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Case 26-2020: A 60-Year-Old Woman with Altered Mental Status and Weakness on the Left Side

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PRESENTATION OF CASE

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Dr. Meridale V. Baggett (Medicine): A 60-year-old woman presented to this hospital with altered mental status during the pandemic of coronavirus disease 2019 (Covid-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The patient had been in her usual state of health until 1 week before admission, when cough and headache developed. One day before admission, vomiting and diarrhea developed. That day, the patient was last seen by her husband at 3:00 p.m. before she went to sleep. The husband reported that the patient awoke screaming at 1:00 a.m. on the day of admission, and emergency medical services (EMS) were called. When EMS personnel arrived, the patient was reportedly lethargic and unable to answer questions. The blood glucose level, obtained by fingerstick testing, was 60 mg per deciliter (3.3 mmol per liter; reference range, 70 to 110 mg per deciliter [3.9 to 6.1 mmol per liter]). Intravenous dextrose was administered. A repeat fingerstick glucose measurement was 127 mg per deciliter (7.0 mmol per liter), and the lethargy abated. The patient was brought by EMS personnel to the emergency department of this hospital.

In the emergency department, the patient reported weakness on the left side of her body and persistent headache. She reported that when she had awoken at 1:00 a.m., she was unable to move or speak, was afraid she was going to die, and began screaming for help. She reported no aura, urinary or fecal incontinence, or neck pain. She had recently moved from Puerto Rico and lived in a suburb of Boston. She did not speak English and was marginally housed, sleeping in the living room of a friend's apartment with her husband. Several people living in the apartment had had cough and fever.

The patient had a history of diabetes mellitus, hypertension, and schizophrenia. Medications included aspirin, glipizide, hydrochlorothiazide, lisinopril, and risperi-

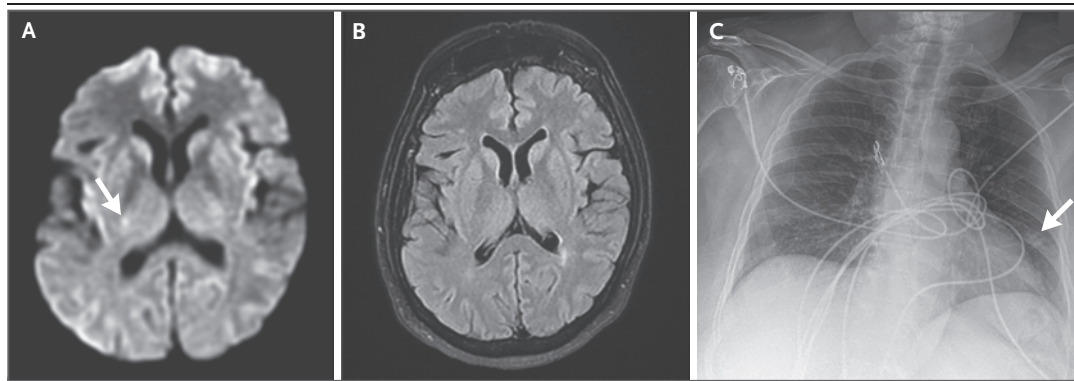


Figure 1. Imaging Studies of the Head and Chest.

MRI was performed 2 hours after presentation. A diffusion-weighted image (Panel A) shows a punctate focus of restricted diffusion within the posterior limb of the right internal capsule (arrow). No corresponding abnormality is observed on a T2-weighted fluid-attenuated inversion recovery image (Panel B). A chest radiograph (Panel C) obtained 2.5 hours after presentation shows a nodular focus in the left midlung field (arrow).

done. She had no known drug allergies. She drank alcohol occasionally and did not smoke tobacco or use illicit drugs.

On examination, the temperature was 37.4°C, the blood pressure 114/62 mm Hg, the heart rate 94 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 94% while the patient was breathing ambient air; the body-mass index (the weight in kilograms divided by the square of the height in meters) was 30.5. The patient was alert and interactive. She was oriented to person and place but not to time. The cranial-nerve examination was normal. Strength in the left arm and left leg was 4/5, and strength in the right arm and right leg was 5/5. She had difficulty manipulating small objects placed in the left hand. The left arm showed pronator drift and orbiting. Sensation to light touch was intact. The remainder of the physical examination was normal.

