

A rare case report: Concurrent COVID-19 and acute cerebrovascular ischemic stroke in a patient with Sheehan's syndrome

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Received: 2020-11-07.

Accepted: 2021-02-10



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J Clin Med Kaz 2021; 18(3):58-61

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Abstract

Introduction: SARS-Corona Virus-2 (SARS-CoV-2/COVID-19) is a novel member of coronaviridae family. This new disease first appeared in China in December 2019, and can cause severe respiratory failure in advanced cases. COVID-19 was announced as a pandemic in March 2020 by the WHO. It has infected 76 million people and has caused the death of more than 1.5 million people until December 2020. Common symptoms of this disease are fever, cough, shortness of breath, anosmia, and fatigue. But atypical presentations have also been reported. Here, we present a COVID-19 patient with an unusual neurological symptom.

Case: 82-years-old female patient with a history of hypertension and Sheehan's syndrome came to the emergency room with the complaint of fever, shortness of breath and left hemiplegia. Although nasopharyngeal swab PCR test was negative (twice), acute phase reactants were elevated and chest CT revealed typical findings of COVID-19 pneumonia, so the patient was diagnosed as COVID-19. Since the patient had left hemiplegia, a cranial CT and diffusion-weighted MRI were performed to see whether a central neurological pathology was present. Both imaging revealed the findings of acute ischemic stroke (AIS). Afterwards, the patient was hospitalized and was started on Hydroxychloroquine, acetylsalicylic acid (ASA), favipiravir and methylprednisolone. At the 7th day of follow up, the nasopharyngeal swab PCR test was performed and found as positive. On the 10th day of treatment, the symptoms and acute phase reactants regressed. Left hemiplegia of the patient also regressed and she was discharged from the hospital at the 12th day of admission without a sequelae.

Discussion and conclusion: Since there has been a recent evidence of strong relationship between COVID-19 and acute ischemic pathologies due to pathophysiology of COVID-19, we should be suspicious of acute ischemic stroke in a COVID-19 patient with neurological symptoms, especially when the patient had a history like Sheehan's syndrome disease may aggravate or hide the symptoms.

Key words: Sheehan's syndrome, COVID-19, cerebrovascular disease

Introduction

SARS-Corona Virus-2 (SARS-CoV-2/COVID-19) is a novel member of coronaviridae family that first appeared in China in December 2019, causing severe acute respiratory failure [1-3]. The severe infectious disease caused by COVID-19 was announced as a pandemic in March 2020 by the WHO. It has infected

76 million people and caused the death of more than 1.5 million people until December 2020 [4]. Although there may be atypical presentations, common symptoms are mostly fever, cough, shortness of breath, anosmia, and fatigue. The disease can cause severe conditions such as ARDS, multiple organ failure, coma, and death, especially in elderly patients [5, 6]. Fortunately, most patients with

COVID-19 can be cured and far fewer infected people result in death. In a study including more than 40,000 COVID-19 patients, 81% of patients had mild manifestations, 14% had severe manifestations, and 5% had critical manifestations [7]. Two well observed complications of COVID-19 so far, are thromboembolic and neurological complications. Thromboembolic complications include pulmonary embolism and acute stroke (even in patients younger than 50 years of age without risk factors), while neurological complications include encephalopathy, stroke, movement disorders, motor and sensory deficits, ataxia, and seizures [8].

Infarction of the pituitary gland after postpartum hemorrhage is called Sheehan's syndrome and it is one of the causes of hypopituitarism [9]. In developed countries, postpartum hemorrhage now less often results in Sheehan's syndrome than previously, largely due to improvements in obstetrical care [10, 11]. At the time of diagnosis, 55 percent had panhypopituitarism and 45 percent had partial hypopituitarism [12]. Evaluation of postpartum hypopituitarism should be performed whenever it is suspected after a delivery associated with unusually heavy blood loss. If the blood loss is severe and especially if it is associated with hypotension, the patient should be evaluated and treated for adrenal insufficiency immediately [9]. In this case report, we tried to present a patient with a history of Sheehan's syndrome, who was diagnosed with COVID-19 and acute stroke concurrently.

Case-presentation

A 82-years-old female patient with a history of hypertension and Sheehan's syndrome came to the emergency room with the complaint of fever, shortness of breath and left hemiplegia. On physical examination, her blood pressure was 90/60 mmHg, heartbeat: 95/min spo2: 94 %, and fever: 39.3oC. Her Glasgow Coma Scale score was 15, she had crepitant rales especially in the left hemithorax on thoracic auscultation, she had tachypnea and dyspnea, her heart sounds were rythmic but tachycardic, she had weakness in the left extremities, and other system examinations were normal. Important lab test results of the patient included Na: 146 mmol/L, CRP: 33.86 mg/mL, Ferritin: 318 ml/ng, D-dimer: 987 ugFEU/L (Table 1).

