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Published online 2021 June 20 **Case Report**

Meningitis Induced by Severe Acute Respiratory Syndrome Coronavirus 2: A Case Report

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Abstract

Introduction: Coronavirus disease 2019 (COVID-19) emerged in December 2019 in China and caused a catastrophic pandemic in 2020. Significant manifestations of COVID-19 are related to the respiratory system; however, other organs, such as the brain and heart, can also be involved.

Case presentation: A 44-year-old-male was hospitalized in our referral emergency center due to being febrile and dizzy. He experienced five episodes of convulsion in the hospital. Within a day, the respiratory symptoms developed. The polymerase chain reaction of cerebrospinal fluid (CSF) was positive for COVID-19. The analysis of CSF and findings of chest computed tomography scan revealed that the case was infected with meningitis induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and pneumonia.

Conclusions: It has been reported that neurological symptoms of COVID-19 can appear earlier than other symptoms. To the best of our knowledge, few articles have represented COVID-induced meningitis. This case study reported the first case of meningitis induced by SARS-CoV-2 in Iran.

Keywords: SARS-CoV-2, Meningitis, Fever, Confusion, Convulsion

1. Introduction

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the most recent coronavirus family member. It first emerged in Wuhan, China, in December 2019 and rapidly spread all around the world. With the help of the angiotensin-converting-enzyme 2 (ACE-2) receptor, the virus can involve different body cells, particularly alveolar cells (1). Fever, dry cough, and tiredness are common clinical symptoms associated with the respiratory system (1, 2). C-reactive protein (CRP) and lactate dehydrogenase (LDH) may increase through the disease, and lymphocytopenia is a common indicator of COVID-19 (1). Some patients developed neurological manifestations prior to respiratory symptoms, such as a headache, vomiting, nausea, and fever (1, 3). Despite several reports on encephalitis caused by SARS-CoV-2, few cases represent meningitis (4, 5). Following, polymerase chain reaction (PCR) can confirm the existence of SARS-CoV-2 both in the lung and cerebrospinal fluid (CSF) (6). To date, no definite medications or vaccines have been applied for the treatment of or prevention from COVID-19, respectively (2). This issue highlights the fact that prompt diagnosis of the disease plays an essential role in controlling the pandemic (7).

This case report presented a COVID-19 patient with several convulsion episodes and confusion, with delayed respiratory symptoms. He was diagnosed with meningitis induced by SARS-CoV-2 and pneumonia.

2. Case Presentation

An Iranian former healthy 44-year-old man presented to the hospital with a 5-day history of high-grade fever and weakness on July 9, 2020, in Mashhad, Iran. The confusion was added to his initial symptoms, which brought him to the emergency room. He was a nonsmoker engineer without a remarkable family history except that his father was infected with SARS-CoV-2.

On general physical examination, his vital signs included body temperature at 38.9°C, blood pressure at 130/80 mmHg, respiratory rate at 35 breaths/min, heart rate at 110 beats/min, with an oxygen saturation of 93%. He was dizzy and opened his eyes to verbal commands. Moreover, meningeal irritation signs were absent, and the neurological examination was normal. After admission, he had sudden generalized convulsions three times a night. However, his fever was controlled, and he received treatment with Phenytoin and Diazepam; however, the convulsion happened two more times. His complete blood cell (CBC) test demonstrated the concentration of normal blood components, except for neutrophilia and lymphopenia. The detailed results of the CBC are presented in Table 1. . Furthermore, the elevation of CRP (144 mg/L), LDH (543 U/L), Interleukin-6 (6pg/ml), and D-dimer concentration (820) was observed in the blood test. Other clinical tests were normal.

