Stroke - next wave of complications from covid-19

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Abstract

Risk factors and hospital events associated with the occurrence of stroke in covid-19 are not yet well known. We analyzed four patients aged 51, 39, 81, and 42 years (represented as cases 1, 2, 3, and 4, respectively), who were admitted with SARS-CoV-2 RT-PCR or antigen positive reports. Inflammatory markers like C-reactive protein (CRP), D-dimer, ferritin, leucocytes, platelets, lactate dehydrogenase (LDH), and liver biomarkers were assessed. All the patients had abnormal NCCT head imaging with hypodense areas involving the left occipital, thalamus, and corona radiata causing ischemic infract or effacement of adjacent sulcal spaces infract. Case 1 and 3 patients survived the treatment and were discharged. While Case 2 and 4 patients underwent sudden cardiac arrest despite all resuscitation efforts. These patients possessed altered sensorium, hemiparesis, hemiplegia, and seizures, along with common respiratory symptoms. While blood biomarkers and NCCT imaging have shown the severity of patients, these tests must be carried out worldwide to decrease the severity of therapy at its early stage. Early biomarker detection might assist physicians to increase prognosis during early infection periods. Thus, more research would improve the results worldwide.

Keywords: stroke, covid-19, NCCT

Introduction

The COVID 19 outbreak caused by the SARS- CoV-2 virus has been declared as a pandemic by the World Health Organization in March 2020 [1]. Acute respiratory syndrome is the most common manifestation of this disease [1, 2]. It was known that the SARS-CoV-2 virus has the ability to bind effectively to the ACE-2 receptors of the host [1]. Therefore, the distribution of ACE receptors across various places in the human body suggests the existence of a wide range of multisystem interactions [3]. We need to get in-depth knowledge of the possible connection, clinical symptoms, severity, and treatment results of Covid-19 infections because of the significant rise in infections in India during the second wave and the severity of neurological sequelae. COVID-19 individuals are found to have an abnormal immune response, which causes the production of numerous inflammatory cytokines and chemokines, showing dysregulated biological pathways [4, 5]. Approximately 30-50% of individuals who develop severe sepsis and accompanying thrombosis, haemorrhage, and organ failure also have COVID-19-induced coagulopathy (CIC) [5-7]. It was also noticed that the degree of coagulopathy is proportional to severity. Patients in the intensive care unit (ICU) are the most seriously affected by this pathology. In a marked number of COVID-19 patients, altered coagulability can lead to pulmonary embolism and other thrombotic events such as cerebrovascular events [8]. Patients would present altered D-dimer, fibrinogen and ferritin levels [9]. In addition, increasing the use of blood thinners to resolve the issue can lead to microbleeds, and haemorrhages [8]. Here, we describe four critical cases of COVID-19 with altered sensorium, hemiparesis, hemiplegia, and seizures. This report described the cases that were admitted to LOKPRIYA HOSPITAL (Reg. no.: RMEE1900995), Meerut, a primary case facility (COVID-19 section) in Western Uttar Pradesh, where most of the patients were uneducated and from lower socioeconomic backgrounds.

Case 1

A 51-year old male patient (UHID-11156) with no co-morbidities was presented with difficulty breathing for 6 days, with vitals, PR 100/min, BP 132/86 mmHg, RR 34/min, temperature 98.4F and SpO2 74% in RA (Table 1). The patient's COVID-19 antigen test was positive and they were shifted to ICU. He was placed on continuous oxygen via NRBM and maintained a SpO2 of 90-92%. Patient relevant investigations were HRCT chest S/O CTSI 18/25. The patient's clinical investigation suggested elevated levels of TLC, neutrophils, CRP, D-Dimer, ferritin, LDH, and HBA1c. While, the lymphocyte count declined drastically. In the course of the treatment, on day 3, the patient started complaining of weakness in his right upper limb and lower limb. On examination, the plantar were found to be extensor on the right side and flexor on the left side. The B/L pupil were normal size and normal reactive, power in the right upper limb was 3/5 and the lower limb was 4/5. The immediate NCCT of head was done, which was suggestive of subtle hypo dense area of mean

20hu noted involving left occipital, thalamus, and corona radiata region/ ischemic infarct (Fig. 1A). The patient's blood thinner was increased after taking a neurologist's opinion. Later, the patient was managed conservatively on IV fluids, antibiotics, antivirals, steroids, and blood thinners and high flow oxygen. The patient was then discharged with stable vitals at room air with a COVID-19 RT-PCR negative report, with an existing neurological deficit and mild post COVID-19 symptoms.