Table 1 Laboratory Findings

PARAMETERS	At admission day (18 April 20)	At 7th day (25April 20)	Normal range
Glukose (mg/dl)	110	187	70-126
Urea (mg/dl)	40	40	17-43
Creatinine (mg/dl)	0.7	0.45	0.67-1.17
ALT (U/L)	41	17	0-50
AST (U/L)	35	35	0-50
Na (mmol/L)	146	134	136-146
K (mmol/L)	3,8	4.5	3.5-5.1
CRP (mg/L)	33.86	16.3	0-5
PH	7.3	7.45	7.35-7.45
HCO3 (mmol/L)	29	23.9	22-26
PCO2 (mmHg)	47	42	35-48
WBC (k/uL)	11.93	7.48	4600-10200
NEU (k/uL)	4.78	7.05	2000-6900
LYM(k/uL)	1.81	0.410	
HB (g/dl)	12.3	11.8	12,2-18
PLT (k/uL)	183000	164000	142000-424000
DDÍMER (ugFEU/L)	987	13400	
LDH (U/L)	288	538	
FERRITÍN(ml/ng)	318	228	

Although nasopharyngeal swab PCR test was negative (twice), acute phase reactants were elevated and chest CT revealed typical findings of COVID-19 pneumonia such as ground glass opacities in the left inferior lobe, and crazy-paving pattern in the inferior part of this opacity (Figure 1A-B). As a conclusion, the patient was diagnosed as COVID-19. Since the patient had left hemiplegia, doctors of emergency department consulted neurologist, and neurologist ordered a cranial CT and diffusion-weighted MRI to see whether a central neurological pathology was present. Cranial CT showed at the lateral ventricle level that there is a large density reduction in gray and white matter in the parietal and occipital lobes, and there is no evidence of bleeding. These findings were compatible with acute ischemic stroke (Figure 2).

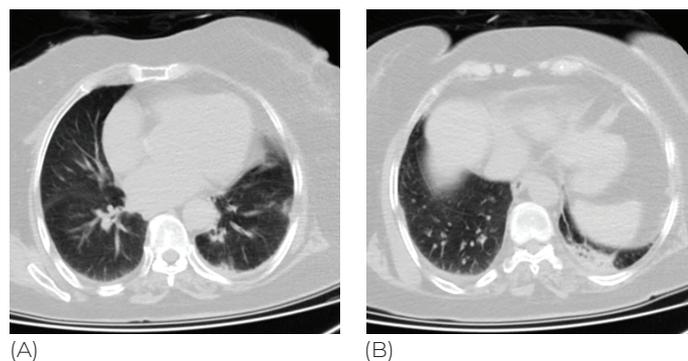


Figure 1. In the left inferior thorax lobe, there were two areas showing the ground glass opacities (A), in the lower area of ground glass opacities, these is crazy-paving pattern (B)



Figure 2. IA t the lateral ventricle level, there is a large density reduction in gray and white matter in the parietal and occipital lobes, and there is no evidence of bleeding.

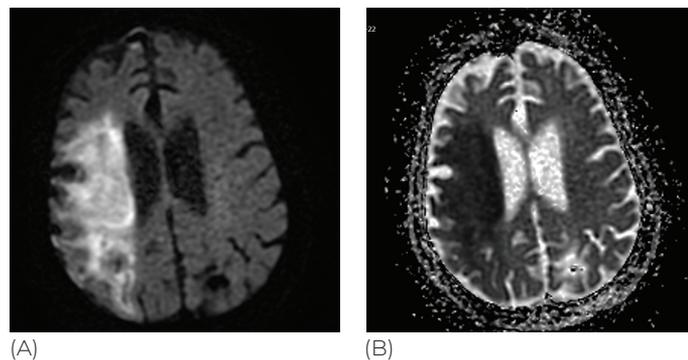


Figure 3. Diffusion image in the same CT section (A) and in the ADC sequences (B). Diffusion reduction was spotted and compatible with acute ischemia in the area fed by the right middle cerebral artery.

After cranial CT showed acute ischemic stroke, cranial MRI and diffusion-weighted MRI was performed. MRI showed diffusion image in the same CT section (Figure 3A) and in the Apparent Diffusion Coefficient (ADC) sequences (Figure 3B) diffusion reduction was spotted and was compatible with acute ischemia in the area perfused by the right middle cerebral artery (Figure 3).

