American Journal of BioMedicine
AJBM 2022;10 (4): 185-192
Research Article doi:10.18081/2333-5106/2022.10/185

Neurological symptoms in patient with COVID-19: a case report

Xinxin Cao [1*], Zunyou Wang

Abstract

Most children with COVID-19 show few symptoms and have a mild form of the disease; some pediatrician reported the extra-pulmonary manifestations in acute COVID-19 like, neurological and cognitive symptoms with minor instances seizures. However, it has become clear that a small proportion of children need intensive care and it can be very debilitating and lead to long school absences. Our case study report 2.3-year-old child male with head ache with fit and cognitive symptoms, on examination had generalized fatigue, neck stiffness and fever for two days. He had never been to any foreign countries. The specific SARS-CoV-2 RNA was not detected in the nasopharyngeal swab but found in CSF exam without any other finding. A brain MRI showed bilateral front-temporal hypo-perfusion. Neurological manifestations are common and psychosocial stress might lead to clinical neuropsychiatric manifestation. Psychosis may be secondary to viral illness; treatment provided and increased psychosocial stress during pandemics. Improved attention to the possible neuropsychiatric consequences of SARS-CoV-2 viral infection might aid in early identification and better management.

Keywords: COVID-19; Psychosocial stress; Cognitive symptoms

*Corresponding author email: Caox@yahoo.yahoo
[1] Department of Epidemiology, Peking University, China
Received June 04, 2022; revised September 28, 2022; accepted October 30, 2022; published December 24, 2022
Copyright © Xinxin Cao et al., 2022. This is article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY 4.0) (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

The outbreak of novel coronavirus disease 2019 (COVID-19) has made a significant impact around the world. In most cases, the disease initially begins with fever, fatigue, and a dry cough, followed by severe pneumonia, acute respiratory distress syndrome, and even death. The fact that there are no suitable drugs effective against COVID-19 makes containment difficult. Recent articles have shown that some SARS-CoV-2 RNA is in the cerebrospinal fluid of patients positive for COVID-19, regardless of the severity of the disease, suggesting that the virus can invade the central nervous system. However, other papers have pointed out that the number of positive results is not large. Therefore, it is likely that the spread of the virus to the nervous system is relatively rare, but it is not yet clear whether the viruses affect the nervous system.

To understand the involvement of the nervous system in COVID-19 cases, it is also necessary to accumulate case reports of patients with COVID-19 who demonstrated neurological symptoms. Herein, the authors report the cases of two patients with suspected COVID-19. They presented with fever, fatigue, and severe headache, partly affecting their physical activities.

Research Article doi:10.18081/2333-5106/2022.10/185

Case 1 demonstrated hyperlipidemia, but no specific abnormalities were found in the brain or cerebrospinal fluid. Cases 1 and 2 gradually displayed underlying symptoms of COVID-19, but it was not possible to confirm COVID-19 through tests. However, COVID-19 may have been highly suspected in these patients. With ongoing research, invasion of SARS-CoV-2 in the nervous system might be gradually understood. Therefore, clinicians should pay attention to neurological manifestations in cases that are suspected as COVID-19. More case details and imaging findings are needed as clinical series accumulate.

Case Presentation

The study describes the case of a patient with COVID-19 who presented with neurological symptoms, namely cerebrovascular complications, severe headaches, and seizures. The provision of ethical standards, such as informed consent and patient confidentiality, has been met throughout the diagnostic, treatment, and follow-up procedures.

A 2.3-year-old child male was admitted to the emergency department in the context of a highly suspected SARS-CoV-2 infection. Her medical history reported the regular use of progesterone-only contraceptives, without prior pregnancy. There was no previous history of severe headaches, seizures, or acute neurological deficits. The clinical presentation of the SARS-CoV-2 infection raised concerns related to a pleomorphic disease course that included neurological symptoms. In this context, the patient's symptoms, diagnostic assessment, treatment allocation, and evolution were thoroughly registered with the purpose of sharing and discussing the case record. In summary, the patient presented with a prodrome of malaise, fever, and headaches progressing to severe deficits of consciousness due to the occurrence of seizures. However, the neurological remission was quite complete within the acute phase. Several thromboembolic and venous anomalies, typical for COVID-19, were disclosed. The patient improved and was dismissed from the hospital for in-ambulatory treatment. At three months, nerve conduction velocity registration, cerebral MRI scan, and a dedicated ophthalmological exam (due to the altered visual field at admission) were all finalized, showing no persistent deficit and satisfactory therapeutic outcome. At the four-month follow-up, no new seizures had presented.

