Case Report

COVID-19 Accompanied with Intracerebral Hemorrhage: A Case Series

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Received 2020 May 12; Revised 2020 August 25; Accepted 2020 September 06.

Abstract

Introduction: The new coronavirus, also known as COVID-19, can potentially involve in the central nervous system. The most important neurological manifestations include dizziness, headache, hypogeusia, hyposmia, ataxia, seizure, ischemic stroke, cerebral hemorrhage, encephalopathy, encephalitis, meningitis, seizure, cerebral vein thrombosis, and Guillain-Barre syndrome.

Case Presentation: In this case series, we reported five patients with consciousness alteration and focal neurological deficit and neuroimaging that is consistent with intracerebral hemorrhage. In all patients, there was an association with COVID-19 infection.

Conclusions: While the neurological manifestation of COVID-19 has not been appropriately defined, it is possible that a number of patients, particularly those who suffer from a severe illness, had central nervous system involvement. Thus, the neurologists should be aware of the likelihood of any neurological symptoms of COVID-19 infection.

Keywords: COVID-19, Neurological Manifestation, Intracerebral Hemorrhage, Coronavirus

1. Introduction

Despite its worldwide report, the neurological manifestation of COVID-19 has not been well defined. From 221 COVID-19 cases in a single center of China, Li et al. (1) reported 11 ischemic stroke, 1 cerebral venous thrombosis, and 1 hemorrhage stroke. Mao et al. (2) reported neurological symptoms in 78 (36.4%) of 214 Chinese patients, including dizziness, headache, hypogeusia, hyposmia, ataxia, seizure, ischemic stroke, and cerebral hemorrhage. Also, Helms et al. (3) reported neurological signs (e.g., agitation, confusion, executive dysfunction, encephalitis, encephalopathy, and ischemic stroke) in 49 of 58 French patients with severe COVID-19. Several studies reported encephalitis, meningitis, seizure, cerebral vein thrombosis, and Guillain-Barre syndrome associated with COVID-19 infection (4-8). Sharifi-Razavi et al. (9) reported three cases of adult patients with ischemic stroke and novel coronavirus 2019 infection.

In this study, we first reported the association of cerebral hemorrhage with COVID-19 at Bou-Ali Sina Hospital on March 15, 2020 (10). Recently, other studies have reported the association of cerebral hemorrhage and COVID-19 (11, 12). Second, we described the clinical symptoms and also radiological and laboratorial characteristics of patients hospitalized to Bou-Ali Sina Hospital with ICH in association with COVID-19.

2. Case Presentation

2.1. Case 1

On March 28, 2020, a 78-year-old woman was taken to the emergency room with acute left hemiparesis, nausea, and impaired orientation. She had a low-grade fever but no respiratory or gastrointestinal symptoms. She had a history of ischemic heart disease (IHD) and was under treatment with aspirin and atorvastatin. There was no prior history of trauma. On the admission time, the patient was confused, and the first vital signs were blood pressure (BP): 130/76, heart rate (HR): 62, respiratory rate (RR): 14 breath/min, body temperature (T): 38.3°C, and O2 saturation 97% on room air.

Neurological examination revealed right hemiparesis. Medical Research Council (MRC) scale grade 3. Deep tendon reflexes (DTR) were 2+ brisk at left, and 1+ and cutaneous plantar responses were extensor on the left side. There was no sign consistent with the hemorrhagic process on the whole body examination. Cardiopulmonary and abdominal examinations were normal as well.
On April 8, 2020, a 78-year-old man referred to the emergency room with acute right hemiplegia, nausea, vomiting, and confusion. He had dry coughs in the past few days. He had a history of ischemic stroke, HTN, and dyslipidemia. He was taking aspirin, atorvastatin, losartan, metoprolol, and folic acid supplement. He had no prior history of trauma. On the admission time, the patient had confusion, and the first vital sign showed the following: BP: 170/90, HR: 52, RR: 15 breaths/min, T 37.8°C, and O₂ saturation 97% on room air. Neurological examination revealed that spastic hemiplegia could affect the left side of the body due to previous ischemic stroke (MRC scale grade 1) at both upper and lower limbs and acute right flaccid hemiparesis (MRC scale grade 3). Sensory and cerebellar examinations were impossible to evaluate due to the decreased level of consciousness. DTRs were brisk at left and 1+ at right upper and lower limbs. Cutaneous plantar responses were extensor on both sides. There were no skin rashes, mucosal hemorrhages, or any signs of trauma after examining of whole body. The first laboratory test showed WBC: 9900 (neutrophil 7425, lymphocyte 1980). Platelet: 151000/microL, CRP: 18 mg/dL, ESR: 42 mm/h, PTT: 30 sec, PT: 12.5 sec, and INR: 1. Also, other routine lab tests, such as electrocardiogram and echocardiography, were normal. RT-PCR from a nasopharyngeal swab sample was positive for COVID-19.

This patient was treated with hydroxychloroquine, lopinavir/ritonavir (LPV/RTV), azithromycin, and conservative management for ICH.

