Case Report

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Neuropsychiatric Disorders in Covid-19 - Symptoms of Infection or A New Disease Entity Triggered by Infection?

Alicja Sierakowska[1], Beata Łabuz-Roszak[2,3], Joanna Bobrowska[4], Michał Braczkowski[5], Krzysztof Kandziora[6] and Dariusz Soszyński[5,7]

[1]*Student Society of Neurology at the Department of Neurology, Institute of Medical Sciences, University of Opole, Poland*

[2]*Department of Neurology, Institute of Medical Sciences, University of Opole, Poland*

[3]*Neurology and Stroke Unit, St. Jadwiga's Regional Specialized Hospital in Opole, Poland*

[4]*Department of Pediatric Neurology, St. Jadwiga's Regional Specialized Hospital in Opole, Poland*

[5]*Department of Physiology, Institute of Medical Sciences, University of Opole, Poland*

[6]*MR Laboratory, Helimed, St. Jadwiga Regional Specialized Hospital in Opole, Poland*

[7]*Department of Human Physiology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Faculty of Medicine, Poland*

***Corresponding author:** Michał Braczkowski, Department of Physiology, Institute of Medical Sciences, University of Opole, Opole, Poland

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ABSTRACT

Abbreviations: CT: Com-Putted Tomography; MRI: Magnetic Resonance Imaging; EEG: Electroencephalographic; ENG: Electroneurographic; CNS: Central Nervous System

Introduction

Neuropsychiatric disorders are a common manifestation of COVID-19, due to the significant affinity of SARS-CoV-2 for the central nervous system. We report the case of a 16-year-old patient with suspected catatonic disorders and dysfunction from the autonomic nervous system, with coexisting SARS-CoV-2 infection. After treatment, significant improvement was achieved in both the patient's neurological and psychiatric status. Cases of COVID-19 coinfection as well as catatonia have been reported previously in the literature, but nevertheless further studies on this topic are needed.

Case Description

A 16-year-old patient was admitted to the Pediatric Neurology Department of St. Jadwiga's Regional Specialized Hospital in Opole for disorders of consciousness, speech and gait since the morning hours of the day of admission. After being brought before the Emergency Medical Team, he was conscious, but did not make verbal contact, lying down with visible drooling. According to the mother's account, the symptoms began the day before bedtime, at which time the patient fasted, and involuntary urination also occurred. The boy had been in quarantine for two weeks due to contact with an infected COVID-19 person at school. Four days before admission, he reported a worsening of his condition, with a temperature of 38 degrees C. During transport by ambulance, an antigen test for Sars-Co-V2 was performed and was positive, which was also confirmed by PCR testing during hospitalization. In addition, in history, the patient's mother reported a history of head trauma, which occurred in November 2021. There was no loss of consciousness at the time, he was consulted in the ED, and complained of difficulties with speech, swallowing, and feeling unwell. A com-putted tomography (CT) scan of the head without contrast showed no pathology. The reported symptoms resolved spontaneously. According to the mother's account, narcotic use was unlikely, which was confirmed by urine toxicology tests. The patient was not treated for chronic diseases. On admission, the patient was in an average general condition, cardiopulmonary efficient, conscious, but did not make logical verbal contact. In addition, he did not obey commands. He did not present features of psychomotor agitation. In the examination of available cranial nerves without deviations, excessive salivation with difficulty in swallowing was evident. He presented convergent strabismus, however, according to his mother's account, it was found at an earlier stage. Increased muscle tone was observed in the four extremities with predominance in the lower extremities, although the patient's active resistance during the examination could not be excluded. The boy was uncooperative during the test of muscle strength, but he kept his raised limbs in the position set by the examiner.