Dr. R. Gilberto Gonzalez: Magnetic resonance imaging (MRI) of the head was performed 2 hours after presentation. Diffusion-weighted images showed a punctate focus of restricted diffusion within the posterior limb of the right internal capsule; no corresponding abnormality was observed on fluid-attenuated inversion recovery images (Fig. 1A and 1B). A chest radiograph (Fig. 1C) obtained 2.5 hours after presentation showed a nodular focus in the left midlung field.

Dr. Baggett: A test of a nasopharyngeal swab for SARS-CoV-2 RNA was positive. Laboratory test results are shown in Table 1. The results of

urine toxicologic screening were normal. Treatment decisions were made, and the patient was admitted to the hospital.

DIFFERENTIAL DIAGNOSIS

Dr. Aneesh B. Singhal: This 60-year-old woman with hypertension, diabetes mellitus, and schizophrenia presented to this hospital with acute psychosis and focal neurologic deficits on the left side during the Covid-19 pandemic. One week earlier, she had begun to have headache and cough, and more recently, vomiting and diarrhea had developed; an initial evaluation confirmed the diagnosis of SARS-CoV-2 infection. Although infection with SARS-CoV-2 provides an explanation for her prodromal symptoms, could this patient's acute psychosis and weakness on the left side also be associated with Covid-19? Because our understanding of the clinical manifestations of SARS-CoV-2 infection is still evolving, it is important to consider other causes that may be contributing to her presentation.

BRIEF PSYCHOSIS

Could this patient's abrupt onset of screaming from the fear of dying and an inability to move indicate an episode of brief psychosis? Brief psychosis is usually precipitated by extreme life stress and can be a component of schizophrenia.¹ In this patient with schizophrenia, factors such as social isolation, insomnia, a language barrier, fear of the development of Covid-19, and

Table 1. Laboratory Data.*

Variable	Reference Range, Adults†	On Admission
Hematocrit (%)	36–46	36.7
Hemoglobin (g/dl)	12–16	12.1
White-cell count (per μ l)	4500–11,000	10,520
Differential count (per μ l)		
Neutrophils	1800–7700	9080
Lymphocytes	1000–4800	700
Monocytes	200–1200	700
Eosinophils	0–900	0
Platelet count (per μ l)	150,000–400,000	279,000
Prothrombin time (sec)	11.5–14.5	13.0
Prothrombin-time international normalized ratio	0.9–1.1	1.0
D-dimer (ng/ml)	<500	1263
Sodium (mmol/liter)	135–145	137
Potassium (mmol/liter)	3.4–4.8	4.2
Chloride (mmol/liter)	100–108	98
Carbon dioxide (mmol/liter)	23.0–31.9	24
Urea nitrogen (mg/dl)	8–25	56
Creatinine (mg/dl)	0.60–1.50	1.87
Glucose (mg/dl)	70–110	115
Ferritin (μ g/liter)	20–300	450
Lactate dehydrogenase (U/liter)	110–210	278
C-reactive protein (mg/liter)	<8	49.5
Creatine kinase (U/liter)	60–400	198

* To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

housing insecurity may have triggered psychosis.² However, brief psychosis associated with schizophrenia typically lasts more than 1 day, so it is unlikely to account for her altered mental status.

Hypoglycemia, which can manifest as psychosis,³ should be considered in this case, given the patient's development of lethargy and subsequent decrease in symptoms after the administration of dextrose. However, her glucose level was 60 mg per deciliter, and symptoms of hypoglycemia usually develop when the level drops

below 45 mg per deciliter (2.5 mmol per liter). Other metabolic or toxic encephalopathies can be ruled out on the basis of her prompt cognitive improvement and negative results of toxicologic screening.

Seizures can cause psychosis and may resemble schizophrenia.⁴ However, this patient had no history of seizures, and Covid-19 does not appear to increase the risk of seizure.⁵⁻⁷

NEUROPSYCHIATRIC MANIFESTATIONS OF COVID-19

Can this patient's apparent episode of psychosis be a manifestation of encephalitis associated with SARS-CoV-2 infection, resulting either from direct infection or from an immune, inflammatory, cytokine, or neural receptor-mediated mechanism?⁸ Coronaviruses primarily affect the lungs but have widespread systemic and cerebral effects. Neuropsychiatric symptoms have been associated with other coronavirus infections; hence, an association with Covid-19 would not be surprising.^{6,9} There is a long association between viral pandemics and psychiatric symptoms such as acute psychosis, delirium, insomnia, mania, depression, and suicidality. The medical literature from the time of the Russian (1889–1890) and Spanish (1918–1920) influenza pandemics is replete with reports of fearful experiences (e.g., “psychoses of influenza” and “influenza nervosa”).¹⁰ Similarly, von Economo's encephalitis (encephalitis lethargica) (1917–1928)¹¹ was associated with several neuropsychiatric features. Encephalitis remains a possible cause of this patient's brief psychosis, but I will also consider the diagnosis of stroke.

