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Spontaneous Intracerebral Hemorrhage in a Patient with Asymptomatic 2019 Novel Coronavirus Disease

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Dear Editor,

A 53-year-old woman visited our emergency department with sudden left hemiparesis that occurred two hours ago. She was diagnosed with 2019 novel coronavirus disease (COVID-19) 5 days ago after screening tests were performed due to close contact with a patient with COVID-19, a member of Shincheonji congregants, Daegu. She had no known medical history, such as hypertension, head trauma, and medication use.

Acute stroke code was activated, and a neurologist wearing personal protective equipment (PPE) checked the patient's condition in the ambulance. She did not have any symptoms of COVID-19, including fever, cough, shortness of breath, and diarrhea. Vital signs were as follows: blood pressure, 138/91 mm Hg; pulse rate, 95 beats/min; and temperature 36.9°C. On neurologic examination, she showed dysarthria and left hemiparesis. Brain computed tomography (CT) was performed, while she was placed in the negative pressure carrier (Fig. 1A), and showed intracerebral hemorrhage (ICH) on the right external capsule and putamen with the ipsilateral intraventricular extension (Fig. 1B and C). Brain CT angiography did not show vascular malformation (Fig. 1D). Laboratory tests demonstrated normal platelet count (141×10^3/μL), prothrombin time (11.4 s; international normalized ratio 1), activated partial thromboplastin time (25.6 s), and D-dimer level (0.41 mg/L). Other hematologic and chemical tests were also unremarkable. A real-time reverse transcription polymerase chain reaction (RT-PCR) assay from nasopharyngeal swab confirmed COVID-19. However, there was no evidence of pneumonia or cardiomegaly on chest X-ray.

She was isolated in the negative pressure ward. She received preventive antiepileptic drugs and analgesics for headache. Because she had no symptoms of COVID-19, antiviral drugs were not initially administered. The systolic blood pressure was maintained <140 mm Hg during hospitalization without any antihypertensive medication. After 13 days, she complained of aggravated headache and drowsiness. Follow-up brain CT revealed partial absorption of ICH and intraventricular hemorrhage but aggravation of perilesional edema with mass effect (Fig. 1E and F). Because of the possibility of vasogenic edema and vasculitis by COVID-19, dexamethasone was administered, and symptoms improved. Since real-time RT-PCR showed repetitive positive results for COVID-19, hydroxychloroquine (200 mg three times daily) and azithromycin (500 mg daily for five days), was prescribed on hospital day 22. On hospital day 30, the test for COVID-19 became negative. She became alert, and left hemiparesis [upper extremities Medical Research Council (MRC) 3, lower extremities MRC 4] has been improving. After monitoring in quarantine for two weeks, the patient was scheduled to transfer for rehabilitation.

This case is remarkable in that spontaneous ICH occurred in a patient with asymptomatic COVID-19. Although several cases of stroke in patients with COVID-19 have been reported, most were ischemic strokes and accompanied by severe COVID-19.[1,2] Recently, two cases of ICH have been reported in patients with COVID-19, and all had respiratory failure

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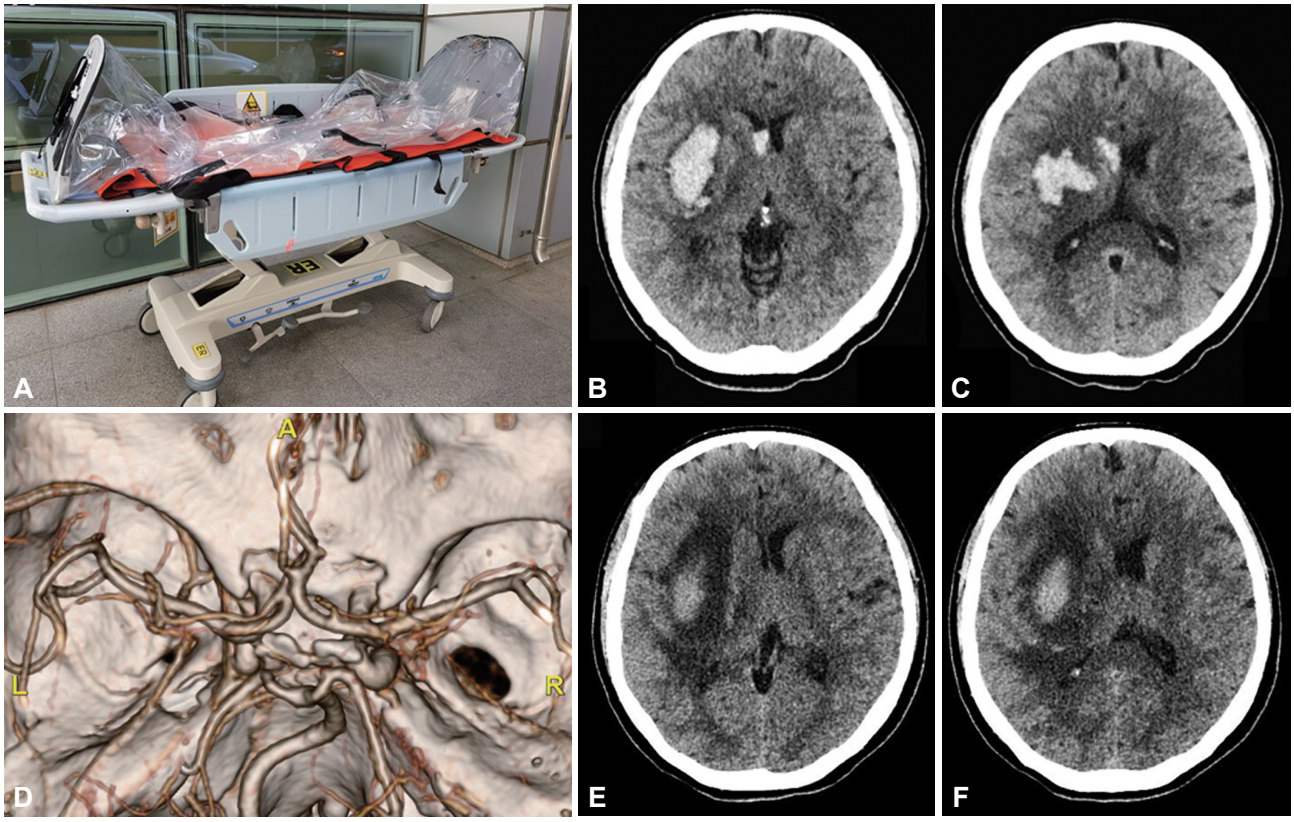

