number of dead cell fragments in the focus of inflammation causes the chronic course of acute inflammation and the development of coagulopathies. Coagulopathy manifests itself in the form of hypercoagulability, with excessive activation of blood clotting factors and increased susceptibility to thrombus formation.

The syndrome is characterized by damage to vascular endothelial cells, loss of intercellular communication, apoptosis, and disturbances in the blood coagulation system. For this reason, the development of many scattered microthrombi in patients is observed, especially in the pulmonary veins. The aggravation of the above-mentioned disorders leads to disorders in the central nervous system, kidney and liver failure, and eventually to the dysfunction of all organs and systems. According to the results of many studies, the amount of von Willebrand factor, VWF factor synthesized in the endothelium has been determined in patients with severe disease. Activation of endotheliocytes causes the release of Willebrand factor. As a result of activation of coagulation hemostasis based on the cascade mechanism, the Willebrand factor causes the adhesion of platelets and leukocytes to the damaged part of blood vessels and the formation of microthrombi. The severity of the clinical course of COVID-19 is closely related to the amount of Willebrand factor secretion, and the higher the concentration of Willebrand factor, the more severe the disease. As a result, thrombotic microangiopathies, occlusion of microcirculatory vessels, and angiogenesis disorders develop. The amount of P-selectin involved in the emigration of leukocytes to the inflammatory zone was found to be high in the blood plasma of patients with severe disease. It should be noted that thrombomodulin plays a significant role in the formation of pathological thrombi in the disease. Thrombomodulin is an integral membrane protein, acting as a thrombin receptor on the membrane of endothelial cells of blood vessels, providing anticoagulant and antifibrinolytic activity. Binding of thrombin to thrombomodulin leads to activation of Protein C, which is considered the main physiological anticoagulant. In addition, Protein C has anti-inflammatory and anti-apoptotic activity. Thrombomodulin expression decreases due to damage to the endothelium of numerous blood vessels in coronavirus infection. In conclusion, in the treatment of patients infected with COVID-19, the use of antecoagulants and antiaggregants together with the use of steroid and nonsteroid drugs to reduce the cytokine spectrum and reduce blood vessel damage helps to reduce the progression of the disease and thrombosis.

Conclusion. The results of many studies indicate that damage to the endothelium of blood vessels is maintained for a long time during the infection of COVID-19. As a result, thrombomodulin expression disorders and Protein C deficiency occur. Activation of blood coagulation factors causes thrombosis in the blood vessels of many organs. As a result, thromboembolic complications occur. For this reason, the use of anticoagulant therapy is included in the standard of care for the infection of COVID-19. Effective use of anticoagulant therapy helps

prevent the development of thromboembolic complications. Taking into account the long-lasting endotheliopathy of the disease, it is necessary to monitor the coagulogram in patients.

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