STROKE

The neuropsychiatric consequences of stroke, such as depression, are common and well recognized. Acute stroke can unmask latent symptoms of schizophrenia and infrequently can trigger psychosis, mania, delirium, hallucinations, delusions, and other neuropsychiatric syndromes such as Anton's syndrome, the Capgras syndrome, and the Cotard syndrome. Stroke-induced psychosis has been associated with lesions that affect the prefrontal and occipital cortexes and with disruption of neural networks resulting from subcortical lesions in the thalamus and basal ganglia (often on the right side),¹² as well as the midbrain, pons, and cerebellum.

Both encephalitis and stroke are possible

causes of the patient's brief psychosis. Can the patient's headache and focal neurologic deficits help narrow the differential diagnosis to the most likely diagnosis?

HEADACHE AND FOCAL NEUROLOGIC DEFICITS

In this patient with ongoing headache and focal neurologic deficits, we must consider the diagnosis of community-acquired bacterial meningitis.¹³ The absence of fever and of signs of meningeal irritation makes bacterial meningitis unlikely. Cerebrospinal fluid (CSF) analysis is required for diagnosis; however, lumbar puncture was not performed in this case, presumably because of the ability to promptly perform imaging of the head.¹³

Headache and cognitive changes are common in patients with viral encephalitis. Coronavirus infections, including SARS-CoV-2 infection, can cause meningitis, encephalitis, myelitis, and acute necrotizing encephalopathy, particularly in patients with moderate-to-severe illness.^{6,14}

Embolic stroke (especially to the middle and posterior cerebral arteries), lacunar stroke, cerebral arteriopathies, venous sinus thrombosis, and brain hemorrhages are all associated with headache. The 1-week duration of the patient's preceding headache with associated viral symptoms makes it unlikely that stroke was the cause of her headache. However, stroke cannot be ruled out as a cause of her focal neurologic symptoms. Headache disorders — such as migraine with aura, headache and neurologic deficits with CSF lymphocytosis (also known as the HaNDL syndrome), and familial hemiplegic migraine — are unlikely, given the absence of recurrent migraine headaches.¹⁵

CORRELATION OF CLINICAL AND IMAGING FINDINGS

Does the head imaging performed in the emergency department help us to determine the diagnosis in this case? MRI of the head revealed an acute brain lesion, effectively ruling out conditions that are often invoked in patients who previously had a stroke or psychiatric disease and now have new focal deficits (e.g., poststroke recrudescence [the reemergence of previous stroke-related deficits]¹⁶ and functional neurologic disorders¹⁷).

Brain lesions with restricted diffusion typically indicate stroke, but given this patient's

presentation, I will consider a broader differential diagnosis.¹⁸ Encephalitic and demyelinating lesions can have restricted diffusion, and demyelination has been reported in association with Covid-19–related encephalitis.^{6,14,19} However, demyelinating lesions are usually patchy and associated with leptomeningeal enhancement and moderate-to-severe respiratory illness, characteristics that are not consistent with those seen in this patient. Hypoglycemia can result in the development of lesions of diverse shapes, sizes, and locations that have restricted diffusion and may simulate lacunar infarction. However, lesions associated with hypoglycemia usually result in cerebral swelling, are reversible, and are most often associated with severe, prolonged hypoglycemia, which was not present in this patient.²⁰ Lesions with restricted diffusion can occur with migraine disorders²¹; however, this patient's headache shows no features of migraine,¹⁵ and lesions associated with migraine typically affect the posterior circulation and cross arterial territories. Seizure-induced lesions with restricted diffusion are unlikely in this patient, given that they usually develop after prolonged seizures or status epilepticus and typically appear in the cortical, hippocampal, or pulvinar region.²² Overall, the size and location of this patient's lesion with restricted diffusion, combined with the abrupt onset of hemiparesis, strongly support a diagnosis of acute ischemic stroke.