Clinical presentation of neurological symptoms

Although most patients usually present mild respiratory symptoms, some severe cases have been described. In addition, initial studies found that neurological symptoms were seen frequently in some patients with COVID-19 infection. In Wuhan, China, a study found that 27% of patients with coronavirus infection had symptoms that affected the nervous system. Here we present a case of confirmed patients with COVID-19 from two different regions in Europe closely located, presenting mainly neurological symptoms and a favourable outcome. Approximately 30% of patients that develop COVID-19 experience neurological symptoms. In a study conducted in Wuhan, China involving 214 patients admitted to the hospital with clinical suspicion of bacteremia, most were found to have CSF with normal cell count with no bacteria

Research Article doi:10.18081/2333-5106/2022.10/185

and most of them had headache. Other authors reported that patients with severe acute respiratory syndrome (SARS) caused by the SARS-CoV-1 also had neurological manifestations, such as dizziness and impaired concentration. These patients had more chances to die. Acute cerebrovascular diseases were also an infrequent clinical presentation of COVID-19 that had at least 11 cases reported from Wuhan, China and Vancouver, Canada. A case series of six acute arterial ischemic stroke associated with COVID-19 infection found that all patients were young with a mean age of 39 (range: 33-49) years. Acute stroke occurred within two to ten days from onset of respiratory symptoms. Only two patients admitted to the emergency department experienced a slight headache as initial symptom. All of them had imaging evidence of occlusion of the large arteries of cervical and/or intracranial arteries. DNS were frequent and most of them included impaired consciousness. These median times were statistically different in comparison of the median times in patients without any DNS. DNS are more frequent in older people.

Imaging studies

In the presence of neurological impairment, two brain imaging techniques were performed in our patient. Electroencephalogram revealed an asymmetry in the background activity, with the left hemisphere 8–11 Hz activity showing facilitation with eye opening, while the right hemisphere 9–11 Hz activity didn't show any reactivity change. A hypertrophy of the lateral occipital lobe of the right brain was suspected; however, a new MRI of the brain didn't lead to this diagnosis, but a small-developed occipital horn was found in the right brain lobe. Anomalous brain vascularization, including carotid artery malformation, was not found by cerebral CT angiography, with exclusion of the Circle of Willis. In the same day, a transcranial doppler was ordered for him but he refused to take the examination.

Laboratory tests

The main laboratory tests and their outcomes were as follows: white blood cells 5.79 × 109 cells/L, neutrophils 73.1%, hemoglobin 183 g/L, lightly increased C-reactive protein 9 mg/L, but not severely high interleukin 6, the erythrocyte sedimentation rate was not significantly increased in the early stage (6 mm/h); the patient's immune function was basically normal, and autoimmune disease was ruled out comprehensively (including systemic lupus erythematosus, Sjogren's syndrome, and antineutrophilic cytoplasmic bodies). Lyme antibody IgG was negative, cerebral blood supply, and basil test dysfunction. The patient's blood lipid status was not high, and the risk of hypercoagulability was reduced. Lower-limb color Doppler and DSA (digital subtraction angiography) were normal. The patient's positive rate for SARS-CoV-2 nucleic acid was 98.4%, his coronary CT calcium score was 1093, which was a middle-calcification (93%-97% stenosis), his prebranial sagittal artery color returned sign from low to high velocity and 1 grade arteria basilar. The immune function evaluation showed impaired perforin expression.