2.4. Case 4

On April 9, 2020, a 67-year-old woman was presented with acute left hemiplegia, global aphasia, nausea, vomiting, and rapidly progressive loss of consciousness. She had a history of IHD, HTN, and DM. She was taking aspirin 80 mg, clopidogrel 75 mg, losartan 50 mg BID, and metformin 500 TID. She had no prior history of trauma. On the admission day, the patient was confused with BP: 240/120, HR, 86, RR, 16 breath/min, body T, 36.8°C, and O₂ saturation 93% on room air. Neurological examination showed anosicopic pupils with a smaller left pupil and left hemiplegia (MRC scale grade 1). Sensory and cerebellar examinations could not be evaluated due to her decreased level of consciousness. The DTR of her upper and lower extremities was 2+. Cutaneous plantar responses were extensor on both sides. On cardiopulmonary examination, the patient had shortness of breath. There were no skin rashes, skin and mu-
cosal hemorrhages, or any signs of trauma after examining the whole body.

The laboratory test findings were follows: serum glucose, 217 mg/dL, marked lymphopenia (WBC: 13800, neu-
with hydroxychloroquine, lopinavir/ritonavir (LPV/RTV), due to a decreased level of oxygen saturation and progressive loss of consciousness. She was treated with hydroxychloroquine, beta interferon, azithromycin, ceftriaxone, clindamycin, montelukast, and conservative management for ICH.

2.5. Case 5

On April 10, 2020, an 85-year-old man with a history of fever from 5 days ago, no evaluation and treatment, was referred to the emergency room with acute left hemiplegia, dysarthria, and impaired orientation. He did not have any history of anticoagulant or antiplatelet consumption nor did he have any prior history of trauma, hypertension, and other medical disorders. On the admission time, the patient was confused, and the first vital sign discovered the following: BP: 120/70, HR: 98, RR: 26 breath/min, body T. 37.4°C, and O₂ saturation 80% on room air. At the time of hospitalization, the patient was confused, and the neurological examination showed left hemiplegia (MRC scale grade 2). Sensory and cerebellar examinations could not be conducted. DTR was 1+ at left limbs and 2+ at right limbs. The cutaneous plantar response was extensor on the left side. No signs of trauma and hemorrhage were detected after the whole-body examination.

Primary laboratory test results indicated Leukocytosis (WBC: 14300, neutrophil: 12155; lymphocyte: 2145). Red blood cell: 2.93 × 10⁶/micro liter; hemoglobin: 8.2 g/dL; platelet: 208000/microfiber, CRP: 4 mg/dL; PTT: 30 sec; PT: 12.5 sec, INR: 1. The electrocardiogram and electrocardiography showed moderate left ventricular hypertrophy. RT-PCR from a nasopharyngeal swab sample was positive for COVID-19 infection. Non-contrast brain CT scan demonstrated large right thalamic hemorrhage and intraventricular hemorrhage (A A Lung CT scan revealed mild ground-glass opacities in the basal of both lungs (Figure 1H).

The patient was admitted to the ICU and intubated due to a decreased level of Oxygen saturation and progressive loss of consciousness. She was treated with hydroxychloroquine, beta interferon, azithromycin, ceftriaxone, clindamycin, montelukast, and conservative management for ICH.

3. Discussion

In this study, we reported five infected patients with COVID-19 associated with intracerebral hemorrhage. There was no history of coagulopathy, anticoagulant consumption, and trauma in all cases.

Despite having no history of HTN, case 1 consumed antiplatelet. She had mild lung involvement. There was no reasonable relation between ICH and COVID-19. She did not need aggressive O₂ therapy and was discharged with no important complications after 10 days.

Case 2 had a history of HTN, but he did not take antiplatelet. He needed early intubation and mechanical ventilation. After about 12 hours, he suffered massive upper gastrointestinal hemorrhage, reduced platelet count, and expired 20 hours after hospitalization. His lung involvement was not severe; CRP was negative, and lymphocyte count was normal; there was an underline medical condition, while ICH size was large with intraventricular hemorrhage. On the other hand, we had no microbiological confirmation for COVID-19, and only the radiological aspect was in favor of this infection.

Therefore, it seems his serious condition and final outcome happened due to cerebral hemorrhage, but not for COVID-19 infection.

Case 3 had a history of HTN, antiplatelet consumption, large ICH size, and moderate lung involvement. He first took O₂ with CPAP, but he was intubated after 48 hours. During the hospitalization, he suffered ventilator-induced pneumonia, but gradually his condition improved, and after three weeks, the patient was discharged to home with a relatively stable condition.

Case 4 had a history of HTN and double antiplatelet therapy. She had marked lymphopenia, but her lung involvement was mild. She was admitted to ICU, and after a few hours, she was intubated due to brain edema and midline shift.

Case 5 had no risk factors for hemorrhage but advanced age. His ICH size was large, and lung involvement was severe, with suspicion of bacterial superinfection. It was a history of 5-day fever before hospitalization. The patient was under mechanical ventilation and, eventually, poor prognosis. He was passed away. We could not find any association between patients’ lab data, imaging findings, and patient prognosis for COVID-19 infection.