Presented deep reflexes vivid, symmetrical, without pathology. Cerebellar spontaneity and the Romberg test remained unassessable due to the patient's lack of cooperation. Meningeal signs were negative. In laboratory tests, with the exception of elevated D-dimer levels, the results were not abnormal. CT scans and magnetic resonance imaging (MRI) of the head were within normal limits appropriate for the patient's age, except for chronic sinusitis. MR of the spine showed cervical and thoracic incipient spondylosis and incipient two-level discopathy with modeling of the ventral surface of the spinal cord. After neurosurgical consultation, no indication for intervention. A general examination of the cerebrospinal fluid (PMR) showed normal cytosis and slightly elevated protein levels. A panel for infection with 12 pathogens (HSV1, HSV2, VZV, EBV, CMV, HHV6, Enteroviruses, Haemphilus influenzae, Neisseria meningitidis, Streptococcus pneumoniae, Streptococcus B, Listeria monocytogenes) was negative, as well as no antibodies to autoimmune encephalitis. The result of the electroencephalographic examination (EEG), apart from movement artifacts, showed no abnormalities. In addition, an electroneurographic examination (ENG) of the lower extremities was per-formed, which showed slowing in conduction velocity in the motor fibers of the left tibial nerve and damage to the motor fibers of the left fibular nerve and sensory fibers of both fibular nerves of an axonal nature, in addition, lesions at the level of the L4-L5 spinal roots on the right side were demonstrated. Performed chest X-ray, which showed inflammatory changes that may correspond to SARS CoV-2 infection. The abnormalities withdrew on follow-up examination. During the first days of hospitalization, due to the lack of independent food intake and difficulty swallowing, the patient was fed through a gastric probe. As a result of the lack of spontaneous micturition, the boy was catheterized. Treatment included hydration fluids, benzodiazepines, due to the suspected catatonia or psychosomatic background of the complaints. A gradual improvement in the patient's clinical condition, the return of logical contact and the resolution of other symptoms were achieved. The boy began to take meals on his own, was rehabilitated locomotionally, and after spionization moved independently. Due to the presence of bacteria and leukocytes in the urine, furasidine was used. The patient was consulted several times psychiatrically and psychologically, and mild cognitive impairment was found, with no psychotic or affective disorders. He was also tested with the Stanford Binet Scale, according to which the current level of intellectual functioning was at an age-appropriate norm. In tests of auditory-verbal memory, there was a slow progression of scores below the age norm, but with a preserved ability to consolidate memory material and decode after temporal deferral. The range of visuospatial memory was also below the age norm. The disposition to process and organize memory material remained preserved. The

above results tended to indicate a secondary nature to the patient's emotional state, affect and anxiety. Personality questionnaire tests showed high scores especially in the area of autonomic nervous system sensitivity. The emotions present suggested a strong and long-lasting character with a tendency to fall into anxious states. After 23 days of hospitalization, the patient was discharged home in good general condition. The patient was referred to the mental health clinic and the neurology clinic for further follow-up and observation.

Chest X-ray showed an image of the lung fields without focal thickening, without fluid in the pulmonary-final angles; the cardiac silhouette was not enlarged. The «bundle-tree»-type thickenings in the parasternal compartments present on MRI were present in the right hilar region on X-ray. These changes are characteristic of the COVID-19 course.

On head MRI, the signal intensity of the brain's white and gray matter remained normal. Diffusion images of the brain showed no features of water restriction in the extracellular space. The ventricular system remained undilated and non-displaced. The brain water supply and ventricle IV without features of abnormality. The cerebellar amygdala at the level of the great aperture; the subarachnoid spaces were not dilated; the signal intensities of the optic nerve, vestibulospinal nerve and pituitary gland were normal.

The EEG examination was performed with the eyes open in the awake state. The recording varied with a lot of movement artifacts, mainly from blinking and eye movements. The bioelectric activity consists of symmetrical irregular alpha waves with a frequency of 9.8-11.2 Hz and an amplitude in the posterior leads of up to 35 uVz with the participation of few slow theta waves of 6-7 Hz and fast beta activity, the predominance of which is marked in the anterior leads. The recording was modified by movement artifacts, without significant features of abnormalities of a paroxysmal nature. Within normal limits for age (Figures 1-6).