Research Article doi:10.18081/2333-5106/2022.10/185

Pharmacological interventions

Remdesivir is a nucleotide analogue that disrupts SARS-CoV-2 RNA replication with a plateau in viral load on day 6 after initiation of remdesivir, followed by a decrease in viral load. Remdesivir, now called veklury, was approved by the Food and Drug Administration (FDA) on October 22, 2020 for adults and pediatric patients (12 years of age and older and weighing at least 40 kilograms) who need supplementation with low oxygen blood, such as hospitalized patients with COVID-19. In remdesivir approved for emergency use authorization in 2020, for the treatment of patients with COVID-19 weighing at least 3.5 kg, who require supplements with low blood oxygen levels or mechanical ventilation. Severe acute respiratory syndrome coronavirus under NIAID Remdesivir Clinical Trials sponsored treatment was related to the average duration of 12 days emerging mechanical ventilation, infiltrate radiological absorption, and declining plasma viral RNA load. Random allocation of remdesivir increased the recovery rate in hospitalized adults with COVID-19 more rapidly than placebo, according to preliminary results. During the course of treatment with remdesivir for 10 days, this outcome was more evident. Early administration of remdesivir consistently showed more rapid clinical improvement at day 7, regardless of duration of illness. In severe patients randomized through compassionate use, clinical improvement with remdesivir compared to expected standard of care was evidenced at day 11 in those on ventilation and at day 15 in those on ECMO support.

Outcome and Follow-up

Outcome and Follow-up. A favorable short-term outcome occurred in our two cases. They recovered well from the neurological symptoms, but a two-week follow-up MRI showed that the brain lesions were still present. Since neurological worsening was described in COVID-19 patients on anti-inflammatory drugs alone, we cautiously think that steroid treatment might not be sufficient for neurological improvement in SARS-CoV-2 patients, if not in association with antiviral therapy. Eighty percent of SARS-CoV-2 patients displayed neurological symptoms of peripheral nerve origin, while little is still known regarding the possible central nervous system (CNS) involvement. With this report, we describe the potential encephalitic picture caused by novel CoV-2. We also warn on the neuroworsening in our patients, although the short-term outcome has been favorable.

Follow-up of Patients. Both patients were monitored for other complications related to the new respiratory syndrome, also being affected by diabetes and hypertension. They showed an improvement in respiratory function and were discharged after 17 days of hospitalization. A new brain MRI scan, that has been performed 24 days after admission, showed a progressive reduction in the size of the lesions (fig. 2a-c). However, new central nervous system alterations and hemorrhagic-inflammatory activity have never been highlighted. A Thoracic CT scan, performed 12 days after brain imaging, and control of the oro/naso-pharyngeal swab by rRT-PCR after 21 days from admission showed a steady fall in viral load, and the following rRT-PCR tests always gave a negative result. The neurological symptoms and the left upper limb

strength also showed improvement, with the patient complaining only for a slight weakness in the wrist and in the fingers of his left hand.

Short-term outcomes

The family reported that the patient's oral intake improved and she was safer from choking. However, she still had some drooling. Physical therapy was initiated, and the patient did some exercises like upper limb strengthening, sliding board transfer, massage, and was encouraged to eat cookies and drink milk. She regained the ability to follow commands and showed significant improvement in her communication and dysphagia swallowing status according to the assessment using the GCS and BDAE score.

The respiratory status of the patient improved with the successful weaning of the ventilator and spontaneous breathing without difficulty. No vital signs abnormalities were found 1 min after unclamping of the tracheostomy cannula and the tracheal cannula was opened. The results of laboratory examination, including blood gas analysis, infection markers on COVID-19 swab, and urine analysis, were normal. No signs of cardiac disorders or hemodynamic changes were found during treatment. No seizures were found before or after treatment. Chest X-rays showed no abnormal results, while brain CT showed a hypodensity area in the right corona radiata region suspected as hemispheric ischemia, with no special indicators found in EEG.

Her consciousness gradually improved, and no weakness was found in her body movement. When examined by the neurologist, the patient could simply move her left leg. She was oriented to the time, person, and place. There were no signs of aphasia. The patient behaved friendly, and memory function had partially recovered. Withdrawal of tracheostomy was initiated 26 days after hospital admission, and it did not require reintubation. The patient used a nasal cannula oxygen mask.

