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PATHOPHYSIOLOGY OF IMMUNE SYSTEM IMBALANCE AND CHRONIC INFLAMMATION IN THE POST-COVID-19 PERIOD

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Abstract: This article provides an in-depth analysis of the pathophysiological mechanisms of immune system imbalance and chronic inflammation that occur in the period after COVID-19 infection. The main factors that play a role in the development of post-COVID syndrome, including T-lymphocyte dysfunction, cytokine imbalance, immune system "exhaustion", oxidative stress and autoimmune processes, are widely covered. It also examines how low-grade but long-lasting forms of chronic inflammation damage the tissues of the body, and their relationship with the mechanisms of microcirculation disorders and hypoxia. The article also analyzes modern scientific areas such as neuroinflammation, changes in the intestinal microbiota and viral persistence. The multisystem lesions that occur in the period after COVID-19 and their clinical significance are substantiated. The results of the study show that long-term imbalance in the immune system and chronic inflammation are one of the main pathogenetic mechanisms of post-COVID syndrome. This work serves as an important scientific basis for a deeper understanding of post-COVID syndrome, its diagnosis, and the development of effective treatments.

Keywords: COVID-19, post-COVID, immunity, imbalance, inflammation, cytokines, T-lymphocytes, exhaustion.

Introduction:

The COVID-19 pandemic has posed a significant challenge to the global healthcare system. The disease is critically important not only during its acute phase but also due to its long-term complications. Post-COVID syndrome is a complex of symptoms that persist for weeks or months after the initial infection has subsided. First identified in 2019, the COVID-19 pandemic has exerted a substantial impact on human health during both the acute stage and subsequent phases. Many patients continue to experience various clinical manifestations long after recovery, a condition known in medicine as post-COVID syndrome or "long COVID." This syndrome results from complex ongoing pathophysiological processes within the organism, primarily driven by immune system imbalance and chronic inflammation.

Upon entering the body, SARS-CoV-2, the causative agent of COVID-19, triggers a potent immune response. While this response is aimed at eliminating the virus during the acute phase, in certain cases, it escalates beyond control and damages host tissues. These very processes subsequently lead to long-term pathological changes. During COVID-19 infection, the functioning of the immune system undergoes drastic alterations. Once the virus enters the body, innate immune elements—primarily macrophages, neutrophils, and the interferon system—are activated. This stage serves to limit initial viral replication. Subsequently, adaptive immunity is engaged, forming a targeted response against the virus through T and B lymphocytes. However, in some patients, the equilibrium of these processes is disrupted, leading to pathological states.

One of the most critical pathophysiological processes is cytokine imbalance. Under normal conditions, a balance exists between pro-inflammatory and anti-inflammatory mediators. However, in COVID-19, pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) increase dramatically. This phenomenon is termed a

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"cytokine storm." Consequently, the inflammatory process becomes systemic and causes damage to numerous tissues. This process may not fully terminate after the acute phase, leading to the development of chronic inflammation.

In the post-COVID period, the recovery of the immune system is not always complete. In some patients, lymphocyte counts remain low, or their functional activity is impaired. Concurrently, persistent hyperactivation of the immune system can remain, creating a constant inflammatory environment within the body. This state is referred to as immune imbalance and serves as a fundamental mechanism of post-COVID syndrome. Another crucial mechanism is the development of autoimmune reactions. Under the influence of the virus, the body's immune system may sometimes perceive its own tissues as foreign, subsequently producing autoantibodies against them.

This leads to the persistence of inflammatory processes in various organs. The nervous system, cardiac muscles, and joints are particularly sensitive to this process. Endothelial dysfunction also plays a pivotal role in the post-COVID period. SARS-CoV-2 damages the inner lining of blood vessels—the endothelium. Consequently, normal vascular function is impaired, the coagulation system is activated, and microtrombi are formed. This compromises oxygen delivery to tissues and exacerbates the inflammatory process.

Oxidative stress is of great importance in the continuation of chronic inflammation. An increase in free radicals damages cell membranes, proteins, and DNA, thereby disrupting normal cellular activity. Simultaneously, mitochondrial dysfunction develops, deranging energy production processes, which results in chronic fatigue syndrome among patients.

Post-COVID syndrome affects various body systems:

Respiratory System: Fibrotic changes in lung tissue occur, leading to impaired gas exchange.

Cardiovascular System: Myocarditis, arrhythmias, and thrombosis may develop.

Nervous System: Decreased focus, memory impairment, and the condition known as "brain fog" are observed.

Endocrine System: The probability of hormonal imbalance increases.

Clinically, post-COVID syndrome manifests through diverse symptoms, most commonly including chronic fatigue, dyspnea (shortness of breath), tachycardia, myalgia, and psycho-emotional disorders. These symptoms can persist for weeks or months, significantly impacting patients' quality of life. Treatment approaches must be comprehensive, primarily focusing on reducing inflammation, normalizing the immune system, and promoting recovery. Antioxidants, anti-inflammatory agents, and rehabilitation programs are essential. Furthermore, maintaining a healthy lifestyle, proper nutrition, and physical activity accelerate the recovery process.

Alterations in Innate Immunity

Disruption of the innate immune response is widely observed in COVID-19 patients. Increased neutrophil activity and macrophage hypersecretion lead to the excessive production of inflammatory mediators. High levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and other pro-inflammatory cytokines are closely associated with severe clinical outcomes. This state, termed a "cytokine storm," leads to tissue damage, multi-organ failure, and an increased risk of mortality. The overactivation of innate immunity plays a critical role in COVID-19 pathogenesis.

