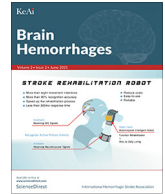




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Case Report

SARS-CoV-2 infection with pneumonia and stroke

Muhammad Hassan^{a,b,*}, Fibhaa Syed^{a,c}, Fatima Mustafa^{a,d}, Hafiza Faiza Mushtaq^{a,e},
Naveed Ullah Khan^{a,b}, Mazhar Badshah^{a,f}

^a Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), Islamabad, Pakistan

^b Resident Neurologist, Department of Neurology, SZABMU, Pakistan

^c Department of Internal Medicine, SZABMU, Pakistan

^d Resident General Surgery, Department of General Surgery, SZABMU, Pakistan

^e Resident Obstetrics and Gynecology, Department of Obstetrics and Gynecology, SZABMU, Pakistan

^f Department of Neurology, SZABMU, Pakistan

ARTICLE INFO

Article history:

Received 8 December 2020

Received in revised form 21 December 2020

Accepted 22 December 2020

Available online 2 February 2021

Keywords:

Covid-19

SARS- CoV-2

Stroke

ABSTRACT

Background: Covid-19 pandemic has been manifested mainly as respiratory and constitutional symptoms. Though, it may demonstrate the involvement of other systems i.e. cardiovascular system (CVS), central nervous system (CNS) or gastrointestinal system (GI).

Discussion: Systemic manifestation of Covid-19 requires further research. Recent surveys revealed a few alarming facts about Covid-19, that, when it hits the brain, can cause some serious complications like; psychosis, stroke and dementia.

Case Presentation: Here, the case is about two patients, having PCR confirmed Covid-19 and radiographic evidence of stroke, who eventually died during hospital stay. Data collection was done after informed consent and in retrospective manner.

© 2021 International Hemorrhagic Stroke Association. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co. Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Coronavirus disease, caused by SARS-CoV-2, has been a global pandemic, now. More than 31.3 million cases have been reported to date¹. This aerosol infection caused by SARS-CoV-2 possess a wide range of symptoms, varying from being asymptomatic to fatal, from simple cold, cough and flu to severe pneumonia, respiratory distress, kidney failure, multi-organ failure, even neurological and cardiovascular manifestations^{2,3}. Invasion through hematogenously and through cribriform plate explained the neuroinvasive potential of virus⁴. Neurological manifestations described in 214 patients in Wuhan, China as 36.4% of all patients with cerebrovascular accidents, altered sensorium⁵. This case reports of 2 SARS-CoV-2 patients confirmed by PCR, who developed ischemic stroke during their hospital stay.

1.1. 1st case report

A 67-year-old male, known case of type-2 Diabetes Mellitus (DM), hypertension (HTN), Ischemic heart disease (IHD), smoker, doctor by profession, and with no travel history in recent time pre-

sented to emergency room (ER) with the complain of shortness of breath (SOB) with mild cough and low-grade fever (undocumented). His receiving vitals were B.P: 110/80 mmHg, Pulse: 98 bpm, Respiratory rate: 18/min with 92% oxygen saturation on room air and was afebrile. Neurological examination was GCS: 15/15, pupils bilateral equal and reactive to light, moving all four limbs. Systemic enquiry revealed bilateral coarse crepitations on chest auscultation. After initial management in the ER, he was consulted by the On-call registrar of Covid-19 isolation ward for the ground glass appearance of his Chest X-Ray with pneumonic patches in the middle lobe of the right lung. He was taken over by the isolation ward after PCR confirmed the SARS CoV-2 infection. All baselines were within normal range except for the total leukocyte count (TLC) that showed marked lymphopenia (As shown in [table 1](#)). C-reactive protein (CRP) and D-dimers and serum ferritin, all were slightly elevated. Electrocardiogram (ECG) was unremarkable. He was started on Injectable antibiotics (ceftriaxone 1gm BD, azithromycin 500 mg OD) and his routine medications for diabetes (Inj. Insulin R + NPH), HTN and IHD (Aspirin 75 mg OD, Rosuvastatin 10 mg HS, Losartan 50 mg OD) were also continued. Though, he was received in a relatively promising condition and remained static till his 4th day of admission; when his GCS suddenly deteriorated to 10/10 (E₄ M₆ V₀) with aphasia and left sided hemiparesis with ipsilateral plantar up-going, unable to maintain saturation on room air so was immediately put-on oxy-

* Corresponding author at: Department of Neurology, Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), Islamabad, Pakistan.