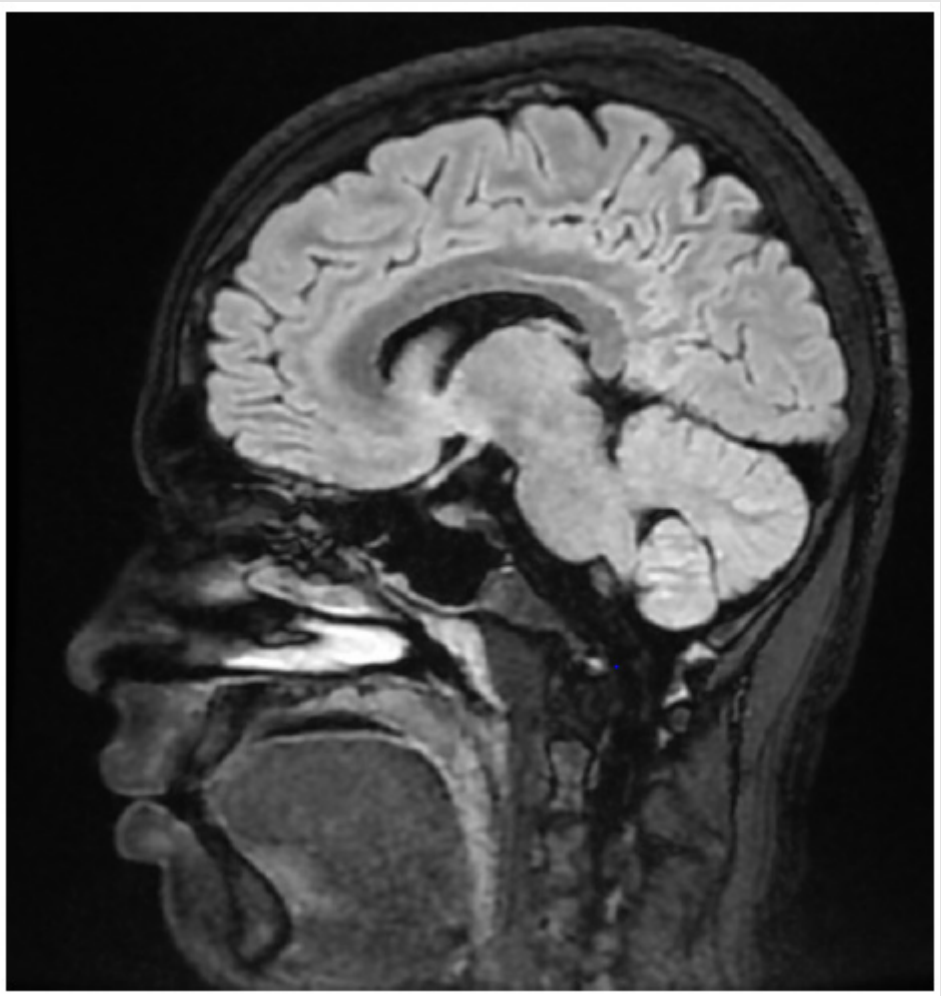

Figure 1: T2 Flair Sagittal projection.

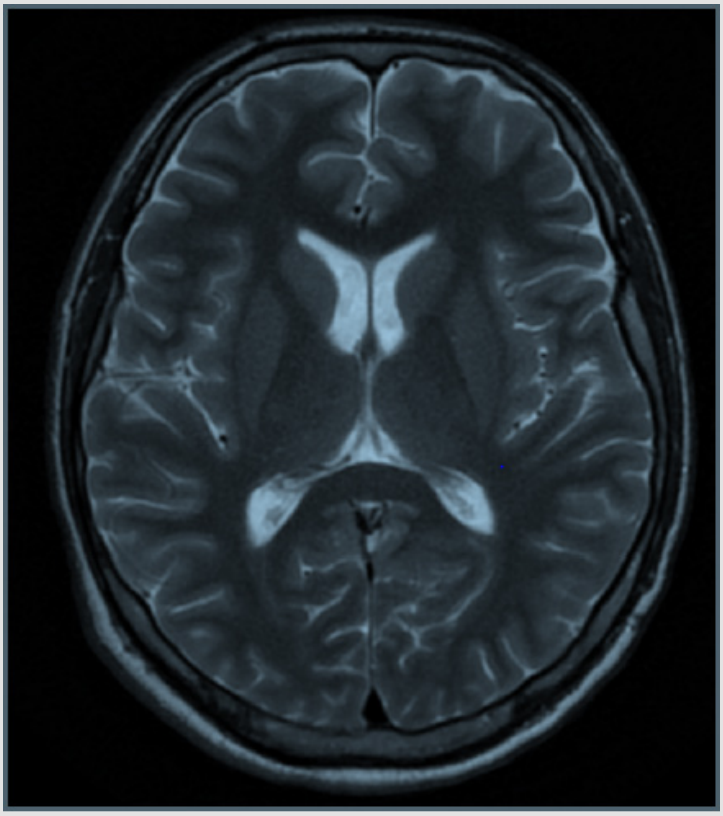

Figure 2: T2 transverse projection.

