CRCP Case Reports in Clinical Practice

Case Report

Journal Homepage: http://crcp.tums.ac.ir

The Possible Associaton Between Cerebral Venous Thrombosis and COVID-19 Infecton in a Patent WithSickle Cell Disease: A Case Report

Athena Sharifi Razavi[1], **Narges Karimi**[2*]

1. Clinical Research Development Unit of Bou-Ali Sina Hospital, Mazandaran University of Medical Science, Sari, Iran.
2. Associate Professor of Neurology, School of Medicine, Immunogenetics Research Center, Toxoplasmosis Research Center, Clinical Research Development Unit of Bou Ali Sina Hospital, Mazandaran University of Medical Sciences, Sari, Iran.

Use your device to scan and read the article online

Citation: Sharifi Razavi A, Karimi N. The Possible Association Between Cerebral Venous Thrombosis and COVID-19 Infection in a Patient With Sickle Cell Disease: A Case Report. Case Reports in Clinical Practice. 2020; 5(Special Issue on Covid-19):19-22.

Running Title: Cerebral Venous Thrombosis and COVID-19 Infection

Article info:
Received: 16 September 2020
Revised: 30 October 2020
Accepted: 01 November 2020

Keywords:
COVID-19; Coronavirus; Cerebral venous thrombosis; Sickle cell disease

ABSTRACT

Background: The most common symptom of the novel Coronavirus Disease 2019 (COVID-19) infection is fever and dyspnea that leads to hypoxia in severe cases. Some COVID-19 patients experience neurological symptoms, including ischemic stroke and intracerebral hemorrhage. Sickle Cell Disease (SCD) is a hypercoagulable state, however, it has not been approved as a significant cause of Cerebral Venous Thrombosis (CVT).

Case presentation: In this case report, we described CVT in an SCD patient who had COVID-19, as well. We reported a 32-year-old man with a history of sickle cell anemia presented with left hemiparesis, headache, and seizure. After evaluation of the patient, CVT accompanied by COVID-19 infection was diagnosed. He was treated with intravenous unsaturated heparin, antiepileptic drugs, and antiviral agents with a favorable outcome. Based on our knowledge, this is the first case study to describe an association between CVT and COVID-19 infection in a patient with SCD.

Conclusion: During the recent pandemic, vaso-occlusive attacks in SCD patients can be evaluated for COVID-19 as an etiological factor.

Introduction

Sickle Cell Disease (SCD) is a multi-organ disorder with potentiation of compromised immune system state. Currently, due to the outbreak of coronavirus disease 2019 (COVID-19), the condition of SCD is complicated [1]. In severe cases of COVID-19 infection, acute respiratory problems and pneumonia, and consequently, diminished cellular oxygenation were observed. This pathological development is strictly correlated with a high risk of vascular obstruction extension in SCD [1]. The pathogenesis of hypercoagulability in SCD is considered to be multifactorial.

*** Corresponding Author:**
Narges Karimi, MD.
Address: *Associate Professor of Neurology, School of Medicine, Immunogenetics Research Center, Toxoplasmosis Research Center, Clinical Research Development Unit of Bou Ali Sina Hospital, Mazandaran University of Medical Sciences, Sari, Iran.*
E-mail: *drkarimi_236@yahoo.com*

The most common neurological complications of SCD include acute cerebrovascular disease, ischemic or hemorrhagic stroke, moyamoya syndrome, Posterior Reversible Encephalopathy Syndrome (PRES), and cerebral fat embolism [2]. One of the significant complications of SCD is the increased risk for blood clots emerging but it has not been recognized as a potential event of Cerebral Venous Thrombosis (CVT) and only a handful of CVT cases have been reported in the literature. The COVID-19 is caused by β-coronavirus, which was first observed in patients with unknown pneumonia in Wuhan, China [3]. The outbreak of COVID-19 has started in China in December 2019 and has rapidly spread worldwide [4]. The typical symptoms observed in patients with COVID-19 are fever, respiratory, and gastrointestinal complications [5].

