



Frequent Convulsive Seizures in an Adult Patient with COVID-19: A Case Report

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) is a novel coronavirus that was extracted from patients with respiratory tract infections. The most common symptoms of patients are fever and respiratory tract involvement. In this report, we describe one patient with frequent seizures probably due to COVID-19 infection for the first time.

Case Presentation: A 30-year-old previously healthy female was admitted with generalized tonic-clonic seizure in the neurology emergency room. The patient complained of dry cough five days before the admission. She had seizures (five times) approximately every 8 hours. Brain MRI was normal and chest CT revealed focal ground-glass opacities. The respiratory specimen was positive for COVID-19 using real-time PCR assay. The symptoms of the patient improved with anticonvulsive and antiviral medications.

Conclusions: To the best of our knowledge, this is the first case study to report an association between frequent seizures and COVID-19. In our opinion, there is a hypothesis about this subject that the etiology of seizure may be due to encephalitis and invasion virus to the brain or toxic effect of inflammatory cytokines.

Keywords: Seizure, COVID-19, Novel Coronavirus, Case Report, Convulsion

1. Introduction

Coronavirus disease 2019 (COVID-19) is a novel coronavirus that was extracted from patients with respiratory tract infection of unknown causes on December 31, 2019, in Wuhan, Hubei, China (1-3). The infected patients' symptoms ranged from asymptomatic to severe (4). The most common complaints of patients are fever (98%), cough (76%), dyspnea (55%), myalgia, and fatigue (44%) (5-7). Some pieces of evidence reported gastrointestinal involvement, acute cardiac injury, and acute kidney injury due to COVID-19 (7, 8). Mao et al. (9) reported neurological manifestations of patients with COVID-19. The most common symptoms were dizziness, headache, hypogeusia, and hyposmia (9). Severe patients had ischemic or hemorrhagic stroke, and loss of consciousness (9). At this time, the likelihood of COVID-19 should be considered primarily in patients with fever and/or respiratory tract symptoms who had close contact with a confirmed or suspected patient of COVID-19 (1). Real-time polymerase chain reaction (real-time PCR) and next-generation sequencing were used for definitive diagnosis of this novel coronavirus (5). To the best of our knowledge, up to now, no seizure was reported due to COVID-19. In this report, we describe one patient

with frequent seizures probably owing to COVID19 for the first time.

2. Case Presentation

A 30-year-old previously healthy female was admitted with generalized tonic-clonic seizure in the neurology emergency room in Bou Ali Sina Hospital, Mazandaran Province, Iran. The patient had no history of drug and alcohol abuse. She complained of dry cough five days before admission. Three days prior to admission, she had fever (T = 38°C axillary) and fatigue. The first generalized tonic-clonic seizure (GTC) of the patient occurred in the sleep, two days before the admission. Then, recurrent seizures (five times) happened approximately every 8 hours. Also, one seizure attack arose in the hospital, at the admission time. As the seizure ended, the patient was sleepy and confused for thirty minutes to one hour. The patient was conscious between attacks. She neither had a history of epileptic seizures nor a family history concerning seizure disorders. At the time of hospitalization in the Emergency Department, the body temperature was 38.8°C, blood pressure 130/70 mmHg, heart rate 98 beats/minute, respiratory

rate 20/minute and oxygen saturation of 96% on room air. The bedside serum glucose level was 108 mg/dL. In terms of neurological examination, the patient was drowsy with disorientation to time. The cranial nerves were intact. Pupils were midsize and reactive to light and accommodation. There was no optic disc swelling bilaterally. The patient was able to move all four extremities and there was no stiff neck and nuchal rigidity. Deep tendon reflexes were normal. Considering general examination, no skin rash was observed and other systems, including cardiac and abdominal examination, were normal. Primary laboratory tests discovered a normal blood sugar, electrolytes, calcium, phosphor, magnesium, liver function test, urea, and creatinine. The blood sample revealed the following results: white blood cell count 5,500 cells per microliter with 26% lymphocytes and 70% neutrophils, mildly elevated erythrocyte sedimentation rate (ESR = 35 mm/hour), and normal C-reactive protein (CRP). Lumbar puncture was done and the cerebrospinal fluid (CSF) showed normal protein, glucose, with five cell counts (all of them were lymphocytes). There was no bacterial growth after 48 hours of incubation. Brain MRI was normal. Given that the patient had cough and fever, the chest computed tomography (CT) was done and revealed focal ground-glass opacities (Figure 1). Respiratory specimens, including nasal and pharyngeal swabs, and CSF sample were tested for COVID-19 using real-time PCR in the Health Center no. 5 (Shahid Ghasemi) Laboratory. This center is under the supervision of Mazandaran University of Medical Sciences. Nasal and pharyngeal samples were positive for COVID-19. The CSF sample was unremarkable for COVID-19 infection. The patient was treated with intravenous phenytoin and levetiracetam. In addition, the patient received chloroquine 200 mg BD and Lopinavir-ritonavir 400/100 mg bd. The patient was monitored for one week. Fever and seizure of the patient were controlled.