E-mail address: drfibhaasyed@szabmu.com.pk (M. Hassan).

Table 1
Laboratory Findings at admission.

Laboratory Findings	Normal Range	Patient 1	Patient 2
WBCs	(4.8–10.8 K/ μ L)	14.45	18.5
Neutrophils	(1.4–6.5 K/ μ L)	9.2	8.8
Lymphocytes	(1.2–3.4 K/ μ L)	0.9	0.8
Platelet Count	(130–400/ mm^3)	175	188
Hemoglobin	(12–16 g/dL)	13.8	14.5
Albumin	(3.5–5.2 g/dL)	4.2	3.6
ALT	(0–41 U/ L)	55	75
AST	(0–41 U/L)	30	28
LDH	(50–242 U/ L)	280	320
Creatinine	(0.7–1.5 mg/dL)	1.2	1.1
PT	(9.95–12.87 s)	10.80	12.0
APTT	(27–39.2 s)	34.5	35.0
D-Dimers	(0–230 ng/mL)	703	892
Ferritin	(15–150 ng/L)	1947	1548
CRP	(0.00–0.40 mg/ dL)	26.3	53.9

gen (Nasal Cannula @5L). Immediate CT-Brain was planned which turned out to be consistent with an acute right middle cerebral artery infarct- Right MCA dot sign (hyperdense sylvian fissure) as shown in Fig. 1. A repeat CT scan of the brain was carried out on 6th day of admission since his GCS dropped to 6/15 which demonstrated Total Anterior Circulation Infarct (TACI). Laboratory findings after onset of stroke were listed in table 2. Despite all the possible doctoring and medical care, the patient could not cope up with his life and breathed his last on 10th day of admission.

1.2. 2nd case report

62 years old female with a previous history of IHD, T2DM and osteoarthritis (OA), presented in ER with shortness of breath and drowsiness. The attending vital signs were BP:130/80 mmHg, HR:88 bpm, Temp: 98° F, RR: 20/min with saturation of 94% on room air. The systemic examination was insignificant except for the respiratory system upon auscultation, there were bilateral coarse crepitations all over the chest and chest X- ray showed bilateral consolidations (Radiographic Assessment of Lung Edema (RALE) Score :17/33). PCR for SARS CoV-2 was positive. She was

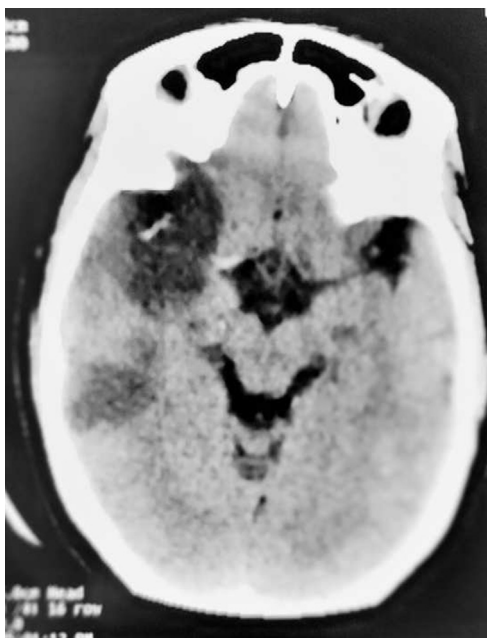


Fig. 1. Non contrast CT Scan Brain showing Right sided MCA dot sign- presenting early infarct.

admitted in Covid-19 isolation. All the baseline investigations were sent, including CRP, serum ferritin and D-dimers, out of which TLC and raised Ferritin and D-dimers took the most of attention (As shown in table 1). Her condition was progressively deteriorating when she developed right sided hemiplegia and worsening of breathing with saturation dropped to 82% with dual oxygen, on 6th day of her admission. Acute MCA infarct, affirmation thus made on the radiologic findings shown by the CT-Scan Brain and HRCT chest showed extensive ground glass opacification with interlobular reticulations/septal thickening in bilateral lungs. Patient was then put on ACMV mode of mechanical ventilator with a PEEP of 12, there she was saturating 88–90% with FiO₂ 1.0. She was being managed on the lines of Acute Respiratory Distress Syndrome (ARDS) and was on injectable broad-spectrum antibiotics (Inj. Piperacillin and Tazobactam). However, the routine medications for her type-2 Diabetes (Insulin Regular), and IHD (Aspirin 75 mg OD, Rosuvastatin 10 mg HS), were being continued since day 1 along-with other supportive measures). Laboratory findings after onset of stroke were listed in table 2. Due to poor functional status, the patient deemed not to be a good candidate for any neurologic intervention or thrombolysis. Despite all the striving and efforts, the patient couldn't survive and died on 11th day of hospitalization.