There is inadequate evidence about the neurological manifestations of COVID-19 in infected patients. In this respect, some studies have reported the concomitant of neurological disorders, including intracerebral hemorrhage, ischemic stroke, recurrent generalized tonic-clonic seizures, and Guillain-Barre syndrome and COVID-19 in the infected patient [6-9]. Mao et al. reported that of 214 patients infected with COVID-19, 74 cases had neurological symptoms with dizziness and headache as the most common complaints [10]. Here, we reported the first case of venous infarction as a result of CVT in an adult SCD patient who was infected with COVID-19 infection.

Case presentation

A 32-year-old man with a history of sickle cell anemia (SCA) was referred to the emergency room (university hospital) with an acute left hemiparesis after awakening. He suffered from a compressive headache, asthenia, and fever from one day before admission. He had a history of splenectomy for about 15 years ago and was taking folic acid (1 mg/day) and hydroxyurea (1 g/day) medications. The patient reported a blood transfusion for up to ten years. He was a nonsmoker with no history of drug or alcohol abuse. He experienced acute painful episodes rarely. At the time of admission, general physical examination was unremarkable and vital signs were as follows: blood pressure: 110/70, respiratory rate:17, the pulse rate: 88, body temperature: 38 C, and O2 saturation: 97% at the room air.

Neurological examination revealed a normal level of consciousness, left hemiparesis (Medical research council scale 3), and extensor plantar reflex on the left side. He was restless and did not cooperate for fundoscopic examination. He had no neck stiffness and meningeal irritation. Early significant laboratory values were as follows: hemoglobin: 8.6 g/dl; hematocrit: 24.9%; white blood cell (WBC): 11150/ml (neutrophil: 7470; lymphocyte:2340); platelet: 430000 / microL; C-reactive protein (CRP): 23 mg/dl, erythrocyte sedimentation rate (ESR): 12 mm/h, Lactate Dehydrogenase (LDH): 530 IU/L, Partial Thromboplastin Time (PTT): 32 sec, Prothrombin Time (PT): 12.5 sec; and International Normalized Ratio (INR): 1. Other routine laboratory tests and Electrocardiogram (ECG) were normal. After primary supportive care, the patient developed a focal seizure, with a trembling left hand. These attacks repeated four times and after the fifth attack, the patient experienced a secondary generalized seizure. No seizures were repeated after antiepileptic infu-

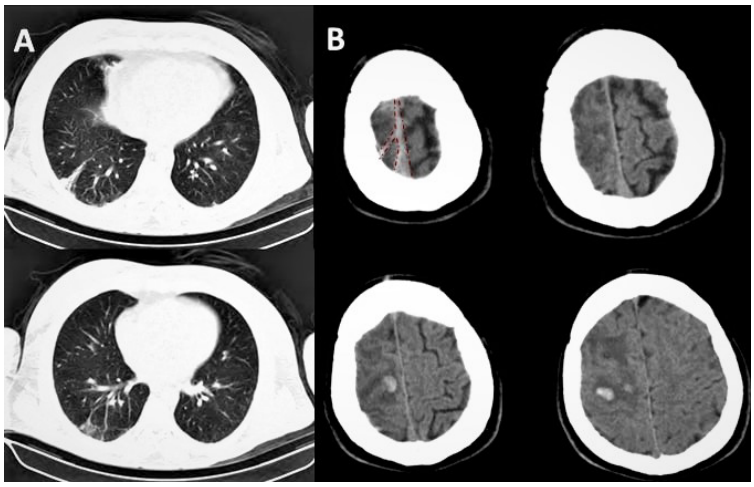

Figure 1. Axial brain CT scan

A. Lung CT scan revealed subpleural ground-glass opacities and linear consolidation in the left lung; B. Axial brain CT scan showed multiple small focal hemorrhages in the right parietal lobe with extensive surrounding edema and "cord sign"(red dashed line).