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Table 1. Laboratory test results of the patient at admission to and discharge from the hospital

	Patient (on admission day)	Patient (on discharged day)	Normal value
WBC (k/µL)	4.9	9.4	4.5-11
Lymph %	15.2	24	20-40
Neutrophil %	78	65	40-60
RBC (M/µL)	5.47	5.15	4.7-6.1
Hb (g/dl)	15.2	14.1	13.8-17.2
Plt (k/µL)	184	328	150-400
Urea (mg/dL)	33	28	7-20
Creatinine (mg/dL)	1.2	o.9	0.84-1.21
LDH (IU/L)	543	397	140-280
AST (U/L)	34	25	5-40
ALT (U/L)	39	20	7-56
CRP (mg/dL)	144	34	<10
ESR (mm/h)	71	32	0-50
O2 Sat %	89	93	95-100
PH	7.47	7.41	7.35-7.45
Pao2	80	92	80-110
PCO2	34	41	35-45
HCO3 (mEq/L)	22	24	22-28
D-dimer (ng/mL)	826	450	<500
TPI (ng/ml)	0.5	-	0-0.04
Procalcitonin (ng/mL)	1.08	0.5	0.10-0.49
Interleukin-6 (Pg/ml)	71	10	0-5

WBC: White blood cells; RBC: Red blood cells; Hb: Hemoglobin; Plt: Platelet; LDH: Lactate dehydrogenase; AST: Aspartate transaminase; ALT: Alanine transaminase; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; TPI: Treponema pallidum immobilization

After the second day of hospitalization, a sepsis workup was applied for the patient due to high-grade fever. Chest X-ray showed peripheral consolidation. A chest computed tomography (CT) scan was requested due to lymphopenia, fever, and lung involvement. The outcome demonstrated typical signs of pneumonia-like diffuse bilateral peripheral consolidation. After a day, dyspnea was initiated, approximately 50% of the lung was involved, and oxygen saturation decreased to 89%. Therefore, CT angiography was applied due to the aggravation of dyspnea, oxygen saturation decrease, and D-dimer increment, which revealed regular features (Figure 1).

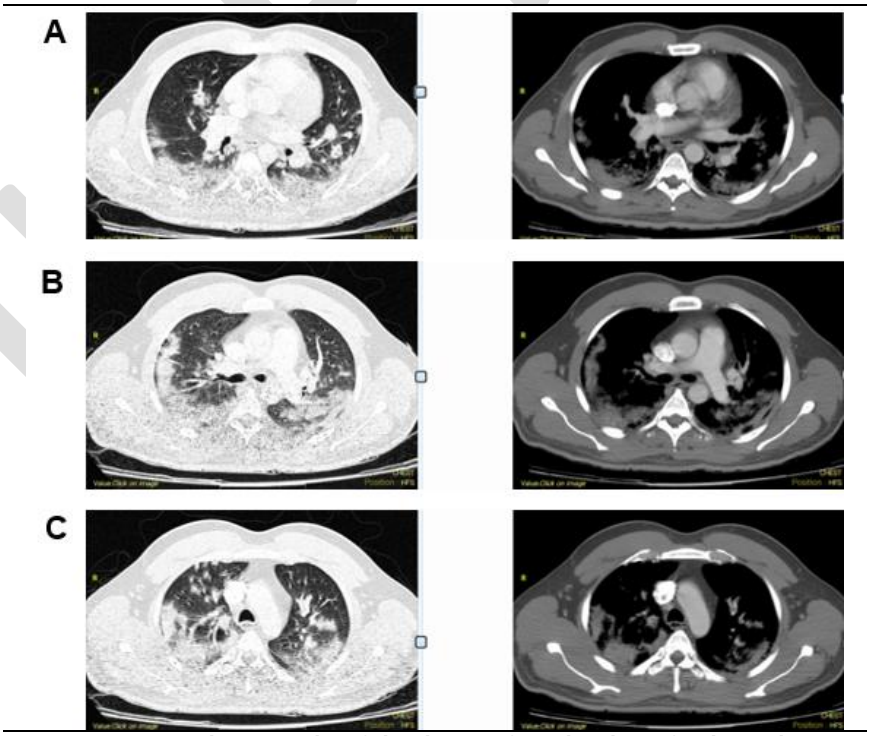

Figure 1. Computed tomography of the chest performed 6 days after hospitalization, demonstrating diffuse bilateral peripheral consolidation in three levels: (A) trachea, (B) carina, and (C) heart. No abnormality was found in the computed tomography angiography of the chest.