It was demonstrated that coronaviruses, and especially β-coronaviruses, to which the COVID-19 belongs do not limit their presence to the respiratory tract and frequently...
References

1. Li Y, Li M, Wang M, Zhou Y, Chang J, Xian Y, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke Vasc Neurol. 2020;5(3):279–84. doi: 10.1016/j.stvr.2020.000431. [PubMed: 32056524]. [PubMed Central: PMC7374460].

2. 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. JAMA Neurol. 2020.

3. Helms J, Kremer S, Merjadi H, Cleere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020;382(23):2268–70. doi: 10.1056/NEJMcc2008597. [PubMed: 32294339]. [PubMed Central: PMC779967].

4. Zhou B, She J, Wang Y, Ma X. A Case of Coronavirus Disease 2019 With Concomitant Acute Cerebral Infarction and Deep Vein Thrombosis. Front Neurol. 2020;11:296. doi: 10.3389/fneur.2020.00296. [PubMed: 32390931]. [PubMed Central: PMC7788982].

5. Karimi N, Sharifi Razavi A, Rouhani N. Frequent Convulsive Seizures in an Adult Patient with COVID-19: A Case Report. Iran Red Crescent Med J. 2020;22(1). doi: 10.5812/irrcmj.102828. [PubMed: 32390931]. [PubMed Central: PMC7309300].

6. Moriguchi T, Harri N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Int J Infect Dis. 2020;94:55–8. doi: 10.1016/j.ijid.2020.03.062. [PubMed: 32251791]. [PubMed Central: PMC7309578].

7. Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. J Clin Neurosci. 2020;76:233–5. doi: 10.1016/j.jocn.2020.04.062. [PubMed: 32312628]. [PubMed Central: PMC758887].

8. Mardani M, Nadji SA, Sarhangipor KA, Sharifi-Razavi A, Baziborou M. COVID-19 infection recurrence presenting with meningoencephalitis. New Microbes New Infect. 2020;37:100732. doi: 10.1016/j.mni.2020.100732. [PubMed: 32798020]. [PubMed Central: PMC7786314].

9. Sharifi-Razavi A, Karimi N, Zarvani A, Cheraghmakani H, Baghbanian SM. Ischemic stroke associated with novel coronavirus 2019: a report of three cases. Int J Neurosci. 2020;1–5. doi: 10.1080/00207454.2020.1782902. [PubMed: 32543268]. [PubMed Central: PMC7309100].

10. Sharifi-Razavi A, Karimi N, Rouhani N. COVID-19 and intracerebral haemorrhage: causative or coincidental? New Microbes New Infect. 2020;38:100669. doi: 10.1016/j.mni.2020.100669. [PubMed: 32323988]. [PubMed Central: PMC763102].

11. Benger M, Williams O, Siddiqui J, Sziroth I. Intracerebral haemorrhage and COVID-19: Clinical characteristics from a case series. Brain Behav Immun. 2020;88:940–4. doi: 10.1016/j.bbi.2020.06.005. [PubMed: 32525049]. [PubMed Central: PMC7276127].

12. Dogra S, Jain R, Cao M, Bilalofful S, Zagzag D, Hochman S, et al. Hemorrhagic stroke and anticoagulation in COVID-19. J Stroke Cerebrovasc Dis. 2020;29(8):104984. doi: 10.1016/j.jstrokecerebrovasdis.2020.104984. [PubMed: 32689588]. [PubMed Central: PMC7242524].

13. Steardo L, Steardo LJ, Zoraci R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. Acta Physiol (Oxf). 2020;229(3). e13473. doi: 10.1111/apha.13473. [PubMed: 32223077]. [PubMed Central: PMC7228251].

14. Asadi-Pooya AA, Simani I. Central nervous system manifestations of COVID-19: A systematic review. J Neurol Sci. 2020;433:116832. doi: 10.1016/j.jns.2020.116832. [PubMed: 32290907]. [PubMed Central: PMC759553].

15. Sankowski R, Mader S, Valdes-Ferrer S. Systemic inflammation and the brain: novel roles of genetic, molecular, and environmental cues as drivers of neurodegeneration. Front Cell Neurosci. 2015;9:28. doi: 10.3389/fncel.2015.00028. [PubMed: 25698933]. [PubMed Central: PMC4313590].
16. Liu R, Pan MX, Tang J, Zhang Y, Liao HB, Zhuang Y, et al. Role of neuroinflammation in ischemic stroke. *Neuroimmunol Neuroinflammation*. 2017;4(8). doi: 10.20517/2347-8659.2017.09.

17. Yang C, Hawkins KE, Dore S, Candelario-Jalil E. Neuroinflammatory mechanisms of blood-brain barrier damage in ischemic stroke. *Am J Physiol Cell Physiol*. 2019;316(2):C135–53. doi: 10.1152/ajpcell.00136.2018. [PubMed: 30379577]. [PubMed Central: PMC6397344].