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CASE REPORT

Acute Ischemic Stroke Induced by Covid-19 Disease - A Case Report

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ABSTRACT

Introduction: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is the agent of Coronavirus disease 2019 (COVID-19), may attack the central nervous system in addition to the respiratory system because of its neuro-invasive features. Increased inflammation, immobilization, hypoxia, and disseminated intravascular coagulation may predispose to the cerebrovascular diseases.

Case Report: A 73 years old man presenting to the emergency service with complaints of dyspnea, cough, and high fever was admitted to the hospital after being diagnosed as having COVID-19 upon findings of ground-glass densities and mild parenchymal involvement which was more prominent in the mid- and lower lobes of the lungs on his computerized tomography scan. His treatment was started with chloroquine, azithromycin, ceftriaxone and enoxaparin. On the neurological exam performed for symptoms of dizziness, imbalance, speech disorder and deviation of angle of mouth; he was conscious, cooperating, oriented limitedly and the right nasolabial groove was indistinct and he had dysarthria and ataxia. Acetyl salicylic acid was added to the treatment because cerebral diffusion magnetic resonance imaging revealed limited diffusion consistent with acute ischemia on the right posterolateral area of the bulbus. The patient whose respiratory distress worsened and who was admitted to the intensive care unit developed cardiac and respiratory arrest and he died despite all efforts of resuscitation.

Conclusion: It should be kept in mind that the elderly patients with Covid-19 with prothrombotic risk factors are also at risk for cerebrovascular disease in addition to the infectious symptoms. In this case report, a patient infected with SARS-CoV-2 and diagnosed as acute ischemic stroke with anamnesis, clinical and radiological findings is presented.

KEYWORDS: SARS-CoV-2, COVID-19, Cerebrovascular Disease, Wallenberg Syndrome, Cytokine Storm.

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HIGHLIGHTS

- SARS-CoV-2, causative agent of COVID-19, is a virus with neuro-invasive features.
- During the disease increased inflammation, immobilization, hypoxia and disseminated intravascular coagulation contribute to development of cerebrovascular diseases.
- Inflammation may be monitored with levels of ferritin, CRP and d-dimer.
- Particularly the elderly patients with risk factors for development of atherosclerosis should be followed closely.

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is the causative agent of Coronavirus disease 2019 (COVID-19), was first detected in China in December 2019 [1]. About 172.000 confirmed cases were detected so far and a total of 4729 patients died of the disease [2]. Remarkable symptoms of COVID-19 include high fever, cough, fatigue, hemoptysis and dyspnea. In the severe cases pneumonia, acute respiratory distress syndrome, sepsis, heart failure, alkalosis, hyperkalemia, acute renal failure, hypoxic encephalopathy and multiple organ failure may occur [3].

SARS-CoV-2 enters the cell by binding to the angiotensin converting enzyme (ACE-2) receptors. ACE-2 receptors which are present on the type II alveolar epithelial cells of human lung are also expressed in the glial cells and in the neurons [4]. SARS-CoV-2 may spread from the respiratory system to the central nervous system either by means of its neuro-invasive features or by altering the endothelial and epithelial cells making the blood-brain barrier or through retrograde axonal route. Thus, neurological conditions are commonly observed in the patients with COVID-19. Several neurological conditions including involvement of the central nervous system (CNS), peripheral nervous system and skeletal muscles have been reported in more than one third of the patients [3]. Signs and conditions indicating involvement of the CNS include dizziness, vertigo, sleep disorders, headaches, loss of conscious, ataxia, seizure, acute cerebrovascular disease (ACD), meningitis, and encephalitis [4].

In COVID-19 increased inflammation, immobilization, hypoxia and disseminated intravascular thrombosis increase predisposition to ACD [5]. This case report reported that acute ischemic stroke accompanied the clinical presentation of COVID-19.

