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Case Report

Cognitive Functions in a 29-Year-Old Male with Post-COVID Syndrome and Long-Term Psoriasis – A Case Study

Miroslava Hristova[1], Radka Massaldjieva[2], Lyubomir Chervenkov[3,4], Penka Atanassova[1]

[1] *Department of Neurology, Medical University of Plovdiv, Plovdiv, Bulgaria*
[2] *Department of Health Care Management, Medical University of Plovdiv, Plovdiv, Bulgaria*
[3] *Department of Diagnostic Imaging, Medical University of Plovdiv, Plovdiv, Bulgaria*
[4] *Research Complex for Translational Neuroscience, Medical University of Plovdiv, Plovdiv, Bulgaria*

Corresponding author: Miroslava Hristova, Clinic of Neurology, St George University Hospital, 66 Peshtersko Shosse Blvd., 4000 Plovdiv, Bulgaria; Email: miroslava.mgh@gmail.com; Tel.: +359882700320

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Abstract

Post-acute COVID syndrome (PACS), or long COVID, is a newly defined condition emerging as a widespread post-pandemic diagnosis with prevalent neuro-psychiatric symptoms and possible neuroinflammation-associated pathogenetic mechanisms.

We present the clinical case of a 29-year-old male patient who had mild COVID-19 infections, autoimmune illness (psoriasis), and suffered a post-COVID aggravation of psoriasis, along with other non-specific neuropsychiatric problems. The patient underwent computer-based neuropsychological testing (the CogState Battery), brain magnetic resonance imaging (MRI), and a clinical interview since he fulfilled the criteria for a PACS diagnosis.

The acquired data showed poor results on most of the neuropsychological subtests during his follow-up visit, structural changes in the MRI, and a possible immune dysregulation with increased levels of immunoglobulin G. These results confirm that the nonspecific neuro-psychiatric post-COVID complaints are associated with objective findings.

Keywords

computer-based testing, immune dysregulation, long COVID, neuroinflammation, neuro-psychological functioning

INTRODUCTION

Post-acute COVID syndrome (PACS), or long COVID, is a new condition emerging as a widespread post-pandemic diagnosis with prevalent neuro-psychiatric symptoms and undeniable medico-social importance. The syndrome affects both patients with symptomatic and asymptomatic infections, and its incidence is ranging from 10% among non-hospitalized patients to up to 85% among those requiring hospitalization.[1] For instance, the REACT-2 study (2021) analyzed the incidence of 29 self-reported persisting complaints among 508,707 recovered patients and the data showed that 37.7% of the participants had one or more long-lasting complaints, but only a third of them had experienced a severe COVID-19 infection.[2] Another study found that 6 months after COVID-19 infection, 50% of the patients showed cognitive impairment and their Montreal Cognitive Assessment (MoCA) scores were below 18 points.[3] While Walle-Hansen et al. obtained similar results with 43% of their subjects showing impaired cognition on MoCA, Lamontagne et al. established that executive functions and memory were predominantly affected,

while orientation and active attention were relatively intact.[4,5] According to Woo et al., 78% of those with a mild or moderately severe COVID-19 infection, experienced post-acute cognitive difficulties, which confirms the high incidence of neuro-psychiatric complaints among patients with PACS.[6]

CASE REPORT

We present the clinical case of a 29-year-old male patient with long-term psoriasis who tested positive for COVID-19 twice–once in 2021 and a second time in 2022. Both times his infection was mild, he had no need of oxygen supplementation or hospitalization. After his first COVID-19 infection, he recovered fully and had no persisting complaints.

Prior to his second COVID-19 infection, his psoriasis was in remission, as he had been receiving biological treatment for 8 years without any adverse effects. Several weeks after his 2022 COVID-19 infection, however, he had a relapse of his psoriasis and an exacerbation of both his skin lesions and psoriatic arthritis. Therefore, he underwent a clinical re-evaluation and a subsequent change of therapy. Currently, he is in remission again and is receiving another biological treatment with the monoclonal antibody risankizumad. The medication is prescribed for patients with moderate to severe psoriasis and is not known to negatively affect cognitive functions according to official data.