STROKE MECHANISM

This patient had pure motor hemiparesis, which is a classic lacunar stroke syndrome.²³ The punctate size of the lesion and its location in the contralateral posterior limb of the internal capsule in this patient with chronic hypertension suggest small-vessel disease (lipohyalinosis) as the mechanism of the stroke.

Other mechanisms are also possible. This patient was taking risperidone, which has been associated with stroke.²⁴ Primary angiitis of the central nervous system (CNS) and a reversible cerebral vasoconstriction syndrome are often invoked in patients with headaches and stroke; however, the clinical and imaging features of these entities were not observed in this patient.²⁵ Finally, cardiac and artery-to-artery embolism cannot be firmly ruled out without appropriate testing, although both seem unlikely on the basis of the clinical and imaging characteristics

favoring the presence of lipohyalinotic small-vessel disease.

STROKE AND COVID-19

Is there a relationship between this patient's stroke and Covid-19? Upper respiratory infections are known to trigger stroke; a case–cross-over study showed an odds ratio of 2.88 (95% confidence interval, 1.86 to 4.47) for stroke occurring within 15 days after a hospital visit for an influenza-like illness, as compared with the same calendar period 1 or 2 years before the stroke.²⁶ Emerging data suggest a much higher risk of stroke with Covid-19 than with influenza.²⁷ Multiple studies have reported on the frequency and characteristics of stroke in patients with Covid-19.^{5,6,28} Ischemic stroke appears to affect men and older adults with cardiovascular risk factors most frequently. Potential mechanisms of stroke associated with Covid-19 include coagulopathy, cardiac embolism due to myocardial injury, and nonadherence to medication, all of which may be common during this pandemic (Fig. 2). However, most patients with Covid-19 who had a stroke also had concurrent advanced systemic illness. This patient had mild viral illness at the time of stroke, and the D-dimer level at the time of admission was not markedly abnormal. It is conceivable that the small-vessel stroke resulted from viral endotheliitis or systemic inflammation, since her subacute headache and transient psychosis could be consistent with viral encephalitis. SARS-CoV-2 may invade the endothelium²⁹; in addition, it is associated with vasculitis,^{30,31} and pathological evidence indicates that SARS-CoV-2 RNA may be present within brain tissue.^{32,33}

In conclusion, this patient's brief psychosis was probably related to direct and indirect effects of SARS-CoV-2 infection, including the socioeconomic effect of Covid-19 in combination with underlying schizophrenia, and to the new infarct in the right hemisphere. The small-vessel stroke resulting from lipohyalinosis was probably triggered by Covid-19, although direct viral mechanisms cannot be ruled out.

DR. ANEESH B. SINGHAL'S DIAGNOSIS

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection resulting in acute psychosis and ischemic stroke.

Figure 2 (facing page). Stroke Subtypes and Mechanisms in SARS-CoV-2 Infection.

Coagulopathy and inflammation (black box) are central to thrombosis within cerebral blood vessels and cardiac embolism, the two major mechanisms of ischemic stroke in SARS-CoV-2 infection. Other possible mechanisms of stroke and sources of cardiac embolism are listed in the lighter boxes. Patients with SARS-CoV-2 infection may have a higher risk of stroke because of coexisting factors such as advanced age, cardiovascular disease, nonadherence to medications, and cerebral microvascular dysfunction. ACE2 denotes angiotensin-converting enzyme 2, and RAAS renin–angiotensin–aldosterone system.

