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Hemorrhagic Posterior Reversible Encephalopathy Syndrome: A Rare Neurological Complication of COVID-19 Infection

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Abstract
Neurological complications of COVID-19 are well documented. However, there are limited reports of posterior reversible encephalopathy syndrome (PRES) associated with COVID-19 in the literature. Herein, we described a 21-year-old man with a history of bipolar disease and opioid addiction who was admitted because of COVID-19 infection. He suddenly experienced a convulsive status epilepticus following hypertension crisis. The patient was intubated and underwent antiepileptic and anti-hypertensive therapy. His brain imaging was compatible with PRES. The patient gradually improved and was eventually discharged after 40 days. On the next month follow-up, the patient was able to walk with a cane without a history of seizure. In this report, we aimed to highlight the less common cerebrovascular complication of COVID-19 infection.
Kewwords: Posterior reversible encephalopathy syndrome; Encephalopathy; COVID-19.

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Introduction

COVID-19 disease first appeared in China in December 2019 and soon became a pandemic. Currently, because of new genetic mutations, different variations of the disease are emerging. Despite the Initiation of global vaccination, the pandemic is still a critical health threat. While the pulmonary manifestations of the disease were prominent at first, nervous system involvement has been increasingly reported. One of the main hypotheses of nervous system involvement is the tendency of the virus to attach to the angiotensin-converting enzyme 2 (ACE2) receptor expressed in both respiratory and nervous systems.[1,2]

The first report of neurological manifestations of the COVID-19 was related to 214 Chinese patients with COVID-19 who developed a wide range of neurological symptoms such as headache, hyposmia, myalgia and even cerebrovascular accidents.[3] Notably, the main reported cerebrovascular autoregulation disorders associated with COVID-19 was attributed to acute ischemic stroke. However, little is known about the occurrence of posterior reversible encephalopathy syndrome (PRES) in this context.[4] The current report focuses on PRES as a cerebrovascular complication of COVID-19 which might lead to significant morbidity.

Case Presentation

A 21-year-old man presented to our emergency department with a chief complaint of opium overdose leading to drowsiness. His medical history was notable for bipolar disorder and heavy smoking. He used olanzapine 5 mg, propranolol 10 mg, and bupropion 75 mg, each consumed twice daily.

Upon admission, the patient was mildly confused with a Glasgow Coma Scale score of 12. In response to a vocal stimulus, the patient opened his eyes, said incomprehensible sentences, and moved his limbs symmetrically. He had a temperature of 37.5°C, blood pressure of 135/75 mm Hg, respiratory rate of 8 breaths/minute, oxygen saturation of 81% on room air with respiratory distress and bilateral pulmonary coarse crackle. However, no evidence of meningismus was evident. Apart from altered mentation, the neurological

examination was unremarkable except for pin-point pupils.

A naloxone infusion was started leading to gradual recovery. Laboratory examination displayed leukocytosis (14 200 cells/mm^3) with decreased lymphocyte percentage (6%). There was also a significant elevation in C-reactive protein (CRP) (85 mg/L), creatinine (4.3 mg/dL), liver profile (alanine transaminase: 930 mg/dL, aspartate transaminase: 340 mg/dL, and alkaline phosphatase: 134 mg/dL), and creatine phosphokinase (CPK) (32 000 U/L) levels from baseline (Table 1).

Radiological examination was notable for bilateral lung involvement in favor of COVID-19 (Figure 1) which was confirmed by nasopharyngeal COVID-19 polymerase chain reaction (PCR). The brain CT was unrevealing.

The patient was then admitted to the internal ward and underwent intravenous ceftriaxone (1 g twice daily), clindamycin (600 mg three times a day), dexamethasone (8 mg twice a day), and oxygen therapy for the COVID-19 infection, and additionally sodium bicarbonate and hydration to manage electrolyte dysfunction.

Notably, he was maintained on his usual medication (olanzapine 5 mg twice daily, propranolol 10 mg twice daily, bupropion 75 mg twice daily) leading to significant clinical recovery. Gradual improvement of laboratory findings also occurred.

On day five, he suddenly developed convulsive status epilepticus following hypertension crisis. On neurological examination, he was comatose and in response to painful stimulation, he only localized and had no verbal or visual reaction. Moreover, the pupils were mydriatic and non-reactive and bilateral Babinski sign was evident. The vital signs were notable for tachycardia (pulse rate of 110), hyperthermia (temperature of 38.5°C), and elevated blood pressure (175/110 mm Hg).