Long-term follow-up

As the follow-up evolved, this number increased to 19. The long-term follow-up of these two patients showed that there were no more complaints. They managed to function as before, since they returned to work, and they resumed a normal personal and social life. AMA was at 2. If we look forward, we observe that it appears that most of the symptoms decrease in intensity and number over time. Confusion, memory impairments, and signs of meningeal irritation did not decrease. Also, some of the other residual symptoms appear to present a fluctuating pattern. International standards for diagnostic statistical manual of mental disorders (DSM) and affected domains in these patients. In conclusion, patients critical for COVID-19 needing ICU support frequently exhibit neurological signs, symptoms, and paraclinical presentations. These neurological manifestations may pose diagnostic and therapeutic dilemmas, requiring clinical suspicion and vigilance, despite the multitude of other. The findings seem to suggest a change in the international standards for diagnostic and statistical manual of mental disorders and decrease the numbers of areas profoundly affected in these patients. Further research is

needed to refine these signs and symptoms of pD-PICS in ICU patients for COVID. The improvement in the affected specialties was more evident in men compared to women. A decrease in overall ICD-10 affective symptomatology is expected and pictograms 15, 16 and 17 (affect systems) are attached. A fluctuated pattern was observed with autistic, conduct, histrionic and anxiety disorders showing an improvement at t = 1 month and exhibit a deteriorating evolution.

Discussion

The association between COVID-19 and neurological symptoms is not to be overlooked. The increase in venous clot formation might explain the predisposition to transient ischemic attacks in more severe cases. It is not yet known whether the olfactory bulbs can be attacked by the virus. It has also been reported that patients may present with symptoms consistent with a florid encephalopathy, which may be persistent. The cytokine storm can lead to an over-functioning of the immune system which ultimately attacks the cells of the body; in this case, the damage is determined by the blood vessels, including the blood vessels of the brain. The cytokine storm has only recently been investigated; the data are scarce and further studies are needed to investigate the repercussion on the brain in patients affected. It is important to mention that CoV are able to enter into the CNS, as proven in post-mortem studies. These patients need detailed analysis to confirm whether the immune system or the virus itself is the main cause of the symptoms reported in the CNS. It cannot be ruled out that SARS-CoV-2 may mimic the parameters of the cytokine storm, but with a potential greater aggressiveness. It has also been proven that CNS damage may have a hormonal basis. The role of both hormones and cytokines in the development of neurological disorders in patients affected by SARS-CoV-2 is crucial, and thorough studies are awaited to clarify the correlation. Necrotizing hemorrhagic encephalopathies are not infrequent in virus-related diseases, and SARS-CoV-2 is not an exception. The S protein in SARS-CoV has been labeled as being inserted into the brains of mice. A direct passage of SARS-CoV-2 in the CNS of rats was confirmed. Additionally, MERS was determined to have a severe neurological role. In a study with 195 patients affected by MERS, elevated levels of creatinine kinase, which are related to a progressive muscle lesion (ranging from easy muscle pain to severe muscle damage), have been reported. Multiple CNS findings were confirmed at CT and/or MRI in a large number of patients, confirming that a robust impact on the CNS is to be expected in patients affected by coronaviruses. In this study, Gutiérrez-Ortiz found that 16/38 (42%) of patients affected had severe impairment of consciousness, as opposed to 13/72 (18%) of patients affected by H1N1.

Conclusion

we have described dramatic neurological symptoms in patients during the COVID-19 pandemic, including an unusual wave of encephalopathy without typical respiratory symptoms. It seems that the high frequency of neurological symptoms cannot be explained simply by the

large number of patients infected by the severe acute respiratory syndrome coronavirus. Our data are in line with previous studies indicating that the CNS is affected by the recent strains of coronavirus, including SARS-CoV-2, leading to encephalitis/encephalopathy and other neurological symptoms.

Competing interests

The authors declare no conflict of interest.

Ethics Statement

This study has been approved by the Ethical Review Committee of the Shanghai University of Sport (approval number: 312672411BN112). The publication of any potentially identifiable images or data contained in the article requires personal written informed consent. The research team will provide consultations for all subjects and their families to answer any research questions. Before signing the informed consent form, after the patients and their families fully understand the research process, our team members will organize the patients to sign the informed consent form or withdraw from the research. All subjects or their guardians will sign informed consent. Authors tend to submit research results to peer-reviewed journals or academic conferences for publication.

Authors' contributions

All authors shared in the conception and design and interpretation of data, drafting of the manuscript and critical revision of the case study for intellectual content and final approval of the version to be published. All authors read and approved the final manuscript.