2. Discussion

This case study narrates first ever Covid-19 positive patients presenting with stroke in Pakistan. A study conducted revealed that the percentage of people developing stroke, later in the disease course of Covid-19 is 5.7%⁶. PCR confirmed SARS-CoV-2 has been detected from CSF of Covid-19 positive patients⁵. Yet another study reported to have 5% incidence of stroke amidst Covid-19 patients, within 2 weeks from the day of onset of disease, but usually amongst those having severe form of disease and other known co-morbidities like HTN, IHD and DM. In the pathophysiology of stroke, the main contributory role seems to be played by the higher inflammatory state and the abnormal coagulation cascade, depicted clinically by raised CRP and D-dimers⁷.

The exact course of events causing the stroke to take place, is still unknown. However, the increased risk of thromboembolism and cardiovascular events in an infective state, could be a cause, since the rate of thromboembolic complications among critically ill patients and those who are under ICU care is 31%⁸. Angiotensin converting enzyme –2 (ACE-2) receptors provide the main doorway to all the coronaviruses including SARS-CoV-2⁹. And thence, SARS-CoV-2 can get an entry into the CNS through these receptors and several other means as well, that might include hypoxic or immune-related injury or direct injury to blood brain barrier. Multiple cases of pulmonary emboli have also been reported. A few

Table 2
Laboratory Findings after onset of stroke.

Laboratory Findings	Normal Range	Patient 1	Patient 2
WBCs	(4.8–10.8 K/ μ L)	18.9	22.7
Neutrophils	(1.4–6.5 K/ μ L)	9.6	9.4
Lymphocytes	(1.2–3.4 K/ μ L)	0.3	0.4
Platelet Count	(130–400/ mm^3)	183	189
Hemoglobin	(12–16 g/dL)	12.7	13.5
LDH	(50–242 U/ L)	375	380
D-Dimers	(0–230 ng/mL)	1209	1980
Ferritin	(15–150 ng/L)	1866	1688
CRP	(0.00–0.40 mg/ dL)	82.6	122.3

autopsies carried out, revealed the presence of macroangiopathic thrombi in lungs and kidneys of SARS-CoV-2 infected patients, but there is no evidence of such findings in brain, yet in the literature¹⁰.

With such limited literature available, thrombi formation due to hypercoagulable state may be rendered as the most probable pathophysiological mechanism, hypoxia and infection may also play their contributory role.

3. Conclusion

Fight against the Covid-19 in terms of control, protection and management remains the mainstay. However, the probability of stroke amongst Covid-19 infected patients must be considered and the management plans must be made accordingly. Further more research is needed to explore the disease course of Covid-19, associated complications and other neurological manifestations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Patients consented for the study and publication.

References

1. <https://Covid.who.int>.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506.
3. Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):819–824.
4. Montalvan V, Lee J, Bueso T, De Toledo J, Rivas K. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. *Clin Neurol Neurosurg*. 2020;194 105921.
5. Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis*. 2020;94:55–58.
6. Mao L, Jin H, Wang M, Hu Y, Chen S, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. 2020;77(6):683–690.
7. Li Z, Huang Y, Guo X. The brain, another potential target organ, needs early protection from SARS-CoV-2 neuroinvasion. *Sci China Life Sci*. 2020;63(5):771–773.
8. Kloka J, Martin C, Gilla P, Lotz G, Zacharowski K, Raimann F. Visualized effect of the Frankfurt Covid aErosol pRotEction Dome-COVERED. *Indian J Anaesth*. 2020;64(14):156.
9. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181(2):271–280.e8.
10. Barton LM, Duval EJ, Stroberg E, Ghosh S, Mukhopadhyay S. Covid-19 autopsies, Oklahoma, USA. *Am J Clin Pathol*. 2020;153(6):725–733.