The patient was intubated. Labetalol and midazolam were infused. Meanwhile, levetiracetam was started with the maximum therapeutic dose. Unfortunately, the seizures continued in the form of focal myoclonus which were gradually controlled by increasing the dose of midazolam and adding sodium valproate. Additionally, by consulting an infectious disease specialist, the antibiotics were escalated to tazocin, vancomycin and ciprofloxacin.

Subsequently, the patient underwent brain CT which revealed bilateral fronto-parieto-occipital hemorrhage with diffuse vasogenic edema (Figure 2). With a suspicion of PRES, the treatments continued. Midazolam was then tapered over 72 hours without recurrence of seizures. Along with improvement of para-clinical findings, the level of consciousness gradually improved. On day 20, the patient woke, had eye contact and was able to obey one-step command. However, he was in decerebrate posture which was mildly improved by baclofen. The repeated brain CT showed mild resolution of hemorrhage and edema. As the patient's condition stabilized, complementary imaging was performed. Similar to brain CT, magnetic resonance imaging (MRI) indicated evidence of subacute hemorrhage in fronto-parieto-occipital lobes and significant vasogenic edema (Figure 3). Nevertheless, the brain MR venography and angiography

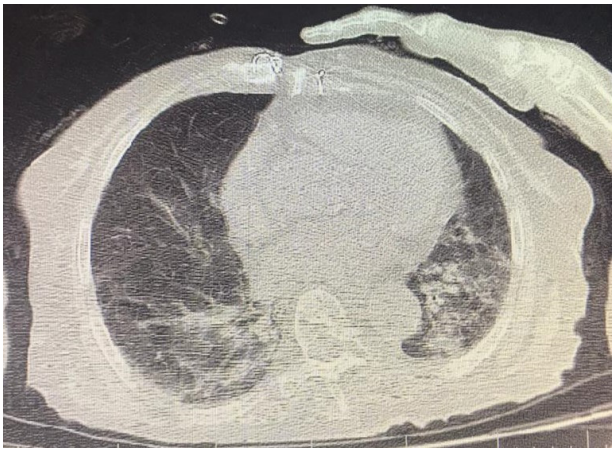

Figure 1. Evidence of Patchy Ground Glass Opacity in Inferior Lobes of the Lungs.

Table 1. The Patient's Laboratory Examination Upon Admission and Discharge

	Normal Range	Admission	Discharge
White blood cells	4000-10000/mcL	14200	6500
Lymphocyte percent	20-40%	6	12
Hg	12-16 g/dL	16	14.5
Platelet	150000- 450000/mcL	120000	245000
Erythrocyte sedimentation rate	0-20 mm/h	46	12
C-reactive protein	0-10 mg/L	84	10
Creatinine	0.6-1.2 mg/dL	4.3	1.1
Alanine transaminase	19-33 mg/dL	930	45
Aspartate transaminase	5-40 md/dL	340	23
Creatine phosphokinase	26 – 308 U/L	32000	210

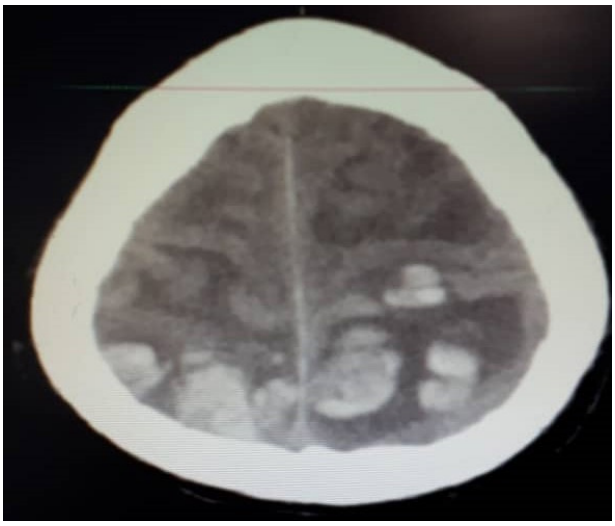

Figure 2. Evidence of Bilateral Parieto-Frontal Hemorrhage With Diffuse Vasogenic Edema.