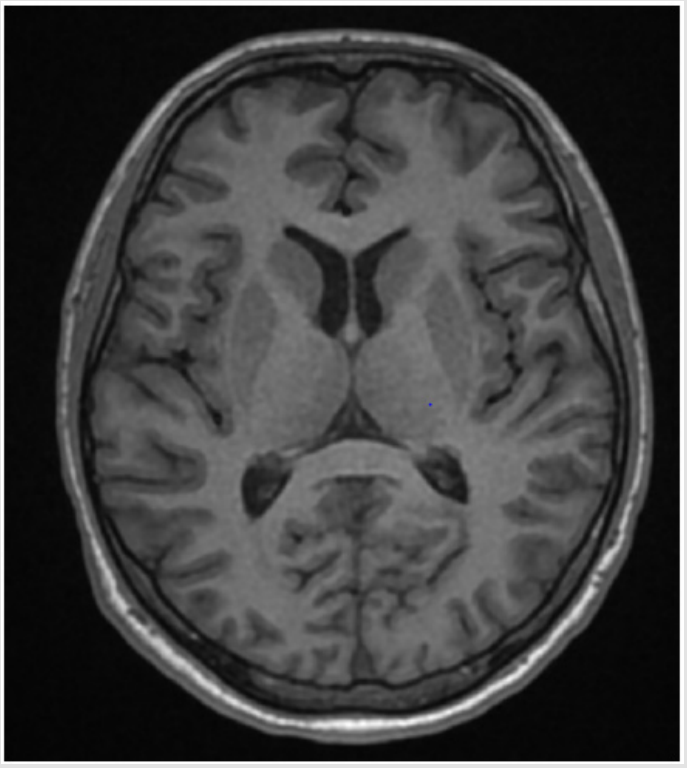

Figure 3: T1 transverse projection.

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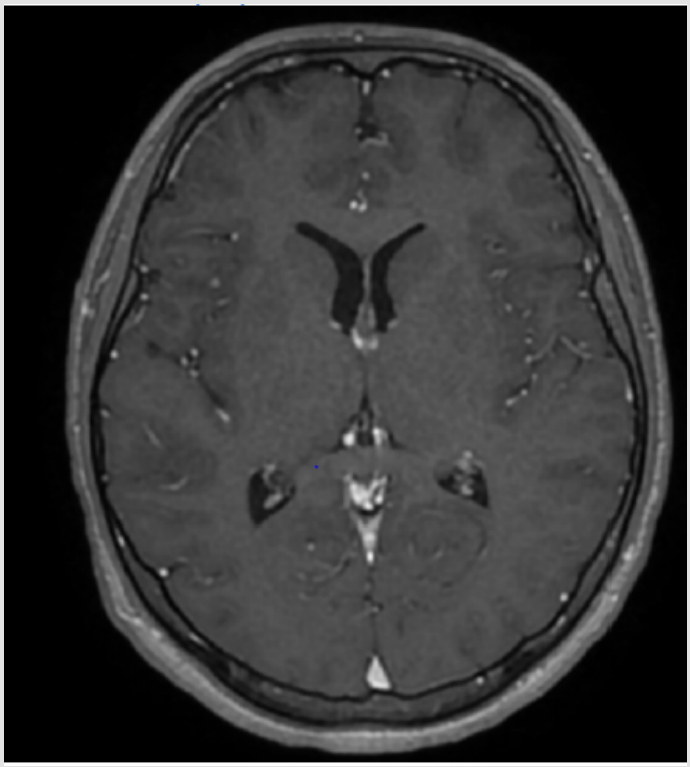

Figure 4: T1 transverse projection.