CASE REPORT

Vital findings of the 73 years old man presenting to the emergency service with symptoms of cough, high fever starting about one week ago followed by dyspnea were as follows: arterial blood pressure 145/95 mm/Hg, temperature 38.2°C, respiratory rate 18 per minute. Physical examination revealed widespread rales which were more remarkable in the middle and lower bilateral pulmonary lobes and pretibial edema on both lower limbs. Medical history of the patients included hypertension, chronic obstructive pulmonary disease, diabetes mellitus (DM) and smoking of 18 packs per year for 30 years. Thoracic computerized tomography (CT) revealed ground-glass densities which were more prominent on the middle and lower lobes and mild parenchymal involvement (Figure 1) and the patient was admitted to the hospital with diagnosis of COVID-19.

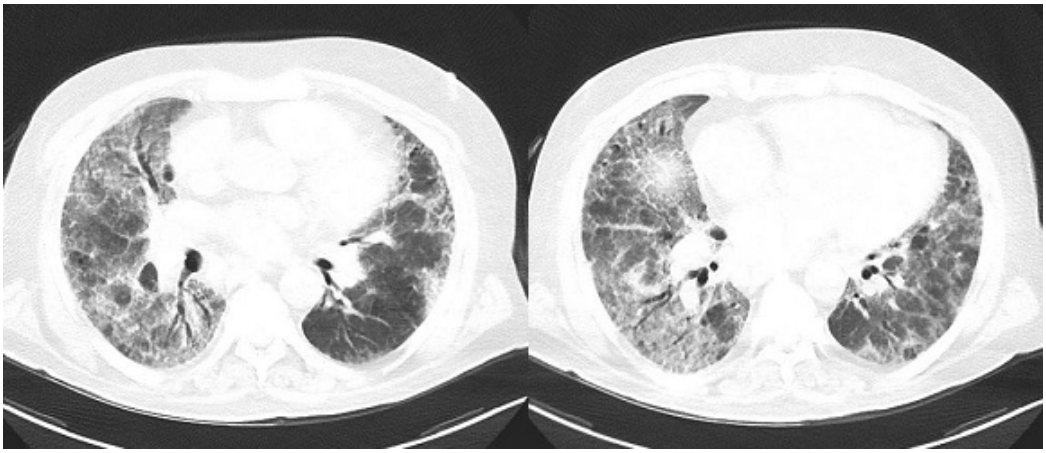

Figure-1: Thoracic CT revealed widespread remarkable rough reticular markings and traction bronchiectasis in parenchymal areas of both lungs. Ground-glass densities were observed which were more prominent in the middle and lower lobes.

His treatment was started with chloroquine at loading dose of 800 mg daily, followed by maintenance dose of 400 mg daily, azithromycin at loading dose of 500 mg daily followed by maintenance dose of 250 mg daily, ceftriaxone at daily dose of 0,5 mg/kg per 12 hours (40 mg bid). Arterial blood gas parameters were pH:7.45, pCO2:2.34, SO2: 85 and HCO3:25 and oxygen treatment was started with nasal canula. Results of routine biochemistry and hemogram investigations and polymerase chain reaction (PCR) results from the nasotracheal smear samples for Covid-19 are given in Table-1.

Table-1: Characteristics of blood hemogram, biochemical and Covid-19 PCR tests of the patient after admission