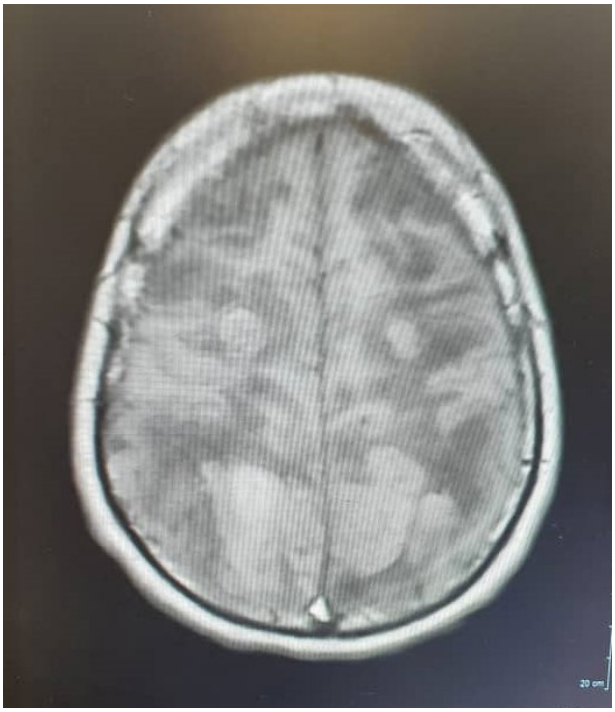

Figure 3. Evidence of Bilateral Parieto-Frontal Hemorrhage With Diffuse Vasogenic Edema.

were unremarkable. Taking all considerations into account, the patient was diagnosed with complicated hemorrhagic PRES associated with COVID-19.

On day 30, the patient was transferred to the ward. The dose of antiepileptic drugs was reduced and taken orally. He was coherent and hemodynamically stable. Eventually, on day 40 the patient was discharged. On discharge, he breathed with a tracheostomy. He was alert and motor strength was 3/5 based on Medical Research Council (MRC) scale. Within the next month of follow up, the patient was able to walk with a cane. Additionally, he did not mention any seizure or blood pressure instability.

Discussion

The second clinical scenario of our patient, similar to many previous PRES reports, included sudden hypertension crisis accompanied by confusional state and seizure. Previous studies have confirmed the neurotropism of the virus by showing an increasing incidence of COVID-induced encephalitis regardless of the severity of COVID-19.[5] However, there are limited reports of PRES in association with COVID-19 infection in the literature. The first report of PRES in association with COVID-19 was described by Kaya and colleagues. They reported a young, otherwise healthy man with COVID-19 who suddenly developed encephalopathy, blindness, and elevated blood pressure. Along with clinical suspicion of PRES, brain MRI revealed bilateral parieto-occipital vasogenic edema with superimposed micro-infarct which was in favor of PRES. Complete clinical and para-clinical recovery was achieved within 10-24 days.[6]

Since the first report of PRES associated with COVID-19, more than ten reports have been published worldwide. Interestingly, in a postmortem study, Coolen and colleagues demonstrated evidence of brain damage associated with PRES in four of the nineteen deceased patients with COVID-19. Their results were in line with the hypothesis of COVID-19 neurotropism and neuro-endothelial disturbances.[7]

While the exact pathophysiology of PRES is poorly understood, endothelial dysfunction related to rapid changes in blood pressure or cytokine storm in a context of severe infection such as COVID-19 in conjunction with impaired autoregulation of cerebral blood flow have been suggested as possible mechanisms. Endothelial dysfunction might increase the permeability of the blood-brain barrier which consequently results in higher susceptibility to blood pressure fluctuations.[8] Moreover, contrary to the belief that reversibility of symptoms is a major feature of PRES, in rare cases it might be complicated with intracranial hemorrhage, subarachnoid hemorrhage, and ischemic infarct that results in a serious neurological deficit.[9] Recently, there was a case series of eight critically ill patients with COVID-19 associated with acute disseminated leukoencephalopathy which evolved into cystic degeneration of white matter lesions. All patients had a poor functional outcome as two patients died and six of the cases survived with modified ranking score (mRS) of 5 at the time of discharge.[10] Another report described a 39-year-old man with COVID-19 infection who developed serial seizure and confusion following hypertension crisis. With a diagnosis of hemorrhagic PRES, antiepileptic therapy and tight blood pressure control was advocated leading to significant recovery,

while the patient was still hemi-paretic.[11]

Similar to a case described by Mozhdehipanah and colleagues,[11] the initial presentation of our case was acute confusion attributed to opium overdose and COVID-19 infection was incidentally diagnosed. However, the second scenario of convulsive status epilepticus and hypertension crisis raised the suspicion of PRES in association with COVID-19 infection which was confirmed by radiographic features and gradual recovery of the symptoms by tight blood pressure control.

