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Postcovoid syndrome in children: clinical and neurological aspects of the problem

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Abstract: Postcovoid syndrome is a pathological condition of the body after a coronavirus, which can be accompanied by various symptoms: both of somatic and neurological origin. The coronavirus can penetrate the central nervous system, affecting neurons and glial (auxiliary) cells. Neurological manifestations are not leading in the clinical picture of diseases caused by coronaviruses. Nevertheless, there is evidence of possible lesions of the nervous system and their role in the development of respiratory, sensory and other disorders in patients.

Keywords: neurological, pathological, symptoms

Postcovoid syndrome is a pathological condition of the body after a coronavirus, which can be accompanied by various symptoms: both of somatic and neurological origin. The coronavirus can penetrate the central nervous system, affecting neurons and glial (auxiliary) cells. Neurological manifestations are not leading in the clinical picture of diseases caused by coronaviruses. Nevertheless, there is evidence of possible lesions of the nervous system and their role in the development of respiratory, sensory and other disorders in patients.

In the previous period before the pandemic, coronavirus isolates were isolated from the brains of patients with multiple sclerosis. Some authors consider coronaviruses to be opportunists of the central nervous system (CNS), more tropic to glial structures and playing a certain role in the development of meningoencephalitis, epileptiform disorders, chronic headache, cognitive and behavioral disorders. Several potential mechanisms can be identified in the pathogenesis of neurological disorders: direct virus-induced damage to the nervous tissue, hypoxia, parainfective immune-mediated mechanisms and disorders from other organs and systems caused by the activation of systemic inflammation [7,9].

Currently, several possible mechanisms of damage to the nervous system in COVID-19 have been proposed. It is believed that the SARS-CoV-2 virus can enter the brain through the olfactory tract in the early stages of infection, causing inflammation and demyelination. Early studies have shown that the main host cell receptor for SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2). Given that ACE2 is expressed both in neurons and in glial cells, direct viral invasion of the central and peripheral nervous system is not excluded, which may be a mechanism of neurological symptoms in COVID-19. The mechanism of virus penetration into the cell by interacting with the APF2 receptor is realized through a "spike" glycoprotein (S-protein).

The viral particles bind to the APF2 receptors, then interact with the cell, injecting their RNK into it inside. In a cage SARS-CoV-2 RNK triggers the virus

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replication process. Binding of the coronavirus to these receptors can lead to direct damage to neurons. Some authors consider the high frequency of olfactory and gustatory dysfunctions in COVID-19 as evidence of the neurotrophy of the virus. Other mechanisms of damage to the nervous system in a new coronavirus infection are also considered. The development of a cytokine storm in COVID-19 increases the permeability of the blood-brain barrier, creating the possibility of penetration of viruses, immune cells, bacteria, and inflammatory agents into the structures of the central nervous system. It is possible that the development of respiratory failure in COVID-19 is associated not only with the involvement of the lower respiratory tract in the pathological process, but also with a viral lesion of the respiratory center in the medulla oblongata [1,3]. The possibility of virus penetration through the blood-brain barrier is confirmed in single studies that revealed SARS-CoV-2 RNA in the cerebrospinal fluid (CSF) of COVID-19 patients by genome sequencing [4,5,6].

The pathogenesis of COVID-19, according to several authors, is that this infection is associated with early functional depletion of the activity of cells of innate (NK cells) and acquired (CD8+ cytotoxic lymphocytes) immunity, although not everyone agrees with the theory of the suppression of innate immunity caused by the virus. What everyone agrees on today is that a serious illness is associated with a cytokine storm, by analogy with those pathological variants of the immune response that are triggered in some rheumatic diseases (the so — called MAS — macrophage activation syndrome or secondary HLH-secondary hemophagocytic lymph histiocytosis, when a systemic inflammatory response is activated, manifested by the defeat of many organs and systems).

Neurological manifestations in COVID-19 both at the beginning of the pandemic and during the second wave are distinguished by their polymorphism, wide prevalence and occur in patients of any age. Despite the worldwide spread, the epidemiological and clinical features of COVID-19 among children remain largely unclear. According to recent studies, only 0.9% of positive cases were associated with COVID-19 with children under 15 years of age. The results showed that COVID-19 occurs in 0.39-12.3% of children. it was also noted that children have a lighter course of the disease and complications, and adverse outcomes are much less common [1,2,8]. The authors conclude that children of all ages were sensitive to SARS-CoV-2, and there were no significant gender differences. The clinical manifestations of COVID-19 cases in children were less severe than in adult patients [6,8].

It should be noted that difficulties in making a correct diagnosis often arise since primary COVID-19 in children usually occurs without or with minor respiratory symptoms. Damage to the nervous system in COVID-19 is observed quite often along with damage to the lungs, liver, kidneys, cardiovascular, endocrine system, etc. Symptoms develop both in the acute phase of the disease and in later periods and are highly specific (impaired sense of smell or taste, headaches, dizziness, confusion,

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cognitive impairment, and many others). In 36.4% of cases, neurological symptoms are manifested in COVID-19.