	27th		**28th**		**30th**		
Covid-19 PCR (Smear from the upper respiratory tract)	Negative		Negative		Positive		
Indicators (Normal range)	**Detection time (April-May)**						
	27th	**28th**	**29th**	**30th**	**01st**	**02nd**	**03th**
White blood cell (4,5-11 x 10^3. /µL)	6,15	4,83	6,26	8,80	8,6	9,20	15,2
Neutrophil (1,8 -6,4 x 10^3. /µL)	4,91	4,23	5,16	7,91	5,10	7,19	13,37
Lymphocyte (1,2-3,6x 10^3 /µL)	0,84	0,39	0,67	0,42	0,34	1,17	0,81
Eosinophils (0,1-0,5 x 10^3 /µL)	0,07	0,07	0,01	0,02	0,14	0,13	0,01
Red blood cell (3,83-5,08 x 10^6/µL)	4,53	4,85	4,47	4,46	3,97	3,96	3,03
Monosit (0,3-0,8 x 10^3 /µL)	0,32	0,19	0,36	0,91	0,32	0,66	0,91
Hemoglobin (11,7-15,5 g/dl)	11,8	12,7	11,6	11,4	11,2	9,4	8,7
Platelet (156-373 x10^3 /µL)	226	228	250	252	258	403	425
PT (9,2-12,8 sn)	11,2	14,5	12,9	13,4	16,5	12,4	11,4
INR (0,8-1,2 INR)	1,20	1,12	1,09	1,01	1,43	1,07	1,01
APTT (25,1-38 sn)	28,8	27,4	25,9	27,1	23,6	26	22,1
C-Reactive Protein (0-0,5 mg/dl)	18,1	16,6	13,9	30,4	48,6	84,1	111,6
Ferritine (24-336 ng/mL)	311	335	320	716	945	526	726
Procalcitonin (0-0,065ng/mL)	0,1	0,1	0,1	0,9	0,9	0,9	0,7
Alanine aminotransferase (0-35 U/L)	34	46	33	27	38	29	20
Aspartate aminotransferase (0-35 U/L)	42	48	24	27	41	34	41
Serum total protein (6,6-8,3 g/dl)	6,2	6,0	5,6	5,2	5,1	6,65	6,48
Serum albümin (3,5-5,2 g/dl)	2,8	2,7	2,5	2,9	2,7	2,9	3
Creatine kinase (0-145 U/L)	18	21	16	24	36	30	32
Lactic dehydrogenase (0-247 U/L)	286	317	292	423	441	345	437
Fibrinogen (200-393 mg/dl)	1068	982	944	977	1054	1124	1245
D-dimer (<243 ng/ml)	1604	1921	1035	3035	3446	3657	4160

PT: protrobin time, **aPTT**: activated partial thromboplastin time, **INR**: International Normalized Ratio

On the neurological exam performed for symptoms of dizziness, imbalance, speech disorder and deviation of angle of mouth he was conscious, cooperating, oriented limitedly and the right nasolabial groove was indistinct and he had dysarthria and ataxia. The right nasolabial groove was indistinct and the patient had dysarthria and ataxia. Other findings were normal on the neurological exam. NIHSS score was 4. More detailed history of the patient revealed that he had complaints of dizziness, vertigo and speech disorder one day after his admission to the hospital and these findings progressed in one day. Cerebral magnetic resonance imaging (MRI) revelaed hypo-intensity on the apparent diffusion co-efficient sections and hyperintensity on the diffusion sections consistent with acute ischemia on the right posterolateral area of the bulbus (Figure 2).

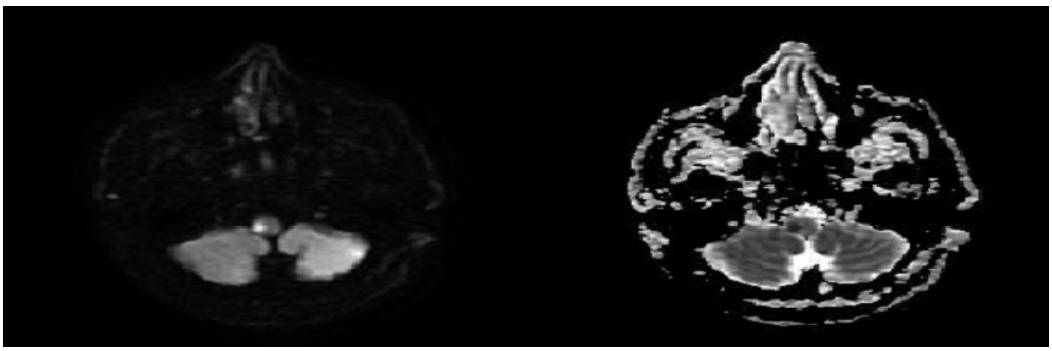

Figure-2: Cerebral magnetic resonance imaging (MRI) revealing hyperintensity on diffusion sections and hipointensity in apparent diffusion co-efficient sections of the right posterolateral area of the bulbus. These findings were considered to be consistent with acute ischemia.