3. Discussion

Coronavirus disease 2019 (COVID-19) is beta coronaviruses, similar to severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 but with a different monophyletic group. Both viruses bind to receptor angiotensin-converting enzyme 2 (ACE2) to enter the cell (10, 11). The most well-known clinical symptoms of this virus are respiratory symptoms. Moreover, Mao et al. (9) described neurological presentations of infected patients with COVID-19. The most common reported symptoms were headache and dizziness. In this report, we reported a case with COVID-19 and frequent seizures, with no past medical history. There are many different viruses that play a role in the development of seizures and convulsions (12). The causes of seizure

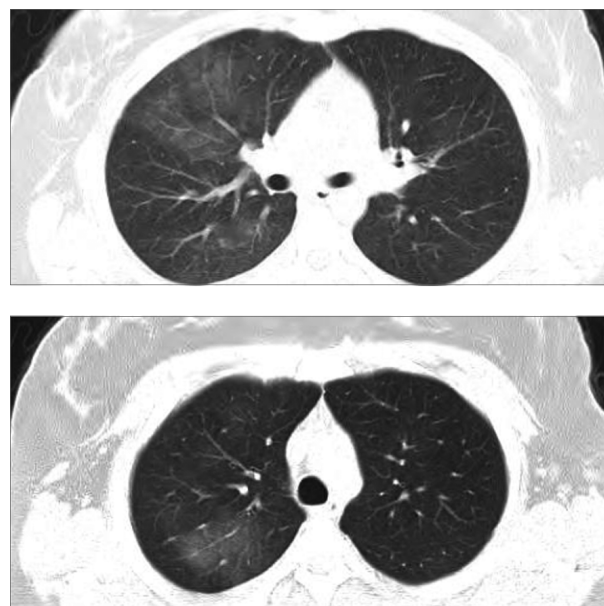


Figure 1. Chest computer tomography in the patient with COVID-19 is shown

may be due to a primary infection or due to reactivation of the latent virus. There are several mechanisms for the etiology of seizure in the patients who suffer from viral infections, including direct infiltration of brain tissue and production of toxins by the virus or production of inflammatory mediators by the brain (13). Huang et al. (2) reported that COVID-19 provokes the inflammatory cascade and as a result, releases inflammatory cytokines, including interleukins 2, 6, 7, and 10, tumor necrotizing α and the granulocyte colony-stimulating factor. Previous studies reported that TNF- α and IL-6 cytokines and C3 of the complement system are the main factors of stimulating the immune system. Consecutively, these cytokines can drive neuronal hyperexcitability via activation of glutamate receptors and play a role in the development of acute seizures (14-16).

3.1. Conclusions

To the best of our knowledge, this is the first case study that reports an association between frequent seizures and COVID-19. In our opinion, there is a hypothesis about this subject that the etiology of seizure may be encephalitis and the invasion of the virus to the brain or toxic effect of inflammatory cytokines.

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Footnotes

Authors' Contribution: Study concept and design: Narges Karimi and Nima Rouhani. Interpretation of data: Narges Karimi and Athena Sharifi Razavi. Drafting of the manuscript: Narges Karimi. Critical revision of the manuscript for important intellectual content: Nima Rouhani and Athena Sharifi Razavi.

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Ethical Approval: Mazandaran University of Medical Sciences approved the publication of this case report.