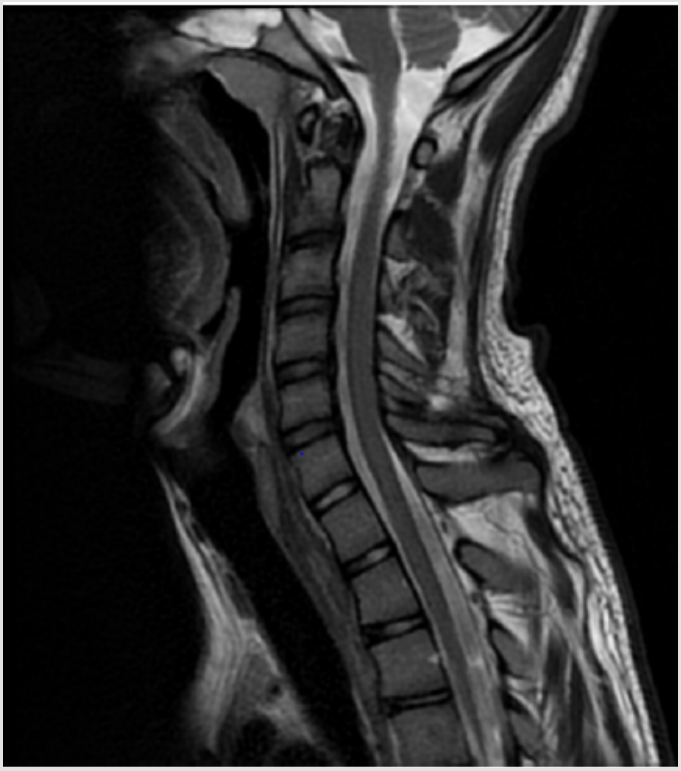

Figure 5: T2 sagittal projection.

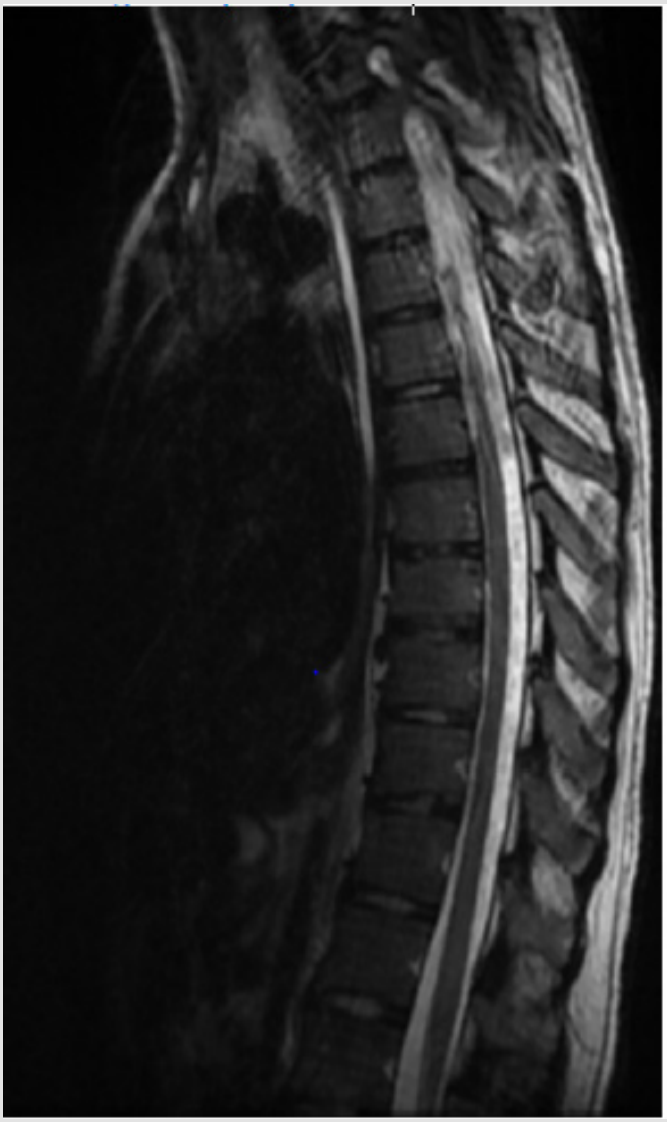

Figure 6: T2 sagittal projection.

Discussion

Coronaviruses, and COVID-19, which belongs to this group, are naturally neuroinvasive. This is evidenced by post-mortem viral RNA isolated from neural tissue in up to 40% of subjects with prior infection. The primary routes of penetration into the central nervous system for the virus are the circulatory system, as well as retrograde neuronal spread. Studies show that in the case of neuronal spread, the gateway should be sought in the situs bone, and more specifically in the olfactory nerve. Another concept suggests that SARS-CoV infection in the central nervous system is not directly caused by the virus. The pathogen remains the trigger for massive meningeal and cerebral inflammation with significant release of inflammatory cytokines [1]. The study by Baig et al. depicts the correlation of the ACE2 receptor with SARS-CoV-2 neurovirulence. Moreover, it suggests the possibility that the S-protein of the pathogen molecule reacts with ACE2 receptors located in the capillaries of the nervous system. In particular, the presence of the above receptors within brain tissue has been previously demonstrated [2]. To date, no specific nervous system symptoms have been observed in the course of COVID-19 infection. Studies dating back to 2020 present an increased incidence of depressive disorders, anxiety, post-traumatic stress disorder, psychotic episodes, as well as non-specific neurological symptoms, delirious syndromes, vascular complications in the nervous system, encephalopathy, neu-romuscular diseases or sleep disorders [3]. Moreover, neuroinflammatory processes were observed during the pandemic period, associated with a massive increase in pro-inflammatory molecules, which are responsible