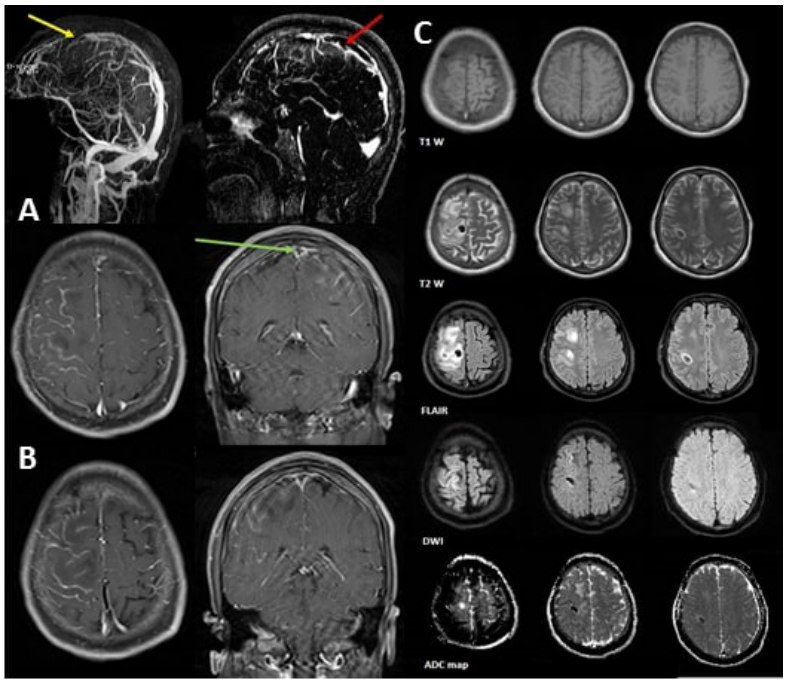

Figure 2. Brain Magnetic Resonance Imaging (MRI) without contrast

A. Magnetic resonance venography consistent with a filling defect in superior sagittal sinus in favor of thrombosis (yellow and red arrows); B. Brain Magnetic Resonance Imaging (MRI) with contrast showed a filling defect in the superior sagittal sinus, known as "empty delta sign"(green arrow); C Brain MRI demonstrated multiple small focal acute hemorrhages in the right parietal lobe with extensive surrounding edema and no restriction pattern in the Diffusion-weighted Image (DWI) and Apparent Diffusion Coefficient (ADC) map sequences.

sion. The patient was transferred to the intensive care unit and after stabilization, a brain CT scan was performed.

Axial brain CT scan showed multiple small focal hemorrhages in the right parietal lobe with extensive surrounding edema and cord sign (Figure 1). Due to the recent pandemic and history of fever, a lung CT scan was also done that revealed a typical COVID-19 infection pattern in the form of sub plural ground-glass opacities and linear consolidation in the left lung (Figure 1). Considering the patient history of SCA, hemorrhagic infarct was suspected and additional imaging was applied. Brain Magnetic Resonance Imaging (MRI) without contrast demonstrated the same findings as the brain CT scan (Figure 2) along with no evidence of restriction pattern in the Diffusion-weighted Image (DWI) and Apparent Diffusion Coefficient (ADC) map sequences. Contrast MRI showed a filling defect in the middle of its path known as "empty delta sign" (Figure 2). In angiographic view, carotid, vertebrobasilar, and Willis circle appeared normal with only mild excessive anastomosis, but not typical for moyamoya (Figure 2). The venous phase was consistent with a filling defect in the superior sagittal sinus in favor of thrombosis (Figure 2).

In transcranial Doppler (TCD) evaluation, there was no evidence of high arterial pressure (MCA peak systolic velocity 49 cm/sec). The patient was treated with exchange transfusion, intravenous unfractionated heparin (1000 u/h), phenytoin (a loading dose of 1000 mg and then 100 mg), three times a day, levetiracetam (2000 mg per day), and other symptomatic managements. The nasopharyngeal swab sample for Real-Time Polymerase Chain Reaction (RT-PCR) was inconclusive for COVID-19. But because of the lung CT pattern and history of fever, the patient was treated with hydroxychloroquine and Lopinavir/Ritonavir (LPV/RTV).