Case 2

A female patient aged 39yrs (UHID-11153) presented with a complaint of fever and cough for 5-6 days, followed by shortness of breath for 3 days. Patient vitals at the time of presentation were PR 80/min, BP 116/66 mmHg, RR 28/min, SpO2 88%, temperature 98.7F, and RBS 110. The patient was tested positive for COVID-19 rapid antigen test. The blood panel investigation of the patient suggested elevated levels of TLC, neutrophils, CRP, D-Dimer, and procalcitonin. While, the lymphocyte count declined drastically (Table 1). HRCT CHEST S/O was CTSI 13/25. On the 5th day of admission, there was a drop in oxygen saturation (64-68%), which was an indication of respiratory failure, after which ABG was done and the patient was kept on BiPAP support. On the 6th day, the patient had an episode of GTCS followed by loss of consciousness, after which the patient was intubated and was taken on mechanical ventilation due to low saturation levels and a fall in GTCS. An immediate NCCT head (Fig. 1B) was done, which showed s/o hypodense area of mean 19hu noted involving left temporo occipital region, left thalamus and left corona radiata causing effacement of adjacent sulcal spaces infarct. The patient was then managed extensively in the ICU with IV fluids, antibiotics, heparin infusion, antivirals, and other supportive treatments. The patient was on mechanical ventilator support and was taken on inotropic support IVO falling blood pressure. On the 7th day of hospitalization, the patient went into sudden cardiac arrest. Immediate CPR was started under ACLS guidelines. Despite all possible resuscitation efforts, the patient could not be revived.

Case 3

An 81-year old male (UHID-11705) presented with a fever for 8 days and shortness of breath for 5 days. The vitals at the time of admission were noticed to be BP 130/80 mmHg, PR 102/min, RR 26/min, Temp 100.4F, SpO2 82% (taken on O2 support at 12 L/min). The patient was COVID-19 RT-PCR positive and was admitted for further management. The patient's relevant investigations were presented in Table 1, where an increase in TLC, neutrophils, D-Dimer, ferritin, LDH, PT/INR, fibrinogen and PCT were noticed. The patients' HRCT S/O CTSI was 17/25. On the 3rd day of admission, the patient suddenly developed altered sensorium and right-sided upper and lower limb weakness. On examination he was E4v3M5, plantar right sided extensor and left side flexor, B/L pupil was normal size, normal reactive, urgent NCCT head (Fig. 1C) was done which showed s/o hypodense area of mean 17HU noted involving left temporo occipito parietal region causing effacement of adjacent sulcal spaces- likely infarct. A Neurologist opinion was taken, advising against antiplatelets and LMWH. On the 5th day of hospitalization, the patient's sensorium improved but the weakness persisted. The patient was then managed conservatively with IV fluids, antibiotics, antivirals, high flow O2 and other supportive management. The patient was discharged on the 10th day of hospitalization on resolution of pneumonia with negative COVID-19 RT-PCR report.