Fig. 1. Patient carrier and brain imaging of the patient. A: Negative pressure patient carrier. B and C: Initial brain CT demonstrated ICH in the right external capsule and putamen and ipsilateral intraventricular hemorrhage. D: Brain CT angiography showed no vascular malformation or steno-occlusive lesion in the intracranial cerebral arteries. E and F: Follow-up brain CT on hospital day 14 revealed partial absorption of ICH and intraventricular hemorrhage but aggravation of perilesional edema with mass effect. CT: computed tomography, ICH: intracerebral hemorrhage.

or pneumonia.[1,3] Because our patient had no symptoms of COVID-19, we could exclude the possibility of secondary stroke related to a medical condition.

The mechanism of ICH, in this case, was uncertain. Most previously reported patients with stroke and COVID-19 were elderly and had multiple vascular risk factors,[1,2] whereas our patient was relatively young and had no apparent risk factors for ICH. Besides, ICH occurred shortly after the diagnosis of COVID-19. Thus, we can speculate that spontaneous ICH may occur related to COVID-19. Several explanations could be possible. The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) enters the cell through the angiotensin-converting enzyme 2 (ACE2) receptor,[4] which is expressed in vascular endothelial cells and neurons.[5,6] Reduced expression and dysfunction of ACE2 followed by SARS-CoV-2 infection may impair blood pressure regulation and endothelial function, so that ICH could occur.[7] Additionally, vasculitis by SARS-CoV-2 infection may lead to ICH. However, considering the high prevalence, we could not exclude the possibility that an acute stroke could occur coincidentally in patients with COVID-19.

COVID-19 could affect the management process of acute stroke. Before the outbreak of COVID-19, if an patient with acute stroke arrived at the emergency department, brain CT and CT angiography were completed within 15 minutes. In this patient, however, it took 36 minutes. The delay in wearing PPE and use of a negative pressure carrier was inevitable, and these processes successfully decreased the risk of contagion. However, the delay could have been reduced if there was prenotification before the arrival of the patient. Recently, Khosravani et al.[8] introduced the concept of protected code stroke and emphasized the importance of prenotification and PPE in the management of hyperacute stroke.

There were other treatment issues in concomitant ICH and COVID-19. Corticosteroids were not recommended in the management of ICH.[9] However, in this patient, corticosteroid was administered because of the possibility of vasculitis by COVID-19 and to avoid surgical treatment. Craniectomy or targeted temperature management was not considered due to the risk of COVID-19 contagion. Because of the concern of virus replication associated with corticosteroid use, we prescribed hydroxychloroquine empirically. Hydroxychloroquine may inhibit the replication of SARS-CoV-2 by interfering with the endosome-mediated viral entry.[10] Recent study showed

that hydroxychloroquine and azithromycin were effective on reducing viral load in COVID-19.[11] Moreover, to reduce the risk of contagion, we minimized frequencies of measuring vital signs, workup, and physician rounds. Fortunately, despite these restrictions, she is recovering fast.

COVID-19 is still spreading rapidly worldwide. Our case suggested that spontaneous ICH can develop in a patient with COVID-19. A further optimized system to balance the management of COVID-19 and acute neurologic disorders should be warranted.

Author Contributions

Conceptulization: Changho Kim, Mi-Yeon Eun. Investigation: Youngseok Kwak, Jaechun Hwang. Supervision: Mi-Yeon Eun. Writing—original draft: Changho Kim, Mi-Yeon Eun. Writing—review & editing: Mi-Yeon Eun.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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