The patient reported experiencing some mood swings and memory difficulties approximately eleven months after his second COVID-19 infection. These complaints did not disrupt his everyday life or professional performance, but nonetheless required greater efforts to achieve his pre-COVID-19 results. Seven months later, at a follow-up visit, he was still complaining of memory difficulties and emotional lability.

A physical examination showed no neurological deficits. Laboratory findings four months after his COVID-19 infection in 2022 showed a titer of serum anti-SARS-CoV-2 immunoglobulin G (IgG) antibodies 114 times higher than the cut-off value, while other blood tests, including the complete blood count, electrolytes, serum proteins, thyroid hormones, anti-thyroid antibodies, and blood sugar, were within normal ranges.

To assess his cognitive functions, we used a computer-based test – the CogState Battery (https://www.cogstate.com), which measures four core cognitive domains: processing speed, attention, visual learning, and working memory. We chose to use the CogState Battery because the test is completely computerized, therefore the administration and scoring are automated and standardized. This reduces the risk of potential administration and interpretation errors, thus providing objectivity to the received data. The stimuli, rules and responses are simple, they have been well-validated and can detect subtle cognitive impairments, making the battery more sensitive than the commonly used MoCA and MMSE (Mini Mental State examination).

The test was performed on a laptop twice – once during the initial interview and a second time at a follow-up visit, 7 months later. Surprisingly, the patient showed poorer results and made more errors during the second testing on all subtests except for One-card learning (OCL) ***(Table 1)****.*

In addition, we performed a magnetic resonance imaging (MRI) scan of the patient's brain in March 2023, approximately 13 months after his positive SARS CoV-2 test. The MRI scan showed an enlarged hippocampal perivascular space in the left hemisphere with a size of 7 mm. No other abnormalities were present ***(Figs 1, 2)****.*

DISCUSSION

The present case study provokes interest in the context of the long COVID-19's rising incidence and its possible inflammatory-associated pathogenesis. Many studies discuss the central role of immune dysregulation and the associated chronic inflammatory state that disrupts the permeability of the blood-brain barrier and leads to prolonged microglial activation, induction of pro-apoptotic processes and in situ synthesis of factors, promoting neurodegeneration with subsequent disruption of neuroplasticity, synaptic function, and myelination.[7-9]

Table 1. Outcome measures from CogState Battery subtests

Subtest	Function assessed	Total errors – baseline	Total errors – follow-up	Correct – baseline	Correct – follow-up
Groton Maze timed chase test (GMCT)	Speed of visual processing	0	1	46	54
Groton Maze learning test (GML)	Executive function	50	59	140	140
Detection test (Has the card turned over)	Psychomotor function	0	1	35	36
One-card learning (OCL)	Working memory	44	39	39	41
Continuous Paired Associate Learning (CPAL)	Delayed visual memory through paired associate learning	67	114	42	42

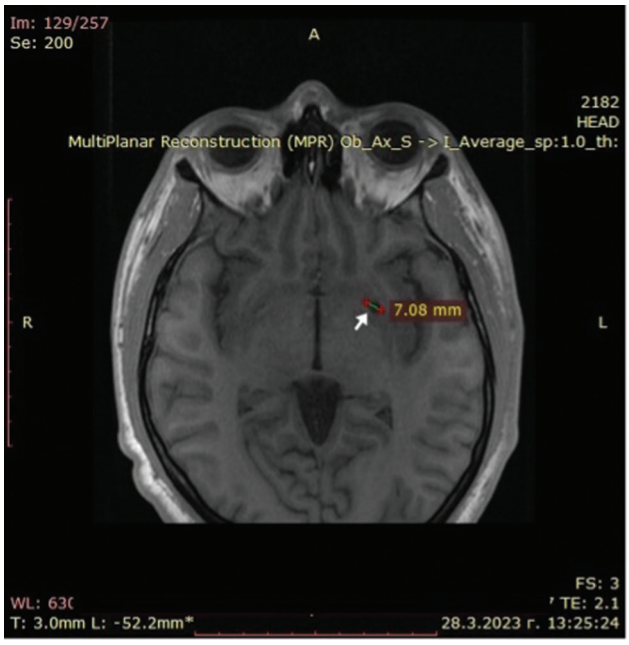

Figure 1. MRI of a 29-year-old patient, T2 FLAIR sequence, axial view. Dilated perivascular space was found near the hippocampus on the left side (white arrow).