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References

- Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet*. 2020;**395**(10223):470-3. doi: [10.1016/S0140-6736\(20\)30185-9](https://doi.org/10.1016/S0140-6736(20)30185-9).
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;**395**(10223):497-506. doi: [10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5). [PubMed: [31986264](https://pubmed.ncbi.nlm.nih.gov/31986264/)].
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet*. 2020;**395**(10223):507-13. doi: [10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7).
- WHO. *Novel coronavirus (2019-nCoV): Situation report-13*. 2020, [cited 2020 Feb 02]. Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200202-sitrep-13-ncov-v3.pdf>.
- Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). *J Gen Intern Med*. 2020. doi: [10.1007/s11606-020-05762-w](https://doi.org/10.1007/s11606-020-05762-w). [PubMed: [32133578](https://pubmed.ncbi.nlm.nih.gov/32133578/)].
- Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology*. 2020;**295**(1):210-7. doi: [10.1148/radiol.202000274](https://doi.org/10.1148/radiol.202000274). [PubMed: [32027573](https://pubmed.ncbi.nlm.nih.gov/32027573/)].
- Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. [Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2020;**43**(0). Chinese. E005. doi: [10.3760/cma.j.issn.1001-0939.2020.0005](https://doi.org/10.3760/cma.j.issn.1001-0939.2020.0005). [PubMed: [32026671](https://pubmed.ncbi.nlm.nih.gov/32026671/)].
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020. doi: [10.1001/jama.2020.1585](https://doi.org/10.1001/jama.2020.1585). [PubMed: [32031570](https://pubmed.ncbi.nlm.nih.gov/32031570/)]. [PubMed Central: [PMC7042881](https://pubmed.ncbi.nlm.nih.gov/PMC7042881/)].
- Mao L, Wang M, Chen S, He Q, Chang J, Hong C, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: A retrospective case series study. *SSRN Electron J*. 2020. doi: [10.2139/ssrn.3544840](https://doi.org/10.2139/ssrn.3544840).
- Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;**579**(7798):270-3. doi: [10.1038/s41586-020-2012-7](https://doi.org/10.1038/s41586-020-2012-7). [PubMed: [32015507](https://pubmed.ncbi.nlm.nih.gov/32015507/)]. [PubMed Central: [PMC7095418](https://pubmed.ncbi.nlm.nih.gov/PMC7095418/)].
- Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zuo W. Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCoV. *bioRxiv 2020*. 2020. doi: [10.1101/2020.01.26.919985](https://doi.org/10.1101/2020.01.26.919985).
- Misra UK, Tan CT, Kalita J. Viral encephalitis and epilepsy. *Epilepsia*. 2008;**49** Suppl 6:13-8. doi: [10.1111/j.1528-1167.2008.01751.x](https://doi.org/10.1111/j.1528-1167.2008.01751.x). [PubMed: [18754956](https://pubmed.ncbi.nlm.nih.gov/18754956/)].
- Libbey JE, Fujinami RS. Neurotropic viral infections leading to epilepsy: Focus on Theiler's murine encephalomyelitis virus. *Future Virol*. 2011;**6**(11):1339-50. doi: [10.2217/fvl.11.107](https://doi.org/10.2217/fvl.11.107). [PubMed: [22267964](https://pubmed.ncbi.nlm.nih.gov/22267964/)]. [PubMed Central: [PMC3259611](https://pubmed.ncbi.nlm.nih.gov/PMC3259611/)].
- Singhi P. Infectious causes of seizures and epilepsy in the developing world. *Dev Med Child Neurol*. 2011;**53**(7):600-9. doi: [10.1111/j.1469-8749.2011.03928.x](https://doi.org/10.1111/j.1469-8749.2011.03928.x). [PubMed: [21518343](https://pubmed.ncbi.nlm.nih.gov/21518343/)].
- Libbey JE, Kennett NJ, Wilcox KS, White HS, Fujinami RS. Interleukin-6, produced by resident cells of the central nervous system and infiltrating cells, contributes to the development of seizures following viral infection. *J Virol*. 2011;**85**(14):6913-22. doi: [10.1128/JVI.00458-11](https://doi.org/10.1128/JVI.00458-11). [PubMed: [21543484](https://pubmed.ncbi.nlm.nih.gov/21543484/)]. [PubMed Central: [PMC3126579](https://pubmed.ncbi.nlm.nih.gov/PMC3126579/)].
- Libbey JE, Kirkman NJ, Smith MC, Tanaka T, Wilcox KS, White HS, et al. Seizures following picornavirus infection. *Epilepsia*. 2008;**49**(6):1066-74. doi: [10.1111/j.1528-1167.2008.01535.x](https://doi.org/10.1111/j.1528-1167.2008.01535.x). [PubMed: [18325012](https://pubmed.ncbi.nlm.nih.gov/18325012/)].