Disorders of the nervous system in COVID-19 are very variable. One of the most common forms of CNS damage in COVID-19 is secondary infectious and toxic encephalopathy. It can be based on direct damage to the blood-brain barrier, hypoxic, dysmetabolic and immune-mediated damage to the nervous system [2,5]. In connection with the new coronavirus infection, the topic of postcovoid encephalopathy has become relevant. "Encephalopathy" is a generalizing name for pathological processes that are diverse in their genesis, the basis of which is the degeneration of brain neurons due to a violation of their metabolism. Encephalopathy is manifested by polymorphic neurological disorders, disorders in the intellectual-amnestic and emotional-volitional spheres. Complaints and neurological symptoms in patients, some authors regarded as manifestations of postcovoid encephalopathy [3,6].

The aim of our study was to study cognitive activity in children with postcephalopathy of postcovid etiology with the help of neuropsychological tests.

Material and methods of research. We examined 27 children with encephalopathy that occurred after a coronavirus infection in children aged 5 to 15 years. The control group consisted of 10 children of the same age without neurological pathology. From neuropsychological tests, we used the Wexler test adapted for children. We considered the Wexler test, first, as a psychological load on the brain, to determine the degree of disorders of the intellectual-mnestic sphere in children with postcovid encephalopathy. Among the instrumental methods, MRT of the brain and EEG were used.

Results and discussion. Neuropsychological symptoms, with various brain lesions, occur not only with gross organic focal brain lesions, but also with more subtle functional changes in the state of brain tissue, and more subtly than technical diagnostic tools, reflect the pathological state of brain structures. The most reliable method for determining cognitive impairment in both cases is neuropsychological tests, which reliably determine the degree of cognitive impairment.

During the neuropsychological examination of children with post-cephalopathy, several disorders of the emotional and behavioral sphere were revealed-rapid mental and even physical fatigue, nervousness, refusal to contact a doctor, decreased concentration of attention and poverty of other psychomotor reactions. A comparative analysis of the data obtained showed that there are significant differences between the indicators of the surveyed groups. In the group of patients, significant differences were revealed mainly in the non-verbal cognitive activity of sick children compared with healthy children. Clinically, this was expressed in the inadequacy of the behavioral response, low orientation of children in the environment, which reflects the degree of non-verbal thinking disorders.

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Table 1.

***Indicators of subtests of the Wexler method in healthy children and in patients with postcovoid encephalopathy* (M±m)**

№	Wexler Subtests	Control group (n=10)	Main group (n=27)
1	"Awareness"	10,54±0,43	8,07±0,86
2	"Understanding"	12,21±0,54	7,65±0,60
3	"Arithmetic"	12,13±0,60	6,76±0,72
4	"Similarity"	13,15±0,53	8,56±0,78
5	"Vocabulary"	10,55±0,63	9,50±0,68
6	"Repetition of numbers"	10,20±0,59	5,60±0,47
7	"Missing details"	11,32±0,33	7,57±0,67
8	"Sequential pictures"	11,47±0,58	6,79±0,43
9	"Koos cubes"	10,45±0,45	7,20±0,54
10	"Folding shapes"	10,18±0,46	6,44±0,65
11	"Coding"	15,45±0,72	8,07±0,73
12	"Mazes"	12,47±0,53	8,75±0,45

When analyzing the SECOND subtest ("Understanding"), 2 points, i.e. the highest score for this subtest, were received by 88% of the healthy children examined, 64% of the children of the main group. If in healthy children we observed our own activity, independence in performing tasks and correcting our own mistakes, then in children of the main groups we observed passivity in performing tasks and reluctance to correct their mistakes independently. A comparative analysis of the indicators of the III subtest ("Arithmetic") between the examined groups showed a high degree of its implementation in healthy children. During testing in the group of children of the main group, the average indicator of this subtest was 1.5-2 times less than in the control group. In the indicators of the V subtest ("Dictionary") there were no significant differences between the examined groups. In both study groups, during the performance of nonverbal tasks, erroneous performances on the "Missing Parts" test, poor quality in "Folding shapes", "Koo's Cubes", "Coding" were very often observed. Nonverbal intelligence is based on visualization and reflects the level of visual memory and attention, constructive thinking, visual-effective thinking, which is associated with the ability to add three-dimensional schemes and the ability to operate with spatial images. When working with the "Encryption" and "Mazes" subtests, the children of the main group experienced more difficulties than the children from the control group, because it was necessary to solve the problem consistently, to keep their actions within the limits set by the verbal instructions. When performing the "Sequential pictures" subtest, the children of the main group

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found it more difficult to organize the parts of the picture into a single whole than the children from the control group.

Conclusion. Thus, the conducted neuropsychological study showed that children with post-cephalopathy have an uneven decrease in intellectual level indicators and are accompanied by a decrease in both verbal and non-verbal cognitive activity.

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