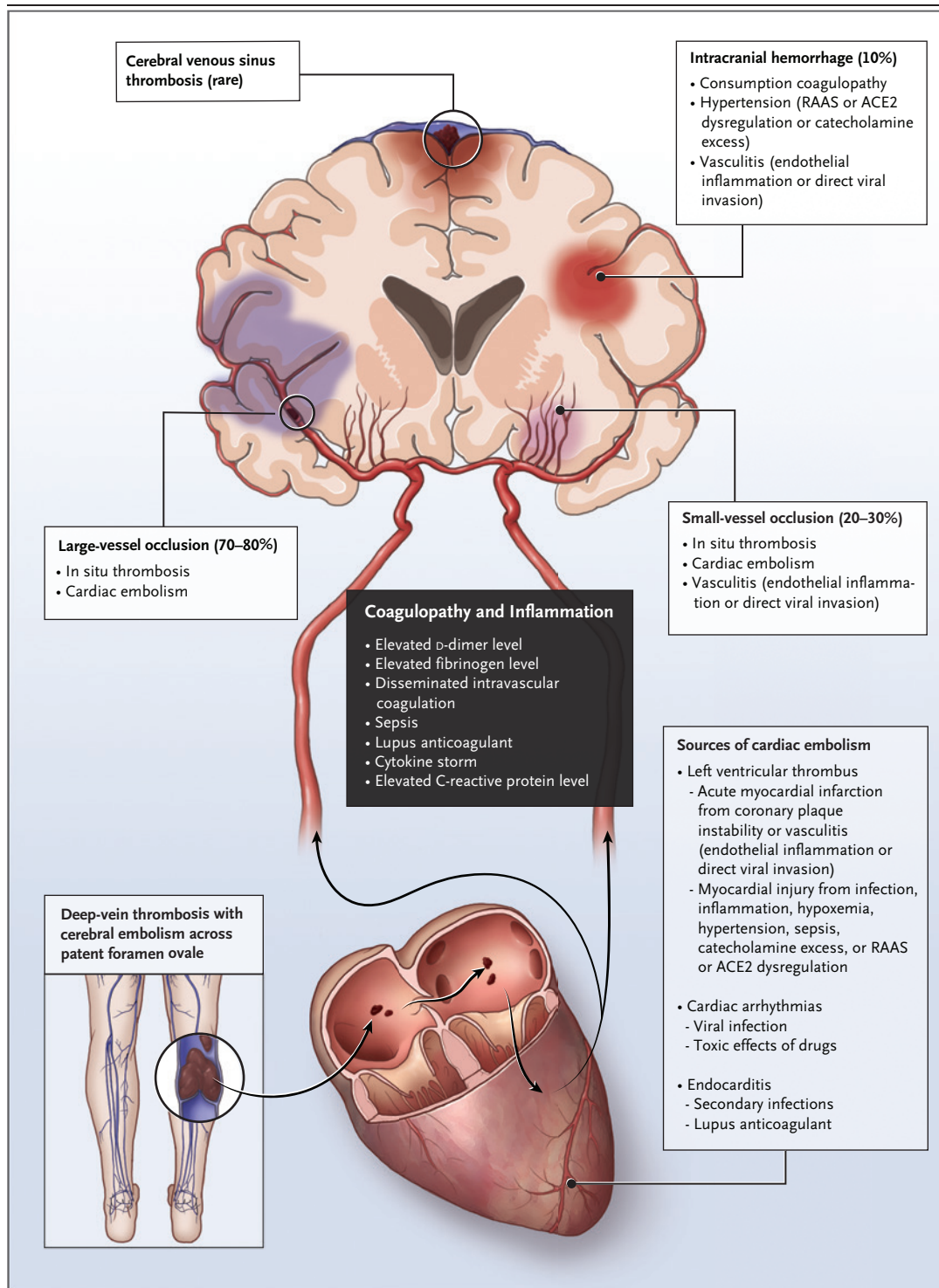
NEUROLOGIC ILLNESS ASSOCIATED WITH COVID-19

Dr. Bart K. Chwalisz: High rates of neurologic dysfunction have been reported in retrospective case series of Covid-19^{5,9,34} (Table 2). One can distinguish between minor neurologic symptoms that are important for diagnostic recognition and case finding and major neurologic disorders that can have an effect on a patient's risk of death and complications. The severity of neurologic findings does not necessarily correlate well with the criteria used for the classification of severity of Covid-19, which are based on features of the respiratory illness.

MINOR NEUROLOGIC SYMPTOMS OF COVID-19

Headache was one of the presenting symptoms in this patient. Minor neurologic symptoms — such as headache, anosmia, ageusia, dizziness, nausea and vomiting, and muscle aches — appear to be rather common, even in mild cases of Covid-19.^{34,37–39,48} The prevalence of neurologic symptoms was reported to be 36.4% in a retrospective series from China⁵ and 57.4% in a series from Spain.³⁴ However, these rates appear to be underestimations; more recently, much higher rates of smell and taste disturbances have been reported from other countries (Table 2). Neurologic symptoms such as headache may be early manifestations of Covid-19 that develop before any respiratory symptoms or abnormalities on chest imaging are present.⁵

Smell and taste disturbances, which appear to be particularly characteristic of Covid-19, even among patients who report no nasal obstruction, include anosmia, ageusia, parosmia, and phantosmia. This patient did not report smell disturbances, but she may have had a decreased



sense of smell at baseline, since odor discrimination can be decreased in patients with first-episode psychosis,⁴⁹ as well as in those with chronic schizophrenia.⁵⁰ In addition to the diagnostic importance of anosmia, the high rate of

this disorder in Covid-19 has led to speculation that the first cranial nerve could be a portal of entry into the CNS. Of note, the olfactory bulb has direct axonal connections to the medial temporal lobe, an area of the brain associated