Acetyl salicylic acid at dose of 300 mg daily was added to treatment of the patient considered to have clinical presentation consistent with ACD upon his history and examination and imaging findings. In regard to the investigations for risk factors, electrocardiogram (ECG) was in normal sinus rhythm and transthoracic echocardiogram (ECO) revealed second degree of tricuspid regurgitation and intermediate pulmonary hypertension. Calcium canal blocker was added to the treatment after the patient with medical history of hypertension was evaluated in the light of all investigations (ECG, ECO). In regard to DM, anti-

diabetic treatment was scheduled and blood sugar was regulated. CT-angiogram ordered for detailed investigation of both anterior and posterior circulatory system of our patient was within normal limits. On the 5th post-admission day, the patient was admitted to the intensive care unit (ICU) and entubated because of development of unconsciousness and decrease in partial oxygen tension (PO2: 48) and oxygen saturation (SO2: 81). The patient with general decline in health status during stay in ICU developed cardiac and respiratory arrest was resuscitated. However, he didn't response to the resuscitation and died.

DISCUSSION

The patient presented here is of importance because he had posterior system ischemic stroke considered to be induced by confirmed COVID-19 infection. It has been reported that 5.7% of the patients with severe infection [3] and about 5% of the patients with COVID-19 develop ischemic stroke during the course of the infection. Mean age at the time of stroke in 71.6 years in COVID-19 disease [3, 6]. Most patients have such risk factors as hypertension, DM and coronary arterial disease [6]. Age of the patient presented here was 73 years, similar to the literature and the patient had risk factors of DM and hypertension.

Severe viral infection leads to activation of complement and increased level of the proinflammatory cytokines such as interleukin (IL)-2, IL6, IL-8, IL-10 and tumor necrosis factor alpha (TNF α) within 7 to 14 days after onset of the symptoms following viremia [6]. Endothelial injury activates the coagulation system along with the immune system response. In addition, endothelial injury creates hypercoagulability by cause excessive production of thrombin and inhibition of the fibrinolysis [7]. Hypoxia occurring in COVID-19, however, increases blood viscosity as well as stimulates thrombosis via signaling due to hypoxia-induced transcription factors. Severe COVID-19 infection causes disseminated intravascular coagulation (DIC) through fulminant activation of coagulation and results in widespread microvascular thrombosis. The virus binds to ACE-2 receptors and decreases their expression, activating the reticuloendothelial activation system. Thus, risk of pulmonary embolism, pulmonary hypertension, and fibrosis increases as a consequence of platelet adhesion and aggregation. Additionally, risk of venous thromboembolism also increases in these patients due to prolonged immobilization. In brief, increased level of lactate dehydrogenase (LDH), ferritin, C-reactive protein (CRP), d-dimer, and Interleukins is considered as an indication of predisposition of the disease to the pro-inflammatory and hypercoagulability [8]. In our patient, levels of LDH, CRP, d-dimer and ferritin indicating predisposition to hypercoagulability were found to be high. Furthermore, timing of stroke in our patient (day 8) is consistent with the time at cytokine storm reported in the literature (day 7-14).

In brief increased inflammation, immobilization, hypoxia, and DIC contribute to occurrence of ACD. In conclusion, predisposition to thrombosis increases remarkably in the presence of severe COVID-19 infection and risk factors for development of atherosclerosis. As can be understood from the findings of thoracic CT and inflammation markers, Wallenberg syndrome consistent with involvement of the posterior circulatory system was considered in our patient due to severe nature of COVID-19 infection and presence of accompanying atherosclerotic risk factors.

COMPETING INTERESTS

The author declares no competing interests with this case.

PATIENT CONSENT

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

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