Based on previous studies, the relationship between COVID-19 and endothelial dysfunction has been well recognized which is considerable as a potential factor to develop PRES.[8,12] Nevertheless, the pathophysiology of PRES in association with COVID-19 remains controversial. Regarding the possible etiological mechanism, we applied tight control of blood pressure and symptom therapy to control seizure and brain edema. Alongside with clinical recovery, resolution of the brain edema in repeated brain CT supported the diagnosis of PRES. An important lesson from our report is a focus on the likelihood of cerebrovascular accidents in a context of mild COVID-19. Hence, a vigilant monitoring is recommended in patients with COVID-19 for a better management of non-pulmonary complications.

Conclusion

The present report indicated PRES as a rare neurological manifestation of COVID-19 which might be attributed to the blood-brain barrier endothelium dysfunction. However, more research needs to be done in this context to confirm our data.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

Ethical Statement

Informed consent was obtained from the patient for publication of this case report.

References

1. Pang J, Wang MX, Ang IYH, Tan SHX, Lewis RF, Chen JI, et al. Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): a systematic review. J Clin Med. 2020;9(3). doi: 10.3390/jcm9030623.
2. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol. 2020;92(6):552-5. doi: 10.1002/jmv.25728.
3. 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. medRxiv. 2020. doi: 10.1101/2020.02.22.20026500.
4. Sabayan B, Moghadami M, Assarzadegan F, Komachali SH, Poorsaadat L, Babaeepour Z, et al. COVID-19 respiratory illness and subsequent cerebrovascular events, the initial Iranian experience. J Stroke Cerebrovasc Dis. 2021;30(1):105454. doi: 10.1016/j.jstrokecerebrovasdis.2020.105454.
5. Khosraviani S, Paybast S, Emami A. Encephalitis as a rare manifestation of novel COVID-19 disease, a para-infection or postinfection complication: a systematic review. Rom J Neurol. 2020;19(3):153-60.
6. Kaya Y, Kara S, Akinci C, Kocaman AS. Transient cortical blindness in COVID-19 pneumonia; a PRES-like syndrome: case report. J Neurol Sci. 2020;413:116858. doi: 10.1016/j.jns.2020.116858.
7. Coolen T, Lolli V, Sadeghi N, Rovaï A, Trotta N, Taccone FS, et al. Early postmortem brain MRI findings in COVID-19 non-survivors. medRxiv. 2020. doi: 10.1101/2020.05.04.20090316.
8. Legriel S, Pico F, Azoulay E. Understanding posterior reversible encephalopathy syndrome. In: Vincent JL, ed. Annual Update in Intensive Care and Emergency Medicine 2011. Berlin: Springer; 2011. p. 631-53. doi: 10.1007/978-3-642-18081-1_56.
9. Hefzy HM, Bartynski WS, Boardman JF, Lacomis D. Hemorrhage in posterior reversible encephalopathy syndrome: imaging and clinical features. AJNR Am J Neuroradiol. 2009;30(7):1371-9. doi: 10.3174/ajnr.A1588.
10. Agarwal S, Conway J, Nguyen V, Dogra S, Krieger P, Zagzag D, et al. Serial imaging of virus-associated necrotizing disseminated acute leukoencephalopathy (VANDAL) in COVID-19. AJNR Am J Neuroradiol. 2021;42(2):279-84. doi: 10.3174/ajnr.A6898.
11. Mozhdehipanah H, Paybast S, Bahadori R. Posterior reversible encephalopathy syndrome as a rare presentation of coronavirus disease 2019: a case report and literature review. J Vessel Circ. 2020;1(2):11-6. doi: 10.29252/jvesselcirc.1.2.11.
12. Pons S, Fodil S, Azoulay E, Zafrani L. The vascular endothelium: the cornerstone of organ dysfunction in severe SARS-CoV-2 infection. Crit Care. 2020;24(1):353. doi: 10.1186/s13054-020-03062-7.