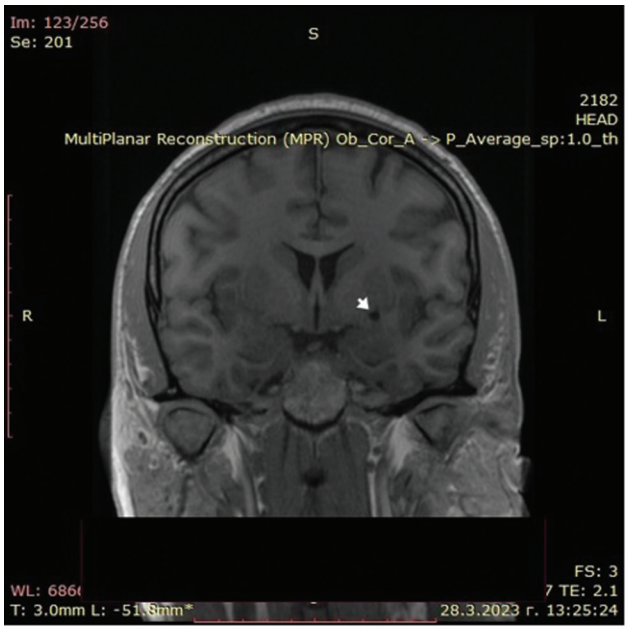

Figure 2. MRI of the same 29-year-old patient, T2 FLAIR sequence, coronal view. Dilated perivascular space of 0.7 cm was found near the hippocampus on the left side (white arrow).

Chronic neuroinflammation is associated with dysregulation of ryanodine ion channels and elevated intracellular levels of calcium, leading to the activation of calcium-dependent enzymes and hyperphosphorylation of the tau protein. The tau protein is physiologically responsible for cell stability and acts as a protector off DNA. In pathologic situations, however, the abnormal tau hyperphosphorylation disrupts the cell's nucleoskeleton and induces cell death. Thus, the pathohistological changes are very similar to those in neurodegenerative tauopathies such as Alzheimer's disease, progressive supranuclear palsy, frontotemporal dementia, etc., indicating a possible neurodegenerative process affecting the CNS.[10,11]

Some authors suggest that during acute COVID-19, there is a state of transient immunosuppression of innate and acquired immunity, with decreased sentinel effect of monocytes/macrophages and suppression of regulatory T-cells, followed by sudden reactivation of the immune system that might cause loss of self-tolerance, inappropriate immune reconstitution and triggering of autoimmunity and autoinflammation that might be associated with some of the persistent symptoms of PACS. Moreover, these events might lead to a post-COVID manifestation of an autoimmune disease or exacerbation of preexisting one, such as psoriasis. So, based on these theories and given the excessively high levels of our patient's anti-SARS-CoV-2 IgG antibodies, we can assume that there is indeed a persistent inflammatory state, suggesting a possible immune dysregulation, that could explain the exacerbation of his autoimmune disease and his persisting neuro-psychiatric complaints.[12]

It is important to note that patients with psoriasis, particularly those with long-term disease, may experience cognitive decline while receiving systemic treatment, as psoriasis is associated with a pro-inflammatory state that can lead to chronic neuroinflammation and potentially promote neurodegeneration.[13] However, the large Rotterdam study concluded that cognitive test results and volumetric and microstructural measures on brain MRI did not differ between psoriasis patients and non-psoriasis subjects.[13] Therefore, we can conclude that the established subclinical cognitive impairments and structural MRI changes in our patient were not associated with his long-term autoimmune disease. This hypothesis is supported by the fact that he experienced no cognitive difficulties or mood swings prior to his second COVID-19 infection.

