

Preclinical Diagnostics of Internal Organ Disorders in Patients with Post-Covid Syndrome

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Abstract This article is devoted to the search for a method that can indicate with great accuracy that a pathological process in some organ has started and there is a tendency for the development of a certain disease even before changes appear in the indications of traditionally used methods for diagnosing this disease.

Keywords Immunochemical analysis of the Eli-Viscero-Test, Method of preclinical diagnosis, Complications of COVID-19, Disorders of internal organs

1. Introduction

COVID-19 is a new disease in the history of mankind, the development of its clinical symptoms, early and late complications has not yet been fully studied. However, it has become clear that in COVID-19, symptoms associated with the SARS-CoV-2 virus are not limited to the respiratory tract, but also lead to many other systemic inflammatory processes, coagulopathies and neurological disorders [1,2,3]. A wide spectrum of presentations from asymptomatic to severe has been identified for COVID-19 [4]. In general, patients exposed to respiratory CoVs present with colds, bronchiolitis, and pneumonia. Clinical manifestations in patients with mild COVID-19 include fever, dry cough and myalgia (fatigue). While a high percentage of patients are asymptomatic or have a favorable prognosis, poorer outcomes have been observed in older patients, as well as patients with underlying medical conditions: cardiovascular disease (CVD), kidney disease, diabetes, high blood pressure, malignancy, obesity and chronic respiratory diseases [5]. High mortality rates with COVID-19 have been observed in patients with these underlying conditions. Within a week of onset, COVID-19 may progress as a severe condition with hypoxemia and dyspnea and rapidly progress to acute respiratory distress syndrome (ARDS). COVID-19 is also associated with damage to various organs and systems such as the lungs, liver, kidneys, heart, gastrointestinal tract, hematological and nervous systems, with a high mortality rate and the induction of multiple organ failure in infected patients [6].

Currently, one of the leading causes of death from acute pathological conditions is considered to be multiple organ failure (MOF), that is, damage and then subsequent

shutdown of the functions of the most important organs and systems of the human body. A number of studies have shown that the severity of COVID-19 is also positively correlated with the level of inflammatory cytokines, the main of which are interleukins (IL) 2, 6, 7 and 10 [7]. In accordance with the literature, even before the development of the COVID-19 pandemic, the role of cytokines, T-lymphocytes, killer T-cells in the pathogenesis of a number of diseases, including oncological processes, was sufficiently studied [8,9]. However, in the development of COVID-19, the significance of these pro-inflammatory elements requires further study. Elevated levels of IL-6 and T cell cytotoxicity are thought to stimulate the immune response and induce a cytokine release syndrome, a “cytokine storm,” which ultimately leads to ARDS, GI damage, and multiple organ failure. A number of studies have reported elevated concentrations of proinflammatory cytokines in the blood of hospitalized patients with COVID-19 [10,11].

Very little is known about the long-term effects of COVID-19. On the other hand, clinical symptoms of damage to organs and systems may not appear immediately after the start of the pathological process, since the body has enormous compensatory capabilities. Even biochemical changes in the blood, although ahead of the clinical manifestation, appear after the loss of a significant number of organ and tissue cells.

Thus, our article is devoted to the search for a method that can indicate with great accuracy that a pathological process in some organ has started and there is a tendency for the development of a certain disease even before changes appear in the indications of traditionally used methods for diagnosing this disease.

The goal is to study the effectiveness of the method for preclinical diagnosis of internal organ disorders in patients who have suffered COVID-19 using the immunochemical analysis of the Eli-Viscero-Test.

2. Material and Research Methods

The method of immunochemical analysis ELI-Viscero-Test allows you to identify and analyze individual profiles of serum immunoreactivity, depending on changes in the relative content of auto-Abs of the IgG class directed to the antigens of visceral organs, which makes it possible to comprehensively assess their condition long before the onset of clinical symptoms with severe the likelihood of predicting diseases, in particular those associated with COVID-19. Methods based on Immunculus technology make it possible to identify pathological changes occurring at the level of specialized cells in certain organs and systems as early as possible and belong to the category of ultra-early diagnostic methods, which allow, based on the results obtained, to individually prescribe the most adequate treatment, including preventive measures and restorative medicine, as well as recommend additional clarifying examinations, mainly to assess the “advancement” of the pathological process and clarify its etiology. A reduced or normal level of auto-AT in the presence of structural and functional disorders confirmed by additional examinations indicates stabilization of the pathological process. An increase in the level of auto-AT during dynamic observation indicates the activation and increase of pathological changes and may be the basis for prescribing preventive therapy.