Case 4

A 42-year old female (UHID-11076) with no known comorbidities was presented with a fever for 7 days, a cough for 2 days, and SOB for 2 days. The vitals at the time of admission were BP 100/60 mmHg, PR 108/min, RR 34/min, Temp 99.4F, SpO2 74-92% on O2 at 15L, GCS E4V5M6. The patient was COVID-19 RT-PCR positive and was admitted to COVID-19 ICU for further management. The patient was managed on high flow O2, antibiotics, antivirals, steroids, blood thinners, antipyretics, antiemetics, nebulization and other supportive treatments. The blood reports of the patient suggested elevated levels of TLC, neutrophils, D-Dimer, ferritin, LDH, PT/INR. The patients' liver function indicators like SGOT and SGPT were also elevated (Table 1). The patients' HRCT CHEST s/o CTSI was 17/25 with ABG s/o Type 1 Respiratory Failure. On the 5th day of hospitalization, the patient went into altered sensorium with irrelevant talking and aggressive behavior. An immediate NCCT head (Fig. 1D) was done which showed s/o subtle hyperdensity noted in left frontal region bleed. An immediate neurologist opinion was taken, and the patient was managed accordingly. On the 6th day of hospitalization, the patient was intubated and IVO falling GCS and oxygen saturation. The patient was managed extensively on IV fluids, antibiotics, antivirals, Inj. Vit K, antiepileptics, and Mannitol and other supportive therapy with mechanical ventilator support was provided. All anticoagulants were withdrawn, and the patient was transfused with Fresh Frozen Plasma and PRBC. On the 7th day of hospitalization, the patient went into sudden cardiac arrest. Immediate CPR was stated under ACLS guidelines, but despite all possible resuscitation efforts, the patient could not be revived and was declared dead.

Table 1: Patient details and clinical investigations

Patient details	Reference range	Case 1	Case 2	Case 3	Case 4
Age (years)	-	51	39	81	42
Sex	-	Male	Female	Male	Female
Fever	F	98.4	98.7	100.4	99.4
Pulse rate (PR) (per min)	60-100	100	80	102	108
Respiratory rate (RR) (beats per min)	16-20	34	28	26	34

Blood pressure (BP) (mmHg)	120/80	NA	116/66	130/80	100/60
SpO_2	≥ 95	74	88	82	74
HRCT Chest S/O CTSI	-	18/25	13/25	17/25	17/25
Co-morbidities	-	No	NA	NA	No
Clinical parameters					
Hemoglobin (Hb) (g/dL)	Male: 13.2-16.6 Female: 11.6-15.0	13.7	9.7	12.2	10.9
Total Leucocyte count (TLC) **(**x 10^3 µl**)**	Male: 4.3-5.9 Female: 3.5 to 5.5	12.8	10.3	10.1	5>19.5
Neutrophils (%)	50-70	94	96	90	96
Lymphocytes (%)	20-45	6	4	10	4
Urea (mg/dL)	18-55	0.39	26	40	14>60
Creatine (mg/dL)	0.6-1.3	1.2	0.8	1.1	0.95>1.1
Sodium (Na) (mmol/L)	136-145	136	141	137	144
Potassium (K) (mmol/L)	3.5-5	3.9	3	3.8	3.1
D-Dimer (mg/L)	<0.50	1084.37	>10000	1063	942
LDH (mg/dL)	up to 100	878	NA	628	628
Ferritin (ng/ml)	up to 100	388.18	NA	149	149
HBA1c (%)	up to 6.3	7.1	6.22	NA	NA
Prothrombin time and international normalized ratio (PT/INR)	11- 13.5/ 0.8- 1.1	12.4/1.06	NA	14.5/1.23	18.1/1.51
Procalcitonin (PCT) (ng/ml)	<0.046	NA	0.19	0.12	0.12
Fibrinogen (mg/dL)	200-400	NA	NA	420	NA
C-reactive protein (CRP) (mg/L)	up to 10	103.7	132.4	10	NA
Platelet count (x $10^9/mm^3$)	1.5-4.5	NA	2.6	3.3	NA
Total Bilirubin (mg/dL)	0-1	0.75	0.39	0.71	0.95
SGOT (IU/L)	10-40	32	29	33	68>905
SGPT (IU/L)	10-45	25	56	43	99>633
Outcome	-	Discharged	Died	Discharged	Died