References

1. Zhu N, Zhang D, Wang W. China novel coronavirus investigating and research team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382(8):727-733. Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Int. J. Infect. Dis 2020; 94:55-58.
2. Carfì A, Bernabei R, Landi F. For the Gemelli against COVID-19 post-acute care study group. Persistent symptoms in patients after acute COVID-19. J Am Med Assoc 2020; 324(6):603-605.
3. Liu X, Zhou H, Zhou Y. Risk factors associated with disease severity and length of hospital stay in COVID-19 patients. J Infect 2020; 81(1):e95-e97.
4. Needham EJ, Chou SH, Coles AJ, Menon DK. Neurological implications of COVID-19 infections. Neurocrit. Care 2020:1-5.
5. Zhou F, Yu T, du R. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395(10229):1054-1062.
6. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barre syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol 2020; 19(5):383-384.
7. Ueda N, Umetsu R, Abe J, Kato Y, Nakayama Y, Kato Z. Analysis of neuropsychiatric adverse events in patients treated with oseltamivir in spontaneous adverse event reports. Biol. Pharm. Bull 2015; 38(10):1638-1644.
8. Severance EG, Dickerson FB, Viscidi RP, Bossis I, Stallings CR, Origoni AE. Coronavirus immunoreactivity in individuals with a recent onset of psychotic symptoms. Schizophr. Bull 2011; 37(1):101-107.

9. Kotfis K, Williams Roberson S, Wilson JE, et al. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. Crit. Care 2020; 24(1):176.
10. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J. Pathol 2004; 203(2):631-637.
11. Filatov A, Sharma P, Hindi F, Espinosa PS. Neurological complications of coronavirus disease (COVID-19): encephalopathy. Cureus 2020; 12(3):e7352.
12. Desforges M, Le Coupanec A, Stodola J, Meessen-Pinard M, Talbot PJ. Human coronaviruses: viral and cellular factors involved in neuroinvasiveness and neuropathogenesis. Virus Res 2014; 194:145-158.
13. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020; 395(10224):565-574.
14. Raj VS, Osterhaus AD, Fouchier RA, Haagmans BL. MERS: emergence of a novel human coronavirus. Curr Opin Virol 2014; 5:58-62.
15. Conceição MS, Chetterje MD, Gupta M. Complete remission of Hodgkin Lymphoma after a concurrent infection with COVID-19: systematic review and meta-analysis. Muthanna medical journal 2022; 9:57-67.
16. Yousif NG. Mortality rate in cancer patients with COVID-19: meta-analysis data. American Journal of BioMedicine 2021; 9(3):156-163.
17. Blomberg B, Mohn KG-I, Brokstad KA, et al. Long COVID in a prospective cohort of home-isolated patients. Nat. Med 2021; 27:1607-1613.
18. Sentongo AE, Voleti N. et al. SARS-CoV-2 vaccine effectiveness against infection, symptomatic and severe COVID-19: A systematic review and meta-analysis. BMC Infect. Dis 2022; 22:439.
19. Azzolini E, Levi R, Sarti R, Pozzi C, Mollura M, Mantovani A, Rescigno M. Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers. JAMA 2022; 328:676-678.
20. Nehme M, Braillard O, Salamun J, Jacquerioz F, Courvoisier DS, Spechbach H, Guessous I. Symptoms After COVID-19 Vaccination in Patients with Post-Acute Sequelae of SARS-CoV-2. J. Gen. Intern. Med 2022; 37:1585-1588.
21. Meza-Torres B, Delanerolle G, Okusi C, et al. Differences in clinical presentation with long COVID following community and hospital infection, and associations with all-cause mortality: English sentinel network database study (Preprint) JMIR Public Health Surveill 2022; 8:e37668.
22. Hajjaji N, Lepoutre K, Lakhdar S, et al. 16 Months Follow Up of Patients' Behavior and Mild COVID-19 Patterns in a Large Cohort of Cancer Patients During the Pandemic. Front. Oncol 2022; 12:901426.
23. Liu Q, Qin C, Liu M, Liu J. Effectiveness and safety of SARS-CoV-2 vaccine in real-world studies: A systematic review and meta-analysis. Infect. Dis. Poverty 2021; 10:132.
24. Jacobs LG, Paleoudis EG, Bari DL-D, Nyirenda T, et al. Persistence of symptoms and quality of life at 35 days after hospitalization for COVID-19 infection. PLoS ONE 2020; 15:e0243882.

American Journal of BioMedicine
Journal Abbreviation: AJBM
ISSN: 2333-5106 (Online)
DOI: 10.18081/issn.2333-5106
Publisher: BM-Publisher
Email: editor@ajbm.net