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CASE REPORTS

Acute stroke in young patients positive for COVID-19: A report of six cases

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Abstract

We report here 6 young patients of stroke with COVID-19 infection. These patients were positive for COVID-19, as confirmed using reverse transcription-polymerase chain reaction (RT-PCR) The patients' mean age was 44.5 ± 1 years, and 83% were young males without cerebrovascular risk factors. Five patients had an ischemic stroke, one patient had intracranial hemorrhage. The mean stroke onset time was 10.2 ± 6.1 days after the COVID-19 diagnosis. Two patients were symptom-free for COVID-19. The mean National Institutes of Health Stroke Scale (NIHSS) score was 9.1 ± 5.3. Three patients had severe COVID-19 pneumonia. Large vessel occlusion was detected in 3 patients with ischemic stroke. Two patients were treated with intravenous thrombolytic, one patient underwent a mechanical thrombectomy, and an elective stent was fitted on another patient. In conclusion, COVID-19 should be considered as a possible cause particularly in young strokes during the pandemic period.

Keywords: coronavirus; COVID-19; SARS-Cov-2; IV-tPA; thrombectomy; stroke

INTRODUCTION

Coronavirus disease 2019 (COVID-19), also known as a severe acute respiratory syndrome (SARS)-Corona Virus (CoV-2), is a disease caused by new types of coronaviruses that mainly affect the respiratory system and present with neurologic symptoms in one-third of hospitalized patients.[1] The most common neurologic findings were dizziness, headache, and loss of smell and taste.[1] Retrospective studies conducted on patients with COVID-19 demonstrated that the stroke incidence was between 2.5 and 6%.[1-3] Although stroke incidence (1.2%) was low in patients with COVID-19 in a meta-analysis, mortality (38%) was high.[3] The incidence of stroke may be underestimated because physicians mayhave missed the stroke symptoms among the intubated and sedated patients managed in the intensive care unit (ICU), or patients with minor stroke might not have been admitted to hospitals during the pandemic period.[3]

Acute stroke is among the most significant life-threatening neurologic complications in patients with COVID-19. Stroke was associated with severe illness and advanced age in COVID-19 positive patients.[1] Unusual thrombosis cases have been identified, including the aorta, carotid, and basilar thrombus with large vessel occlusion.[4,5] The mechanism of stroke in young patients with COVID-19 infection remains controversial. In this study, we report the demographic, radiologic, clinical, and laboratory findings of 6 young patients with acute stroke and COVID-19 confirmed using reverse transcription-polymerase chain reaction (RT-PCR) at our stroke center.

CASE REPORT

This was a single-center study, and the data of the patients were obtained retrospectively from their medical records. Five patients had an ischemic stroke; one patient had a hemorrhagic stroke. Except for one female patient with hypertension, all the other patients were male without risk factors. The median age of the patients was 48 (range, 29-54) years. The mean onset time for stroke was 10.2 ± 6.1 days after the diagnosis of COVID-19.

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Stroke developed after the onset of other COVID-19 symptoms in 4 patients, and 2 patients were diagnosed as having COVID-19 disease concomitantly with stroke. In terms of the etiology of the ischemic strokes according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification, large vessel occlusion was detected in three (60%) patients. Cardiologists performed electrocardiography, echocardiography, and 24-hour Holter electrocardiography examinations in all patients but could not find a cardiac cause in any of the patients. Fasting glucose, Hba1c value, lipids, trombophlia, other infections such as hepatitis, HIV, and syphilis, antiphospholipid antibodies examinations were normal in all the patients. The mean National Institutes of Health Stroke Scale (NIHSS) score was 9.1 ± 5.3. Three of the patients had severe COVID-19 pneumonia as per the international community-acquired pneumonia guidelines.[6] Details of the related findings are given in Table 1. We administered intravenous thrombolytic (IV-tPA) to Patient 2 (at the third hour of the onset of a stroke) and Patient 5 (at the 90 minutes of the onset of a stroke). We inserted an elective stent to carotid artery of Patient 1. Patient 5 underwent mechanical thrombectomy in our stroke unit. However, we observed a rapid re-embolization despite the removal of the clot and performed heparinization. No bleeding was observed in his 24th-hour follow-up CT. The remaining 3 patients were followed up with medical treatment. The neuroimages of the patients are as in Figure 1.