The established hippocampal enlarged perivascular spaces (H-EPVS) have been discussed before as a potential marker of cognitive decline in aging patients. The possible pathogenetic mechanisms of H-EPVS are associated with atherosclerosis and arterial stiffening, abnormal Aβ-amyloid and tau protein aggregation, age related brain atrophy, and disrupted blood-brain barrier, due to nonspecific inflammation.[15] Regarding the association between H-EPVS and cognitive impairments, Jae Eun Sim et al.[16] concluded that the degree of H-EPVS was not associated with sex, smoking, alcohol consumption, hypercholesterolemia, depression, or coronary heart disease. There was however a positive correlation between H-EPVS and age. H-EPVS might be a secondary event, following medial temporal atrophy, which is independently associated with cognitive functions.[14] Based on these conclusions, we can assume that the described 7 mm of H-EPVS in our young 29-year-old patient were not associated with his age or cerebrovascular risk factors. Therefore, we conclude that his brain

MRI abnormalities are a consequence of another primary cause. And based on the lack of another established diagnosis or risk factors we can assume that the 7 mm H-EPVS might be a structural presentation of PACS.

Regarding the patient's cognitive functions, we used several subtests of CogState Battery, presented in **Table 1** to assess delayed visual memory, working memory, attention and executive function as well as speed of visual processing and found more errors in the performance of all subtests, except one. The CogState Battery results show lack of improvement in cognitive functioning months after his recovery from the acute COVID-19 infection, suggesting that subclinical impairments might persist for a prolonged period and left untreated might even worsen on a later stage.

CONCLUSION

The presented case study confirms the hypothesis that even in young people the subjective cognitive complaints of PACS might be associated with objective findings. Here conventional MRI is sensitive enough to discover slight changes of brain structures that can be associated with subclinical cognitive impairments. However, assessing cognitive functions has proven to be a rather difficult task, requiring well-chosen, sensitive, and thorough testing of different cognitive domains in order to uncover the underlying deficits, such as the slight deficit in executive, psychomotor functions, speed of visual processing and delayed visual memory, detected using the CogState Battery.

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Competing Interests

The authors have declared that no competing interests exist.

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Когнитивные функции у 29-летнего мужчины с постковидным синдромом и длительным псориазом – исследование случая

Мирослава Христова[1], Радка Масалджиева[2], Любомир Червенков[3,4], Пенка Атанасова[1]

[1] *Кафедра неврологии, Медицинский университет - Пловдив, Пловдив, Болгария*

[2] *Кафедра управления здравоохранением, Медицинский университет - Пловдив, Пловдив, Болгария*

[3] *Кафедра медицинской визуализации, Медицинский университет - Пловдив, Пловдив, Болгария*

[4] *Центр трансляционных нейронаук, Медицинский университет – Пловдив, Пловдив, Болгария*

Адрес для корреспонденции: Мирослава Христова, Клиника неврологии, УМБАЛ „Свети Георги“, бул. “Пещерско шосе” № 66, 4000 Пловдив, Болгария; E-mail: miroslava.mgh@gmail.com; тел.: +359882700320

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Резюме

Постаст-острый синдром COVID (PACS) или длительный COVID — это новое состояние, возникающее как широко распространённый постпандемический диагноз с распространёнными нейропсихиатрическими симптомами и возможными патогенетическими механизмами, связанными с нейровоспалением.

Мы представляем случай 29-летнего пациента мужского пола, у которого были лёгкие инфекции COVID-19, аутоиммунное заболевание (псориаз) и обострение псориаза после COVID, а также другие неспецифические нейропсихиатрические проблемы. Пациенту провели магнитно-резонансную томографию мозга (МРТ), компьютерный нейропсихологический тест (CogState Battery) и клиническое интервью, поскольку он соответствовал критериям для диагноза PACS.

Полученные данные показали плохие результаты по большинству нейропсихологических субтестов во время его последующего визита, структурные изменения на МРТ и возможную иммунную дисрегуляцию с повышенным уровнем иммуноглобулина G. Эти результаты подтверждают, что неспецифические нейропсихиатрические жалобы после COVID связаны с объективными результатами.

Ключевые слова

компьютерное тестирование, иммунная дисрегуляция, длительный COVID, нейровоспаление, нейропсихологическое функционирование