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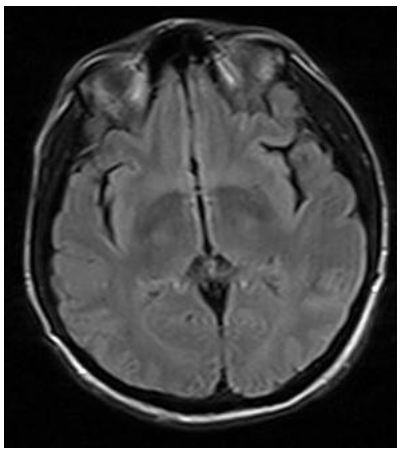

Figure 2. Magnetic resonance imaging of the brain applied 3 days after admission (T2-weighted image), demonstrating convex soft tissue density caused by polyp or retention cyst in the right maxillary sinus

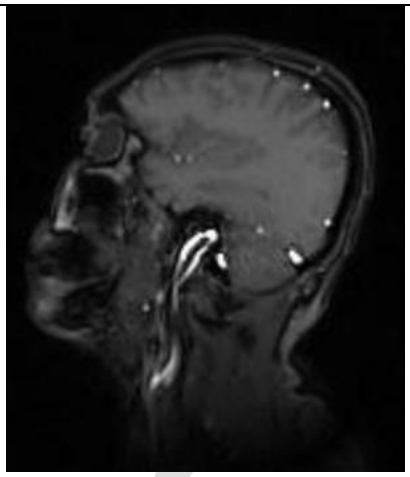

Figure 3. Magnetic resonance venography of the brain performed 3 days after admission, demonstrating a suspicious filling defect in the right jugular vein

Polymerase chain reaction for the nasopharynx was positive for COVID-19. Remdesivir was utilized as the treatment, which controlled fever while the patient was in the hospital. Nevertheless, Interferon was not prescribed due to convulsions. Magnetic resonance imaging (MRI), magnetic resonance angiography, and lumbar puncture (LP) were performed to diagnose the cause of convulsion. Everything was normal in the MRI, except for a convex soft tissue density caused by polyp or retention cyst in the right maxillary sinus (Figure 2). In the magnetic resonance venography, all the brain veins were normal except for the existence of a suspicious filling defect in the right jugular vein (Figure 3). The view of the CSF after LP showed viral aseptic features; therefore, two PCR tests were required for SARS-CoV-2 and herpes simplex virus (HSV). Polymerase chain reaction for the CSF revealed the presence of SARS-CoV-2 and was negative for HSV. Accordingly, the infection with HSV was ruled out, and it was concluded that SARS-CoV-2 infected the CSF. Moreover, the culture and the smear of the CSF were negative (Table 2). Therefore, the diagnosis was pneumonia, accompanied by meningitis caused by SARS-CoV-2.

He was hospitalized for 5 days and administered remdesivir, meropenem, and vancomycin. The oxygen saturation increased to 93%, and he did not experience any convulsions again. C-reactive protein and LDH concentrations decreased to 34 mg/L and 397 U/L, respectively (Table 1). The patient was discharged in good general condition, on July 20, 2020. After a month, clinical tests and oxygen saturation were normal, and no convulsion occurred in his follow-up appointment.