DISCUSSION

Although stroke is a rare complication of Covid 19, it is important due to its high mortality. Severe illness and advanced age were the most commonly reported risk factors of stroke in the Covid 19 patients. However all of our cases were under the age of 55 years. All of our patients had no risk factors except for one patient with hypertension. On the other hand, in Li *et al*.'s study, the patients' median age was 75 (range, 57-91).[7] Our results bear more resemblance to the results reported in the study of Oxley *et al*.[8]

It was reported that physicians might see stroke cases more frequently in the late phases of COVID-19 infection.[1] The mean stroke onset time after the COVID-19 diagnosis was 10 days, as in our patients.[3,7]

Two of our patients were asymptomatic for COVID-19 and were diagnosed as having COVID-19 infection concurrently with a stroke diagnosis. Our study showed that even asymptomatic patients with COVID-19 are prone to stroke. Therefore, physicians should keep in mind that the patients with stroke presenting to emergency wards during the pandemic may have underlying COVID-19 infection. Attention should be paid to the use of personal protective equipment (PPE) during the pandemic to avoid being infected by the virus.

Hypercoagulability associated with COVID-19, such as sepsis-induced coagulopathy, may render patients susceptible to stroke. Multi-organ failure may develop due to endothelial dysfunction, and micro thrombosis develops following a systemic inflammatory response triggered by infection.[9] Zhou *et al*. demonstrated that higher than 1 μg/mL D-dimer levels in patients with COVID-19 were associated with mortality.[10] All of the patients with ischemic stroke included in this study had increased D-dimer levels, indicating underlying inflammtion and hypercoagulability. In a series in which patients with large vassel occlusion were reported, 4 of the 9 patients with initial recanalization underwent early reocclusion within 24 hours.[11] In our patients, we detected large vascular occlusion in half of the patients, and also found early re-occlusion in our patient who underwent thrombectomy. Postmortem histologic analysis of patients with COVID-19 revealed lymphocytic endotheliitis in different organs such as lung, heart, kidney, and liver.[12] ACE2 receptors, to which the virus binds, are located in the alveolar epithelial cells and also in the vascular endothelium in the central nervous system. Patients are at risk of hypercoagulability and cerebral ischemia may also be due to direct viral vascular invasion.

In conclusion, COVID-19 must be considered as a possible cause particularly among the young strokes during the pandemic period. Hypercoagulability may be an important pathogenic mechanism.

DISCLOSURE

Ethical approval: The study received approval by the Ethics Committee of Istanbul Fatih Sultan Mehmet Training and Research Hospital. Informed consent: All of the participants gave their informed consent to participate to the study.

Conflicts of interest: None

Table 1: Clinical details of the 6 cases of young COVID-19 patients with stroke

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	35	53	54	49	29	47
Sex	Male	Male	Male	Female	Male	Male
Medical history	None	None	None	Hypertension	None	None
COVID-19 symptoms	Nausea, vomiting, diarrhea	Cough, dyspnea and fever	Cough, hypogeuzia and fever	Asymptomatic	Asymptomatic	Flu-like symptoms
Neurological examination	He had left central facial paresi, and left-sided hemiparesis (1/5 based on the MRC) score)	He was confused, his eyes deviated to the right side, his speech was paralyzed, and he had left-sided hemiparesis (1/5 based on the MRC score)	He had dysarthria and right-sided hemiparesis (4/5 based on the MRC score)	She had dysarthria, left-sided dysmetria, and dysdiadochokinesia	He was confused, had dysarthria, and global aphasia. He had right-sided hemiparesis (1/5 based on the MRC score)	He was confused, and had dysarthria, and right-sided hemiparesis (3/5 based on the MRC score).
CT chest findings and	Consolidations, ground-glass opacity	Pneumonic infiltrations with frosted glass densities	Patch-style frosted glass densities	Frosted glass densities in the middle zone of left lung	Consolidations ground-glass opacity	Compatible with viral pneumonia
Severity of COVID-19	Severe	Severe	Severe	Non-severe	Non-severe	Non-severe
İnitial treatment	Hydroxychloro-quine, azithromycin, and favipiravir	Hydroxychloro- quine, azithromycin and favipiravir	Hyroxychloro-quine, favipiravir	Hyroxychloro-quine	Hyroxychloro-quine	Favipiravir
Stroke onset time after COVID-19 (days)	5	10	19	Concurrent	Concurrent	7
Admission time (hours)	Wake up stroke	3	6	27	1	3
NIHSS Score	10	15	3	3	15	