The patient was hospitalized and was started on hydroxychloroquine sulfate, acetylsalicylic acid (ASA), enoxaparin sodium (Low Molecular Weight Heparin), azithromycin, favipiravir and methylprednisolone. Her first two COVID-19 PCR test results were negative. Since the severity of symptoms and acute phase reactants progressed on the 6th day of follow up, we wanted to rule out other etiological factors and confirm our diagnosis. Thus, on the 7th day of follow up, the nasopharyngeal swab PCR test for COVID was reperformed and found as positive. Since the patient was suffering from resistant fever and hypoxia (spo₂: 85%), favipiravir 2x200 mg was added to the treatment following the loading dose. In addition, 20 mg methylprednisolone was given to the patient who had been using 4 mg of methylprednisolone due to Sheehan's syndrome. Since TSH level of the patient was in normal range, levothyroxine which was had been used by the patient regularly, was continued as 25 mcg/day. On the 4th day of favipiravir treatment, the patient no longer had fever and/ or hypoxia (spo₂ > %92 in the room air), so favipiravir treatment was discontinued at the 6th day. At the 10th day of treatment, the symptoms and acute phase reactants regressed. As the acute phase levels decrease, with the help of physical rehabilitation, her neurological symptoms also regressed. She was discharged from the hospital on the 12th day of admission without sequelae.

Discussion

The most common symptoms in COVID-19 infection are fever, cough, sputum, and myalgia. But in some cases headache, shortness of breath, abdominal pain / diarrhea, sore throat and chest pain have also been reported [1-3]. Ground glass opacities, consolidation areas, interlobular septal thickening and crazy-paving pattern has been commonly reported in thorax CT [13]. Increased white blood count, neutrophil, CRP, D-dimer and lactate, and decreased albumin, lymphocyte, platelet and hemoglobin levels are well known laboratory findings with COVID-19 and these findings are compatible with mortality [14]. Although standard reference test is seen as PCR in the diagnosis of COVID-19, it is stated that Thorax CT can be used in COVID-19 diagnosis by some sources because of the concerns about sensitivity and the fact that PCR test may be false negative / positive [15,16].

In the chest tomography of our case, there were findings compatible with COVID-19 such as ground glass opacities, although the patient's PCR test was negative, the patient was accepted as COVID-19, and treatment was started. Lab results of the patient were also compatible with COVID-19 with increased Ferritin, D dimer, CRP and raised WBC levels.. In our country, on that date in which this case occurred, the standard treatment of hydroxychloroquine, enoxaparin, azithromycin was given to the patient. However on the 3th day of admission, the exacerbations of symptoms directed us to start advanced treatments such as favipiravir and methylprednisolone. With the help of these additions, COVID-19 symptoms of the patient started to decrease by the 7th day of admission.

Acute ischemic stroke (AIS) is the most commonly reported cerebrovascular event complicating COVID-19. It may presents

with nonfocal deficits, including encephalopathy, and involve multiple vascular territories. This heterogeneity suggests that the mechanisms of stroke in COVID-19 are multiple and may include both specific pathophysiological features of the SARS-CoV-2 virus, including endothelial activation and thrombosis, as well as nonspecific effects of inflammation and coagulation dysfunction, superimposed on preexisting risk factors like hypertension, diabetes, malignancies [17]. In a meta-analysis of 4466 COVID-19 patients, the pooled incidence of AIS was 1.2% with mean age of 63.4±13.1 years. Mean duration of AIS from COVID-19 symptoms onset was 10 ± 8 days in this study (18). The stroke incidence reported in retrospective studies of European and Chinese hospitalized COVID-19 patients varies between 2.5% to 6% [19-21]. In a study of 219 patients hospitalized with COVID-19 in Wuhan, China, those with acute stroke (N = 11; 5.0%) were more likely to be older, to present with severe symptoms, to have cardiovascular risk factors, such as hypertension and diabetes, and a history of cerebrovascular disease [22]. In our case, the patient had a history of hypertension and Sheehan's syndrome (a type of cerebrovascular disorder) which is compatible with these analyses.

The pathophysiological mechanism causing Sheehan's syndrome is simply the interruption of blood flow to the pituitary gland. Considered potential mechanisms causing this interruption are arterial thrombosis similar to that seen in stroke, development of arterial spasm as a result of severe hypotension that is due to massive uterine bleeding, or compression of pituitary vessels due to relatively small sella turcica volume associated with enlargement of the pituitary during pregnancy [23]. In this respect, although there is no clear evidence in the literature, we might suggest that patients with Sheehan's syndrome might be more prone to acute ischemic stroke since there are similar pathophysiological mechanisms related to these two diseases.

Conclusion

Since there has been a recent evidence of strong relationship between COVID-19 and acute ischemic pathologies due to pathophysiology of COVID-19, we should be suspicious of acute ischemic stroke in a COVID-19 patient with neurological symptoms, especially when the patient has a history of cerebrovascular disease such as Sheehan's Syndrome. The hypercoagulability secondary to COVID-19 might further contribute to the thrombotic states such as acute ischemic stroke. More studies and case reports are needed to clarify the relationships between these complex disorders.

Disclosures: There is no conflict of interest for all authors.

Acknowledgements: None.

Funding: None.

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