Table 2. Results of cerebrospinal fluid test from lumbar puncture

WBC=0-1	**RBC=0-1**	**Culture and smear (-)**	**HSV PCR (-)**
COVID-19 PCR (+)	Protein=34 ng/mL	LDH=40 U/L	BS=54

WBC: White blood cells; RBC: Red blood cells; HSV: herpes simplex virus; PCR: Polymerase chain reaction; LDH: Lactate dehydrogenase

3. Discussion

This case study reported a patient with meningitis associated with SARS-CoV-2 along with pneumonia. The patient had fever and dizziness, followed by three episodes of convulsion. The respiratory involvement emerged a couple of days after neurological symptoms. The results of PCR and several tests revealed that the patient was infected with SARS-CoV-2.

Severe acute respiratory syndrome coronavirus is another member of the human coronaviruses that was discovered in 2002-2003. This virus exhibited invasive features outside the respiratory system. The genomic sequence of SARS-CoV and SARS-CoV-2 are so similar to each other that it can be deduced that various characters of these two viruses are alike (7). For instance, both of them use ACE-2 receptors to involve the cells and cause pathogenicity. Furthermore, the neuro-invasive property of the viruses can be concluded (7). Respiratory manifestations have been reported in the majority of COVID-19 patients. Likewise, the World Health Organization has announced dry cough, tiredness, and fever as common symptoms of this disease (2). Some articles presented cases that had developed neurological symptoms sooner than respiratory ones (1, 7, 8). Sia divided neurological symptoms associated with SARS-CoV-2 into two groups (1):

1) Central nervous system (CNS) symptoms, including anosmia, convulsion, seizure, meningitis, headache, dizziness, visual disturbance, and stroke.

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2) Peripheral nervous system (PNS) symptoms, such as myopathy and Guillain-Barré syndrome.

Ye et al. concluded that the immunologic response induced by SARS-CoV-2 could cause unconsciousness and inflammation (8). Similarly, the retrograde movement of the virus in the nerves could transfer the virus to CNS and PNS directly (3). Other mechanisms for the neuro-invasive property of the virus have been mentioned as cytokine storm, molecular mimicry, hypoxia, and coagulopathy (1).

Regardless of several literature reviews on encephalitis caused by COVID-19, to the best of our knowledge, few studies have discussed the meningitis-like manifestations of SARS-CoV-2 (4, 5). Moreover, the pathophysiology of COVID-associated meningitis is not revealed precisely (5). According to de Oliveira et al., fever, headache, pleocytosis, nausea, and higher levels of Interleukin 6 (IL-6) were common clinical manifestations of viral meningitis, which also could be detected in COVID-associated meningitis (5). Furthermore, lymphocytopenia could be an indicator of severe CNS symptoms associated with COVID-19 (1). Some case reports have mentioned patients that their COVID-PCR from the nasopharynx was negative. With neurological symptoms, PCR in the CSF after LP could indicate the existence of SARS-CoV-2, while the PCR of other parts of the body might be negative (9).

Lovati et al. highlighted the importance of differential diagnosis between HSV encephalitis and SARS-CoV-2-induced neurological symptoms. The polymerase chain reaction of CSF can rule out other viral infections. There have been victims of misdiagnosis during the COVID-19 pandemic. Consequently, primary manifestations and differential diagnoses should be taken into account to reduce indirect complications related to misdiagnosis and accelerate the diagnosis of real COVID-19 patients (10).

The findings of the chest CT scan and COVID-19-PCR of the nasopharynx supported the diagnosis of SARS-CoV-2. In the present study, the researchers encountered fever and IL-6 increment, which could be related to meningitis. Furthermore, the strength of our diagnosis was based on the positive COVID-19-PCR taken from CSF.

In conclusion, regarding the fact that there was insufficient knowledge about meninges involvement in COVID-19, this study aimed to add to the literature associated with meningitis presentation of COVID-19. It should be kept in mind that meningitis or neurological symptoms can occur before other typical symptoms of COVID-19, which can help doctors find suspected patients promptly. In addition, the discovery of hidden cases may result in better overcome with the pandemic.

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