Table 1: Clinical details of the 6 cases of young COVID-19 patients with stroke

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Vascular territory	Right middle cerebral artery cortical infarction and right common carotid artery thrombus	Top of basillar artery occlusion	Left middle cerebral artery cortical, and lenticulostriate branches infarction	Left cerebellar hemisphere infarction	Left frontal, parietal, temporal and occipital territory infarction and left internal carotid artery thrombus	Hematoma adhered to the left lateral ventricle
Treatment of stroke	Clot retrieval, stent for stenosis of the right common carotid artery, ASA and clopidogrel, enoxaparin sodium	Intravenous t-PA	Acetylsalicylic acid, enoxaparin sodium	Acetylsalicylic acid and clopidogrel	Intravenous t-PA and clot retrieval, enoxaparin sodium 2x1	Intravenous esmolol hydrochloride
Outcome status	Discharged home	Died in intensive care unit	Discharged home	Discharged home	Discharged to rehabilitation facility	Discharged home
White blood cell (10^3/uL)	7.4	8.3	13.1	9.5	12.7	6
C-reactive protein (mg/L)	10.33	22.33	15.59	1.48	1.21	0.11
Lactate Dehydro-genase (U/L)	930	NA	322	242	178	295
D-dimer(mg/L)	3573.67	7407.78	4169.19	2574.79	1046.42	0,45
Fibrinogen (mg/dL)	683	648	695	397	169	353
Serum ferritin (ng/mL)	752.02	NA	576.48	185	130.30	14.01
ALT(U/L)	102	101	22	19	127	12
AST (U/L)	87	91	21	17	51	18
BUN (mmol/L)	8	15	18	33	10	7
Creatinine (µmol/L)	0.76	0.79	0.77	1.17	0.79	0.65

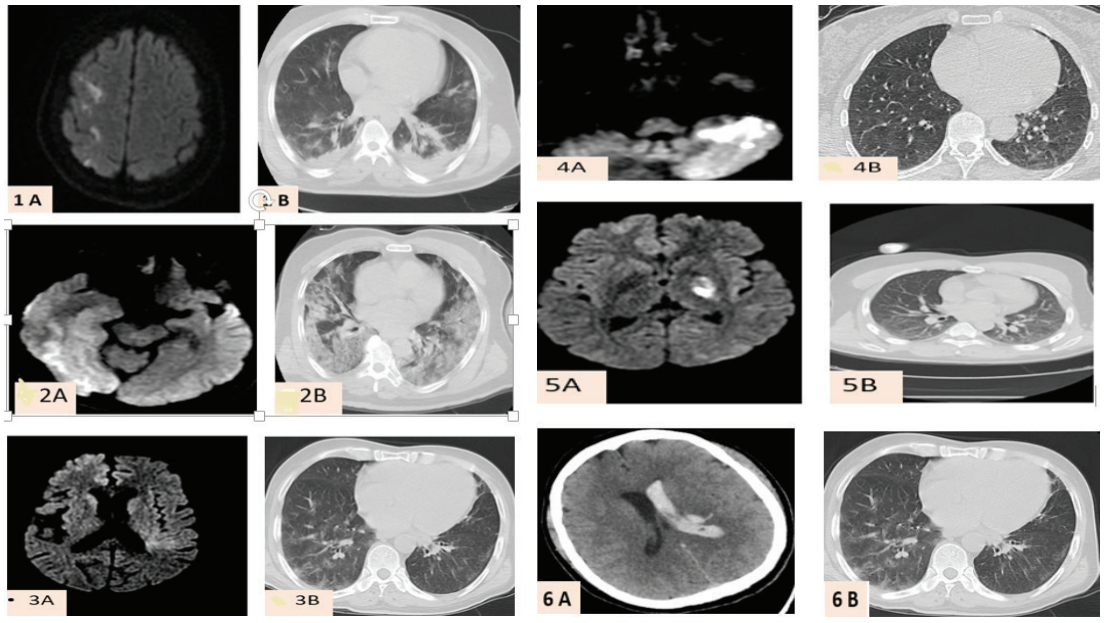

Figure 1. Brain difusion MRI, and lung CT scans of patients.
Imaging of Patient 1 shows right middle cerebral artery cortical infarction (1A); Lung CT scan of Patient 1 shows pleural efusion and ground-glass opacity bilaterally (1B); Imaging of Patient 2 shows bilateral occipitoparietal infarction(2A); Pneumonic infiltrations with frosted glass densitie(2B); Patient 3 shows left middle cereral artery infarction (3A); Patch-style frosted glass densities(3B); Patient 4 shows lef cerebellar hemisphere infarction (4A), Frosted glass densities in the middle zone of left lung(4B); Patient 5 shows left basal ganglion infartion (5A), Consolidations and ground-glass opacity (5B); Brain CT scan of patient 6 shows hematoma adhered to the left lateral ventricle (6A); Lung CT scan of Patient 6 shows ground-glass opacity bilaterally (6B).

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