CORRESPONDENCE

COVID-19 CASES

To rapidly communicate information on the global clinical effort against Covid-19, the Journal *has initiated a series of case reports that offer important teaching points or novel findings. The case reports should be viewed as observations rather than as recommendations for evaluation or treatment. In the interest of timeliness, these reports are evaluated by in-house editors, with peer review reserved for key points as needed.*

Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young

We report five cases of large-vessel stroke in patients younger than 50 years of age who presented to our health system in New York City. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was diagnosed in all five patients.

Cough, headache, and chills lasting 1 week developed in a previously healthy 33-year-old woman (Patient 1) (Table 1). She then had progressive dysarthria with both numbness and weakness in the left arm and left leg over a period of 28 hours. She delayed seeking emergency care because of fear of Covid-19. When she presented to the hospital, the score on the National Institutes of Health Stroke Scale (NIHSS) was 19 (scores range from 0 to 42, with higher numbers indicating greater stroke severity), and computed tomography (CT) and CT angiography showed a partial infarction of the right middle cerebral artery with a partially occlusive thrombus in the right carotid artery at the cervical bifurcation. Patchy ground-glass opacities in bilateral lung apices were seen on CT angiography, and testing to detect SARS-CoV-2 was positive. Antiplatelet therapy was initiated; it was subsequently switched to anticoagulation therapy. Stroke workup with echocardiography and magnetic resonance imaging of the head and neck did not reveal the source of the thrombus. Repeat CT angiography on hospital day 10 showed complete resolution of the thrombus, and the patient was discharged to a rehabilitation facility.

Over a 2-week period from March 23 to April 7, 2020, a total of five patients (including the aforementioned patient) who were younger than 50 years of age presented with new-onset symptoms of large-vessel ischemic stroke. All five patients tested positive for Covid-19. By comparison, every 2 weeks over the previous 12 months, our service has treated, on average, 0.73 patients younger than 50 years of age with large-vessel stroke.

On admission of the five patients, the mean NIHSS score was 17, consistent with severe large-vessel stroke. One patient had a history of stroke. Other pertinent clinical characteristics are summarized in Table 1.

A retrospective study of data from the Covid-19 outbreak in Wuhan, China, showed that the incidence of stroke among hospitalized patients with Covid-19 was approximately 5%; the youngest patient in that series was 55 years of age.[1] Moreover, large-vessel stroke was reported in association with the 2004 SARS-CoV-1 outbreak in Singapore.[2] Coagulopathy and vascular endothelial dysfunction have been proposed as complications of Covid-19.[3] The association between large-vessel stroke and Covid-19 in young patients requires further investigation.

Social distancing, isolation, and reluctance to present to the hospital may contribute to poor outcomes. Two patients in our series delayed calling an ambulance because they were concerned about going to a hospital during the pandemic.

Table 1. Clinical Characteristics of Five Young Patients Presenting with Large-Vessel Stroke.*

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age — yr	33	37	39	44	49
Sex	Female	Male	Male	Male	Male
Medical history and risk factors for stroke†	None	None	Hyperlipidemia, hypertension	Undiagnosed diabetes	Mild stroke, diabetes
Medications	None	None	None	None	Aspirin (81 mg), atorvastatin (80 mg)
NIHSS score‡					
On admission	19	13	16	23	13
At 24 hr	17	11	4	19	11
At last follow-up	13 (on day 14)	5 (on day 10)	NA; intubated and sedated, with multiorgan failure	19 (on day 12)	7 (on day 4)
Outcome status	Discharged to rehabilitation facility	Discharged home	Intensive care unit	Stroke unit	Discharged to rehabilitation facility
Time to presentation — hr	28	16	8	2	8
Signs and symptoms of stroke	Hemiplegia on left side, facial droop, gaze preference, homonymous hemianopia, dysarthria, sensory deficit	Reduced level of consciousness, dysphasia, hemiplegia on right side, dysarthria, sensory deficit	Reduced level of consciousness, gaze preference to the right, left homonymous hemianopia, hemiplegia on left side, ataxia	Reduced level of consciousness, global dysphasia, hemiplegia on right side, gaze preference	Reduced level of consciousness, hemiplegia on left side, dysarthria, facial weakness
Vascular territory	Right internal carotid artery	Left middle cerebral artery	Right posterior cerebral artery	Left middle cerebral artery	Right middle cerebral artery
Imaging for diagnosis	CT, CTA, CTP, MRI	CT, CTA, MRI	CT, CTA, CTP, MRI	CT, CTA, MRI	CT, CTA, CTP
Treatment for stroke	Apixaban (5 mg twice daily)	Clot retrieval, apixaban (5 mg twice daily)	Clot retrieval, aspirin (81 mg daily)	Intravenous t-PA, clot retrieval, hemicraniectomy, aspirin (81 mg daily)	Clot retrieval, stent, aspirin (325 mg daily), clopidogrel (75 mg daily)
Covid-19 symptoms	Cough, headache, chills	No symptoms; recently exposed to family member with PCR-positive Covid-19	None	Lethargy	Fever, cough, lethargy
White-cell count — per mm^3	7800	9900	5500	9000	4900

Platelet count — per mm^3	427,000	299,000	135,000	372,000	255,000
Prothrombin time — sec	13.3	13.4	14.4	12.8	15.2
Activated partial-thromboplastin time — sec	25.0	42.7	27.7	26.9	37.0
Fibrinogen — mg/dl	501	370	739	443	531
D-dimer — ng/ml	460	52	2230	13,800	1750
Ferritin — ng/ml	7	136	1564	987	596

* Reference ranges are as follows: platelet count, 150,000 to 450,000 per cubic millimeter; prothrombin time, 12.3 to 14.9 seconds; activated partial-thromboplastin time, 25.4 to 34.9 seconds; fibrinogen, 175 to 450 mg per deciliter; D-dimer, 0 to 500 ng per milliliter; and ferritin, 30 to 400 ng per milliliter. CT denotes computed tomography, CTA CT angiography, CTP CT perfusion, MRI magnetic resonance imaging, NA not applicable, PCR polymerase chain reaction, and t-PA tissue plasminogen activator.
† The patients were screened for smoking, hypertension, hyperlipidemia, diabetes, atrial fibrillation, congestive heart failure, illicit drug use, and neck trauma.
‡ Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher numbers indicating more severe stroke.

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Disclosure forms provided by the authors are available with the full text of this case at NEJM.org.

We dedicate this case to our inspiring colleague Gary Sclar, M.D., a neurologist who died of Covid-19.

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1. Li Y, Wang M, Zhou Y, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. March 13, 2020 (https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3550025) (preprint).
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