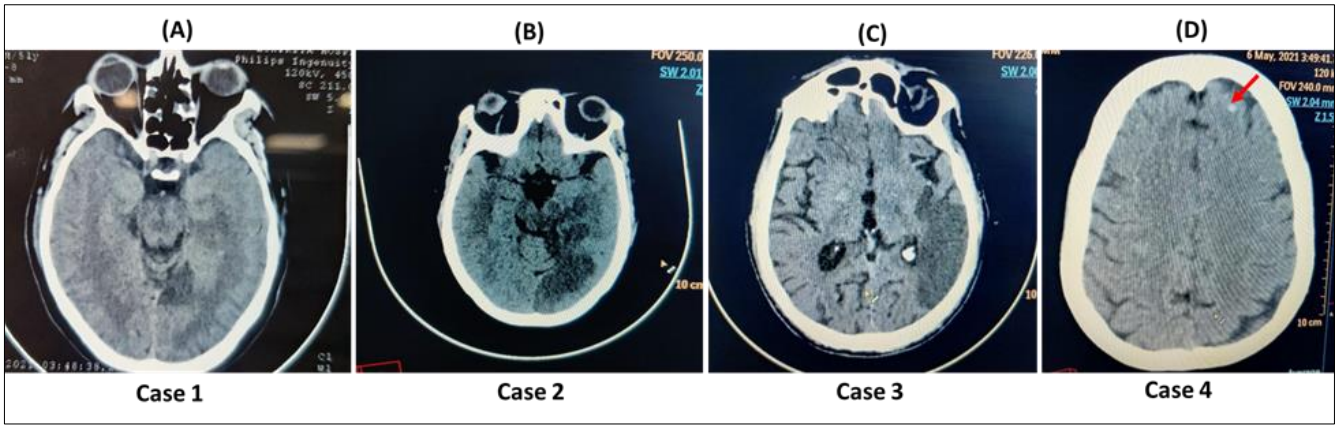

Fig 1: NCCP imaging among the COVID-19 patients

Discussion

Even though the majority of patients with COVID-19 presented with respiratory failure, the second wave of patients also exhibited various neurological symptoms, such as headache, vertigo, dizziness, lack of smell and taste, and CVA (infarct/bleed) [10]. Cerebrovascular events in COVID-19 may be linked to cerebrovascular vasculopathy [11]. In comparison, traditional stroke risk is further increased with sepsis, other illnesses, such as diabetes and hypertension, as well as SARS-CoV2 virus neurotropism [12, 13]. People who acquire COVID-19 seizures are likely to have breakthrough seizures [14]. Approximately 19 out of every 1,000 COVID-19 patients will be identified with the condition of unprovoked altered sensorium, confusion, or agitation, together with focal neurological deficits suggesting an acute stroke, meningitis, and acute myelitis [10].

The above cases discussed show that without any prior neurological history, patients presented or developed these neurological complications that could be attributed to the SARS-CoV2 infection. Therefore, a multidisciplinary approach is needed in the management of COVID-19 patients. From the beginning of the COVID-19 pandemic, potential central nervous system involvement has been hypothesized through various etiological mechanisms, including direct neuro-invasion [15], para-infectious autoinflammatory involvement [16-19] endothelial dysfunction [20], and indirect involvement due to altered homeostasis such as altered coagulative states that cause an increase in ischaemic haemorrhagic lesions [21-25]. Possible underlying microangiopathy may be present in COVID-19-associated

stroke patients due to a significant rise in CRP and D-dimer levels, coupled with thrombocytopenia. Our studied cases also show such clinical findings [26]. Severe thrombocytopenia is seen in about 22 to 58 percent of traditional COVID-19 associated with sepsis patients [27].

Especially common in severe COVID-19 patients, D-dimer and fibrin degradation products are high in people with disseminated intravascular coagulation (DIC) and pulmonary embolism (PE) [28]. Respiratory failure resistant to oxygen treatment and hemodynamic support for septic shock necessitates mechanical ventilation [29]. Different stages of the viral replication cycle and convalescent plasma are being evaluated using antiviral medicines [30]. Although an increase in viral replication and viral disease progression may occur during the initial stage of infection due to the administration of steroids, use of the steroids in small amounts, under control of a timed or titrated programme, may be safe and beneficial in meningitis and various central nervous system demyelinating disorders [31].

In conclusion, a broad range of neurological symptoms are possible with COVID-19 infection. Diagnosing individuals with a primary neurological presentation should be done with great caution, since neurological symptoms are quite frequent in those with severe illness. Further research is needed to discover if neurological problems in these individuals are attributable to the thromboembolic effects of the SARS-CoV2 virus or to over-utilization of anticoagulant treatment.

Disclosure

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