Immunochemical analysis was carried out using the ELI-Viscero-Test method using test kits of the same name. In blood serum samples, individual profiles of serum immunoreactivity were identified and analyzed, depending on changes in the relative content of auto-ABs of the IgG class directed to antigens of the immune system: ds-DNA - the antigenic component of any cell types; an excess of antibodies to it often indicates the presence of an active viral process (less often autoimmune diseases); b2-Glycoprotein I is the main phospholipid-binding protein in blood plasma; an excess of antibodies to it often indicates the presence of antiphospholipid syndrome; Fc-Ig - fragment of immunoglobulin molecules; an excess of antibodies to it often indicates inflammatory processes of any localization; CoM-0.2 - membrane antigen of myocardiocytes; an excess of antibodies to it often indicates degenerative changes in the myocardium; b1-Adrenoreceptors - cardiac isoform of adrenoreceptors; an excess of antibodies to it often indicates changes in the autonomic nervous system of the heart and heart rhythm disturbances (rarely dilated cardiomyopathy); TrM-03 - platelet membrane antigen; changes in the content of antibodies to it often indicate thrombocytopeny and changes in the blood coagulation system; ANCA - cytoplasmic antigen of vascular endothelial cells; an excess of antibodies to it often indicates inflammatory changes in the walls of blood vessels (vasculitis of small vessels); KiM-05 - membrane antigen of glomerular cells of the kidneys; an excess of antibodies to it often indicates degenerative changes in the kidney parenchyma; KiS-07 - cytoplasmic antigen of glomerular cells of the kidneys; an excess of antibodies to it indicates changes in the kidney tissue (often of inflammatory

origin); LuM-02 - membrane antigen of alveolar endothelial cells; an excess of antibodies to it often indicates degenerative changes in the lung parenchyma; LuS-06 - cytoplasmic antigen of alveolar endothelial cells; an excess of antibodies to it indicates changes in the lungs (often of inflammatory origin); GaM-02 - membrane antigen of stomach wall cells; an excess of antibodies to it often indicates degenerative changes in the stomach wall; ItM-07 - membrane antigen of small intestinal wall cells; an excess of antibodies to it often indicates degenerative changes in the wall of the small intestine; HeS-08 - cytoplasmic antigen of hepatocytes; an excess of antibodies to it indicates changes in the liver (often of inflammatory origin); HMMP - hepatocyte mitochondrial membrane antigen; an excess of antibodies to it often indicates degenerative changes in the liver parenchyma; Insulin - excess antibodies to insulin often serves as a marker of chronic pancreatitis and indicates the risk of developing type I diabetes mellitus; Insulin receptors - excess antibodies to peripheral insulin receptors often serve as a marker for the development of type II diabetes mellitus; Thyroglobulin is a specific component of the cytoplasm of thyroid cells; an excess of antibodies to it is a frequent marker of the development of thyroid insufficiency; TSH receptors are a specific component of the membranes of thyroid cells; excess antibodies to it are a frequent marker of the development of thyrotoxicosis (Graves-Basedow disease); AdrM-D/C-0 - membrane antigen of adrenal medulla cells; an excess of antibodies to it often indicates changes in the adrenal parenchyma; Spr-0.6 - membrane antigen common to prostate cells and sperm; an excess of antibodies to it often indicates changes in the prostate (in men) and an inflammatory process in the pelvic organs (in women); S100 - protein S100 - a regulator of many cellular functions (regulation of apoptosis, trophic factor of serotonergic neurons, etc.); an increase in AT to it is often accompanied by changes in emotional status; a common cause of the growth of antibodies to S100 is a papilloma viral infection; GFAP - protein GFAP - specific protein of astrocyte filaments; the growth of antibodies accompanies the proliferation of astroglial cells (gliosis) and electrolyte imbalance in the central nervous system; often accompanies the formation of increased convulsive readiness; MBP - protein MBP is a specific protein of the myelin sheaths of axons; the growth of antibodies accompanies pathological changes in nerve fibers (more often with mechanical damage, less often with demyelinating diseases).