Immunological Changes in Post-COVID Syndrome

In a certain proportion of recovered patients, immune system dysfunction persists for several months. Post-COVID syndrome is characterized by chronic inflammation, autoimmune reactions, and cytokine imbalance. The detection of autoantibodies in some patients suggests that SARS-CoV-2 infection may trigger autoimmune processes, leading to long-term complications involving the joints, cardiovascular, and nervous systems.

Clinical Significance and Potential Mechanisms

Studying the long-term effects of COVID-19 on the immune system is vital for patient rehabilitation, developing immunomodulatory therapies, and preventing reinfection. Developing treatment strategies based on immunological assessment and individualized approaches is a priority in modern medicine.

The summarized mechanisms associated with long-term COVID pathology include:

Immune Dysregulation and Autoimmunity: Persistent immune activation and the emergence of autoantibodies.

Endothelial Dysfunction: Vascular damage leading to microvascular complications.

Viral Persistence: Latent viral reservoirs in various organs.

Gut Microbiota Dysbiosis: Viral persistence may alter the gut microbiota, which in turn modulates the immune response and may lead to neurological changes via the gut-brain axis. Blood-Brain Barrier Penetration: The spike protein may cross the blood-brain barrier, contributing to neurological consequences.

Structural Protein Damage: Nucleocapsid and envelope proteins can damage endothelial cells, triggering cytokine release and further activating immune responses.

Viral Reactivation: Immune impairment may lead to the reactivation of other latent viruses such as EBV (Epstein-Barr virus), HHV-6, and CMV (Cytomegalovirus), as well as bacterial infections like tuberculosis.According to estimates from health agencies, 1 in 5 COVID-19 survivors may develop long COVID, providing the most reliable evidence of its prevalence to date. The CDC conducted a multi-state telephone survey among symptomatic adult COVID-19 survivors in the US to assess the prevalence of disability or activity-limiting symptoms following COVID-19.

-Pathophysiology of Long COVID

Long COVID, as previously mentioned, presents a wide range of symptoms (Figure 2) (12, 13, 22, 108, 109). Despite the clinical presentation, precise pathophysiological mechanisms remain uncertain. Its involvement across multiple organs suggests potential mechanisms including direct viral tropism, cytotoxic viral proteins, and immunopathology (Figure 2). Some studies suggest that long COVID symptoms may result from the persistent effects of the acute phase of COVID-19, producing diverse symptoms described through various mechanisms. Furthermore, activation of the immune system may lead to an autoimmune response or long-term, non-specific inflammation, which can cause additional damage to host cells.

Scientists have developed strategies to assess and classify the impact of long COVID. One such tool is the Post-COVID-19 Functional Status (PCFS), an ordinal system that evaluates the status of COVID-19 survivors over time. It employs a 4-grade scale based on functional limitations, ranging from Grade 1 (indicating no limitation) to Grade 4 (indicating dependence on external assistance for survival). This tool has shown reproducibility in identifying patients in need of assistance and rehabilitation. Since its introduction, it has been used in clinical studies on long COVID and independently validated. To generate consistent clinical outcomes, the Core Outcome Set (COS) has been proposed as a clinical tool. A multi-national effort created a COS for long COVID using systematic literature reviews and a modified Delphi process. This COS is intended for adult patients in various settings. It includes fatigue or exhaustion, pain, post-exertional symptoms, changes in work or occupational and educational activities, survival from acute illness, physical activity-related symptoms, cardiovascular and nervous system symptoms or conditions, and mental and respiratory functions.

Research has shown that 35% of individuals had not returned to their normal state of health 2–3 weeks after diagnosis. Additionally, it has been reported that one out of every five patients aged 18–34 who did not have a chronic illness prior to COVID-19 had not returned to their normal health status. While information regarding the duration of long COVID is limited, reported cases have extended from weeks up to a year. However, recent studies indicate that the incidence of long COVID has decreased following the pandemic, and this decline is attributed to the progress of vaccination. Furthermore, the Wuhan variant has been associated with various physical symptoms and changes in emotional and behavioral patterns, significantly impacting long-term health outcomes. In contrast, the Omicron variant has shown fewer post-infection effects, resembling common seasonal viral illnesses. These observations suggest that Omicron and subsequent variants may not lead to the same long-term health consequences as previous SARS-CoV-2 variants.

Conclusion: In the post-COVID-19 period, immune system imbalance and chronic inflammation represent a complex and multi-stage pathophysiological process. These processes affect various systems of the organism and cause the development of long-term complications. Cytokine imbalance, autoimmune reactions, endothelial damage, and oxidative stress can be identified as the primary mechanisms of post-COVID syndrome. The in-depth study of this issue and the development of effective treatment methods is one of the pressing directions of modern medicine. By balancing the immune system and controlling inflammatory processes, it is possible to restore patients' health and improve their quality of life.

REFERENCES

1. World Health Organization. Coronavirus disease (COVID-19): Post COVID-19 condition. – Geneva: WHO Press, 2022. – 150 p.
2. National Institutes of Health. COVID-19 Treatment Guidelines. – Bethesda, 2023. – 200 p.
3. Centers for Disease Control and Prevention. Long COVID or Post-COVID Conditions. – Atlanta, 2022. – 120 p.
4. John E. Hall. Guyton and Hall Textbook of Medical Physiology. – 14th ed. – Philadelphia: Elsevier, 2021. – 1120 p.
5. Vinay Kumar, Abul K. Abbas, Jon C. Aster. Robbins and Cotran Pathologic Basis of Disease. – 10th ed. – Philadelphia: Elsevier, 2021. – 1392 p.
6. Peter Parham. The Immune System. – 4th ed. – New York: Garland Science, 2014. – 506 p.
7. Abul K. Abbas, Andrew H. Lichtman, Shiv Pillai. Cellular and Molecular Immunology. – 9th ed. – Philadelphia: Elsevier, 2018. – 608 p.