for changes in glial cells, as well as in neural pathways and connections. The above-mentioned organic changes correlated with disadvantage, fear of a severe course of infection, as well as fear. The result was neuropsychiatric symptoms, including episodes of severe depression, bipolar affective disorder, psychotic episodes, obsessive-compulsive disorder, and post-traumatic stress disorder [4]. A similar etiology can be observed in the pediatric population. Stressful events, being forced to spend time at home, grief, domestic violence, abuse of the internet and social media can all be-come predisposing factors in the development of mental illness. As a result of the pandemic, there is an increase in illnesses such as depression, anxiety disorders and post-traumatic stress disorder, which can be caused by experiencing violence in the family or the patient's immediate environment. Moreover, the timing of the pandemic increases the risk of experiencing a life crisis, which also pre-disposes to the above diseases [5,6]. Studies indicate a lower ability to cope with stress during a pandemic, which promotes psychoactive substance use and increased self-harming behavior [7].

Encephalopathy can be a direct result of neuronal invasion of the virus, associated with the entry of immune cells as well as direct virus particle into the PMR. A more severe course is to be expected when the pathogen enters the central nervous system (CNS) by retrograde axonal transport. The above transfer is possible through the olfactory, respiratory, or visceral supply nerves. It then travels directly to the brain, localizing in structures such as the thalamus or brainstem, initiating inflammation and demyelination [8]. The literature reports on the occurrence of catatonia in COVID-19. An example is the case of a 28-year-old woman who had not previously been treated for neurological or psychiatric diseases. She was also not genetically burdened. Symptoms such as talkativeness, mumbling, sleep disturbances, decreased speech ability, as well as decreased food intake and manufacturing symptoms preceded the onset of mutism. In addition, the patient performed repetitive actions for no apparent reason, while refusing to take food and drink. A diagnosis of acute psychosis was made, with catatonic features present in the form of dementia, mutism, stereotypy, withdrawal, negativity and ambivalence. In addition, the affect presented by the patient was rigid, not subject to modulation. A test confirming catatonia with a provocation test with lorazepam was positive, which confirmed the diagnosis [9]. In the case presented here, no clear link could be established between neuropsychiatric symptoms and COVID-19 infection. Excessive drooling and dysphagia are symptoms of autonomic nervous system dysfunction. Leaving the limbs in a set position, low motor activity, increased muscle tension in the limbs, as well as mutism and lack of contact with the environment could indicate catatonic syndrome. As is well known, the symptoms of catatonic syndrome are nonspecific and can occur in a variety of mental illnesses and disorders from the nervous system. Catatonia can occur in the course of schizophrenia, bipolar affective disorder, depression, post-traumatic stress disorder, as a result of the use of psychoactive substances, as well as a consequence of brain diseases and in some somatic diseases. In the presented case, no psychiatric or neurological disease was finally diagnosed, and the patient remains under the supervision of the Neurological and Mental Health Clinic. There is a high probability that neuropsychiatric disorders were present in the course of COVID-19, however, only prolonged observation and the absence of a diagnosis of mental or other somatic disease will allow a definite answer.

Summary

The occurrence of neuropsychiatric disorders in the course of COVID-19 has been confirmed in numerous reports, also SARS-CoV-2 infection can trigger symptoms of a disease that has so far run subclinically, although this requires further research. In some cases, it may not be a cause-and-effect relationship, but only an accidental one. When diagnosing and treating patients infected with SARS-CoV-2, it is important to consider the actual etiology of the symptoms presented. The correct diagnosis is not always straightforward, and often the patient requires prolonged observation and follow-up.

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Michał Braczkowski. Biomed J Sci & Tech Res

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