These antigens are the main targets of autoantibodies, increased synthesis of which is observed in various forms of organ pathology - cardiopathology (cardiomyopathy, rhythm disturbances, etc.), liver pathology (hepatosis, liver cirrhosis, viral, toxic, alcoholic hepatitis), kidney pathology (pyelonephritis, glomerulonephritis), pathologies of the lungs (bronchial asthma, COPD, tuberculosis), pathologies of the gastrointestinal tract (peptic ulcer, gastritis, colitis, etc.), thrombocytopenies and vasculitis of various origins, organic lesions of the nervous system, dysfunction of the adrenal glands, thyroid gland, pancreas, prostate glands,

immunoactivation, immunosuppression (immunodeficiency). In various forms of organ pathology, there is a persistent (more than 3 weeks) increase in the serum content of autoantibodies to one or several antigens of the ELI-Viscero-Test-24 test kit of one or another organ orientation, depending on the localization of the pathological process. A transient simultaneous (nonspecific) increase in the serum content of autoantibodies to a variety of groups of antigens of different organ localization can be observed in acute infectious and inflammatory diseases, regardless of the location of the source of infection. When the acute process subsides (for example, after adequate treatment), after 2–4 weeks normalization of test parameters is noted.

ELI-Viscero-Test-24 was carried out at the Interuniversity Research Laboratory of the Tashkent Medical Academy. Blood samples were taken, cellular elements were precipitated by centrifugation, and serum was collected in the amount required for the study (0.2 ml). The study was carried out using the enzyme-linked immunosorbent assay method in accordance with the protocol instructions supplied with the reagent kit. In the blood serum samples of all patients, the levels of natural autoantibodies (auto-AT) of the IgG class to antigens of the main organs and systems of the human body were examined (using the ELI-Viscero-Test method). The analysis of the obtained data was carried out using the Statistica 6.0 application package.

Analysis transcript

Normal interval parameters for:

- automarkers range from -15 to 10%;
- immune reactivity – from -25 to -5%.

3. Results and Discussion

To determine the effectiveness of the proposed method, 55 patients aged from 28 to 80 years who had suffered COVID-19 and were hospitalized at the Zangiata-2 Covid Center were examined.

All patients were divided into two groups.

The control (A) group included 25 patients who underwent traditional clinical and laboratory research methods, the main (B) group included 30 patients who underwent ELI-Viscero-Test-24. The groups were representative of the age of the patients and the severity of the process. In 10 patients of the main group who had COVID-19 and with concomitant pathology of the kidneys (chronic pyelonephritis), in 40% of cases there was a significant increase in AAT to the KiM-05-300 antigen; KiS, which indicates the likelihood of an inflammatory process in kidney tissue of unknown etiology, in the initial stage or in remission, a 20% significant increase in AAT to the dsDNA antigen; a relative increase in AAT to the KiM-05-300 antigen, which indicates the presence of an active infectious-inflammatory process in the kidney tissue (most likely of viral etiology), 40% - a relative increase in AAT to the KiM-05-40 antigen; KiM05-300; Collagen IV, which indicates the likelihood of

an inflammatory process in the kidney tissue of unknown etiology, in the initial stage or in remission. In 10 patients in the control group, according to clinical laboratory tests of blood and urine, deviations from the norm were observed only in 15% of cases.

In 20 patients of the main group who had COVID-19 and with concomitant pathology of the cardiovascular system (coronary heart disease, angina), in 75% of cases there was a significant increase in AAT to the CoM-0.2 antigen, which indicates the presence of degenerative changes in the myocardium; in 25% there was a relative increase in AAT to the CoM-0.2 antigen and the b1-Adrenoreceptor - which indicates probable changes in the autonomic nervous system of the heart and a disturbance in the rhythm of heart contractions. In 15 patients in the control group, according to clinical laboratory tests and instrumental studies, deviations from the norm were observed only in 31% of cases.

Thus, biochemical (earlier) and clinical (later) signs reflect the already noticeable functional inferiority of the organ.

4. Conclusions

Shifts in the production of specific auto-ABs are the earliest sign of incipient pathological changes. This is explained by the fact that the number of specialized cells of any organ many times exceeds the minimum that is capable of providing the specialized functions of the organ. In this case, the pathological process, accompanied by the activation of apoptosis (exceeding the intensity of regenerative processes), only after several months or even years can reach the stage at which characteristic biochemical changes begin to be detected. Even later, the first clinical symptoms of organ failure will appear.

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