Discussion

The patient was treated for CVT, sickling attack, and COVID-19 together. At that time, he had in favorable condition at the ICU with O2 sat: 98% using cannula and O2: 5 lit/min. The headache was subsided and the seizure did not recur. Now, one question arises: Sickling attack or COVID-19, which one is the cause of CVT? Giannis and et al. evaluated the coagulation state in COVID-19 patients [11]. They reported that the patients with severe respiratory symptoms of COVID-19 infection have impairment in the regulation of the coagu-

lation flow accompanied by intra-alveolar or systemic fibrin accumulations. They can be attributed to the prothrombotic response, which can result in overt clot formation in the vasculature [11]. However, in terms of clinical and radiological symptoms, lung involvement was not severe in our patient. On the other hand, the patient had no history of overt vaso-occlusive attack and he was treated with hydroxyurea, which was recommended for all patients with SCD for the prevention of stroke in the COVID-19 pandemic [12].

TCD was performed for the patient. High blood flow velocity on the TCD is usually a risk factor for stroke in SCD patients. This patient indicated the normal limit for the arterial velocity values in the TCD recording. The mechanism of stroke following COVID-19 infection is unclear. However, several studies have reported the role of pro-inflammatory cytokines in creating the atherosclerosis process and vasculopathy [6, 10]. Thus, during the outbreak of COVID-19, vaso-occlusive attacks in SCD patients can be evaluated for COVID-19 as an etiological factor.

Conclusion

As far as we know, it is the first case of SCD presented with CVT along with COVID-19 infection. Because of the recent pandemic, the physicians should be aware of the possibility of COVID-19 infection as an etiology for disease complications in vulnerable and high-risk patients, such as SCD cases.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgements

The authors would like to appreciate the Vice-Chancellor of Research and Technology of Mazandaran University of Medical Sciences, the patient for his consent, and Dr. Khoshnama for obtaining clinical information about the reported patient.

References

[1] Dexter D, Simons D, Kiyaga C, Kapata N, Ntoumi F, Kock R, et al. Mitigating the effect of the COVID-19 pandemic on sickle cell disease services in African countries. The Lancet Haematology. 2020; 3026(20):30122-8. [DOI:10.1016/S2352-3026(20)30122-8]

[2] Farooq S, Testai FD. Neurologic complications of sickle cell disease. Current Neurology and Neuroscience Reports. 2019; 19(4):1-8. [DOI:10.1007/s11910-019-0932-0] [PMID]

[3] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine. 2020; 20:382-8. [DOI:10.1056/NEJMoa2001017] [PMID] [PMCID]

[4] Center for Disease Control Prevention. First travel-related case of 2019 novel coronavirus detected in United States [Internet]. 2020 [Updated 2020 January 21]. Available from: https://www.cdc.gov/media/releases/2020/p0121-novel-coronavirus-travel-case.html

[5] Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). Journal of General Internal Medicine. 2020; 35(5):1545-9. [DOI:10.1007/s11606-020-05762-w] [PMID] [PMCID]

[6] Sharifi-Razavi A, Karimi N, Rouhani N. COVID-19 and intracerebral haemorrhage: causative or coincidental? New Microbes and New Infections. 2020; 35:100669. [DOI:10.1016/j.nmni.2020.100669.] [PMID] [PMCID]

[7] Karimi N, Sharifi Razavi A, Rouhani Nima. Frequent convulsive seizures in an adult patient with COVID-19: A case report. Iranian Red Crescent Medical Journal. 2020; 22(3):102828. [DOI:10.5812/ircmj.102828]

[8] Zhai P, Ding Y, Li Y. The impact of COVID-19 on ischemic stroke. Diagnostic Pathology. 2020; 15(1):1-5. [DOI:10.21203/rs.3.rs-20393/v1]

[9] Sedagha Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. Journal of Clinical Neuroscience 2020; 76:233-5. [DOI:10.1016/j.jocn.2020.04.062] [PMID] [PMCID]

[10] 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. SSRN Electronic Journal. 2020. [DOI:10.2139/ssrn.3544840]

[11] Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past. Journal of Clinical Virology 2020; 127:104362. [DOI:10.1016/j.jcv.2020.104362] [PMID] [PMCID]

[12] DeBaun MR. Initiating adjunct low-dose hydroxyurea therapy for stroke prevention in children with SCA during the COVID-19 pandemic. Blood, the Journal of the American Society of Hematology. 2020; 135(22):1997-9. [DOI:10.1182/blood.2020005992] [PMID] [PMCID]