

Daytime Hypersomnolence in COVID-19: A Case Report and Literature Review

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Abstract- Coronavirus infectious disease 2019 (COVID-19) is confirmed to develop neurocognitive complications. In the present paper, we describe two patients with laboratory-confirmed COVID-19 and excessive daytime sleepiness. In the present study, we reported two laboratory-confirmed cases of COVID-19 with excessive daytime sleepiness. Patients had drowsiness and mild confusion on presentation. In both cases, CNS infections, including meningitis and encephalitis, were ruled out. Both patients' symptoms remarkably improved following the therapeutic course indicating the direct effect of SARS-CoV2 in sleep modulating centers on the brain. COVID-19 should be considered in patients with excessive daytime sleepiness and drowsiness in the current outbreak.

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Introduction

Coronavirus infectious disease 2019 (COVID-19) with the etiology of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) could cause various signs and symptoms ranging from mild fever and respiratory symptoms to neurological manifestations (1,2). The world health organization (WHO) declared the outbreak and subsequently pandemic of COVID-19 on January 30th, 2020 (3). Coronavirus has neuroinvasive characteristics and enters the central nervous system (CNS), resulting in inflammation and demyelination (4,5). Neurological complications, including convulsions, encephalitis, and change in mental states, are confirmed to have an association with COVID-19 infection (5). In the present paper, we describe two laboratory-confirmed COVID-19 patients with excessive daytime sleepiness emphasizing attention to sleep problems as a presentation of COVID-19.

Case Report

Case one

A 45-year-old woman with the chief complaint of daytime drowsiness and sleep attacks was referred to our sleep clinic. The patient's symptoms included low-grade fever, loss of olfaction and taste senses, neck pain and stiffness, and severe paraspinal muscular pain that had been initiated three days ago. She has recently experienced sleep attacks and severe daytime drowsiness with more than 18 hr/day sleeping time. The patient had no history of medical or psychiatric problems.

On physical examination, vital signs were stable (BP: 120/80 mmHg, PR: 85/min, RR: 13/min, SpO₂: 95%); cardiac and respiratory evaluations were normal; no sign of meningitis (kerning's and brudzinski's signs were normal) was detected. Chemistry profile showed lymphopenia (8%) and elevated C-reactive protein

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(CRP) (WBC: 4500, lymphocytes: 8%, poly: 82%, plt: 220,000/ μ l). Chest X-ray (CXR) showed no abnormality. COVID-19 was detected through the real-time Reverse transcription-polymerase Chain Reaction (rRT-PCR) test.

The patient was treated with Hydroxychloroquine (200 mg BD) and Naproxen (250 mg QID). Her drowsiness was obviously improved during the therapeutic course, and no sleep attack occurred anymore.

Case two

A 76-year-old male presented with a chief complaint of daytime drowsiness. The patient reported sleeping 20 hours a day for the last two days, according to his family statements. The patient had a history of ischemic heart disease and hypertension.

On physical examination, severe drowsiness and mild confusion were detected, and the patient could not effectively communicate. Vital signs were: BP: 130/80 mmHg, PR: 70/min, RR: 18/min, and SpO₂: 90%. Fine crackle in both lungs bases was detected. The remainder of his physical examination (including neurological examination) was unremarkable. In laboratory tests, positive CRP and lymphopenia were detected. SARS-CoV2 was detected in rRT-PCR assay. Chest computed tomography scan (CT scan) showed peripheral ground-glass opacities in both lungs bases.

For the patient, Azitromycine (500 mg daily) and nasal cannula oxygen commenced, and excessive drowsiness remarkably get improved after four days.

Discussion

In the present study, we reported two laboratory-confirmed cases of COVID-19 with excessive daytime sleepiness. Patients had drowsiness and mild confusion on presentation. In both cases, CNS infections, including meningitis and encephalitis, were ruled out. Both patients' symptoms get remarkably improved following the therapeutic course indicating the direct effect of SARS-CoV2 in sleep centers on the brain.

Owing to its higher morbidity and mortality, the global attention to the somatic consequences of COVID-19 has eclipsed the importance of its neuropsychiatric sequels in this epidemic (6). Excessive daytime sleepiness, which is mainly present as chronic drowsiness or irritability, may be misunderstood as a behavioral disorder or lack of attention (7).

Various human organs such as the respiratory tract, skeletal muscles, and nervous system possess ACE2

receptors for SARS-CoV2, which causes direct and indirect neurological symptoms (8). Previous studies have reported neurological symptoms associated with COVID-19, including hypomania, acute cerebrovascular disease, and headache (9). The mechanism that COVID-19 causes excessive sleepiness is unidentified, yet it is maybe due to excessive inflammatory cytokines production or direct virus effect on specific cells within the lateral hypothalamus. The specific cells seated within the lateral part of the hypothalamus produce hypocretin (orexin), which roles as a neurochemical arousal regulator in the brain's wake-sleep circuit (10).

Narcolepsy type 1 (NT1), which is characterized by hypersomnolence, cataplexy, and excessive daytime sleepiness, has been hypothesized to be an autoimmune disease with increasing incidence after the influenza H1N1 pandemic. The occurrence of NT1 in adults with genetic (i.e., human leukocyte antigen) and environmental (i.e., H1N1 influenza virus) predisposing factors supports this notion (11,12).

Increasing the awareness of neuropsychiatric sequels of COVID-19 among clinicians is suggested to minimize the diagnostic delay and further consequences. Besides, further investigations are recommended to underpin the neuropsychiatric and/or autoimmune pathophysiology of this condition.

COVID-19 should be considered in patients with excessive daytime sleepiness and drowsiness in the current outbreak.

References

1. Abkhoo A, Shaker E, Mehrabinejad MM, Azadbakht J, Sadighi N, Salahshour F. Factors predicting outcome in intensive care unit-admitted COVID-19 patients: using clinical, laboratory, and radiologic characteristics. *Crit Care Res Pract* 2021;2021:1-7.
2. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020;77:683-90.
3. Weiss S, Leibowitz JL. Coronavirus pathogenesis. *Adv Virus Res* 2011;81:85-164.
4. Rothan H, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun* 2020;109:102433.
5. Bohmwald K, Gálvez NMS, Ríos M, Kalergis AM. Neurologic alterations due to respiratory virus infections. *Front Cell Neurosci* 2018;12:386.
6. Fotuhi M, Mian A, Meysami S, Raji CA. Neurobiology of COVID-19. *J Alzheimers Dis* 2020;76:3-19.

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7. Postiglione E, Antelmi E, Pizza F, Lecendreux M, Dauvilliers Y, Plazzi G. The clinical spectrum of childhood narcolepsy. *Sleep Med Rev* 2018;38:70-85.
8. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol* 2004;203:631-7.
9. Mohamadi M, Fattahi N, Goodarzi A, Alizadeh-Khoei M, Miri S, Hekmat H, et al. A comprehensive review on COVID-19 infection and comorbidities of various organs. *Acta Med Iran* 2021;59:4-14.
10. Thannickal TC, Moore RY, Nienhuis R, Ramanathan L, Gulyani S, Aldrich M, et al. Reduced number of hypocretin neurons in human narcolepsy. *Neuron* 2000;27:469-74.
11. Jacob L, Dauvilliers Y. Narcolepsy with cataplexy: an autoimmune disease? *Med Sci (Paris)* 2014;30:1136-43.
12. Rocca FL, Pizza F, Ricci E, Plazzi G. Narcolepsy during childhood: An update. *Neuropediatrics* 2015;46:181-98.