Table 2. Reported Neurologic Manifestations of SARS-CoV-2 Infection.*

Manifestation	Percentage of Study Patients
Any neurologic manifestation	36.4% (Mao et al.) 57.4% (Romero-Sánchez et al.)
Decreased taste	5.6% (Mao et al.) 28.8% (Giacomelli et al.) 88% (Lechien et al.)
Decreased smell	5.1% (Mao et al.) 23.7% (Giacomelli et al.) 85.6% (Lechien et al.)
Muscle injury or myalgias	10.7% (Mao et al.) 17.2% (Romero-Sánchez et al.) 23.8% (Goyal et al.) 34.8% (Wang et al.) 44% (Huang et al.)
Dizziness	6.1% (Romero-Sánchez et al.) 16.8% (Mao et al.)
Headache	13.1% (Mao et al.) 14.1% (Romero-Sánchez et al.)
Neuropsychiatric disorder (delirium, agitation, or dysexecutive syndrome) or impaired consciousness	7.5% (Mao et al.) 69% (Helms et al.)
Stroke	2.8% (Mao et al.) Present in case series (Oxley et al.)
Nerve pain	2.3% (Mao et al.)
Vision disturbance or optic neuritis	<1% (Romero-Sánchez et al.) 1.4% (Mao et al.)
Ataxia or movement disorder	<1% (Mao et al. and Romero-Sánchez et al.)
Seizure	<1% (Mao et al., Lu et al., and Romero-Sánchez et al.)
Guillain-Barré syndrome, Miller Fisher syndrome, or ophthalmoparesis	Present in case report (Zhao et al.) and case series (Toscano et al., Gutiérrez-Ortiz et al., and Dinkin et al.)
Acute necrotizing encephalopathy	Present in case report (Poyiadji et al.)
Meningoencephalitis	Present in case report (Moriguchi et al.)
Myelitis	Present in case report (Zhao et al.) Present in case report (Sotoca et al.)

* The study by Mao et al.⁵ (conducted in China) included 214 patients, Romero-Sánchez et al.³⁴ 841 patients, Giacomelli et al.³⁵ (an inpatient study) 59 patients, Lechien et al.³⁶ (an outpatient study) 417 patients, Goyal et al.³⁷ 393 patients, Wang et al.³⁸ 138 patients, Huang et al.³⁹ 41 patients, Helms et al.⁶ 58 patients, Oxley et al.⁴⁰ 5 patients, Lu et al.⁷ 304 patients, Zhao et al.⁴¹ 1 patient, Toscano et al.⁴² 5 patients, Gutiérrez-Ortiz et al.⁴³ 2 patients, Dinkin et al.⁴⁴ 2 patients, Poyiadji et al.⁴⁵ 1 patient, Moriguchi et al.⁴⁶ 1 patient, and Sotoca et al.⁴⁷ 1 patient.

with psychosis. However, it appears that, in most cases, anosmia is a transient symptom that resolves within a week.⁵¹ The rapid resolution suggests that anosmia may be mediated by a transient dysfunction of the olfactory epithelium

rather than by neuronal destruction. Indeed, an analysis of gene expression patterns in various cell types of the upper respiratory epithelium showed that olfactory sensory neurons lack angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) — proteins that have been shown to facilitate SARS-CoV-2 infection. However, these proteins are expressed in supportive cells of the olfactory epithelium, such as basal cells, sustentacular cells, and secretory cells.⁵² Thus, the common occurrence of anosmia among patients with Covid-19 should not be taken as *prima facie* evidence of invasion of the CNS by SARS-CoV-2. However, in at least one case, radiologic changes in the olfactory bulb and gyri recti have been reported, findings that merit further study.⁵³

MAJOR NEUROLOGIC SYMPTOMS OF COVID-19

Major neurologic symptoms of Covid-19 include CNS disorders such as encephalopathy, stroke, and myelopathy, as well as severe neuromuscular disturbances such as rhabdomyolysis,⁵⁴ the Guillain-Barré syndrome,^{55,56} and cranial-nerve dysfunction.^{43,44}

In a retrospective series of patients with Covid-19, neurologic symptoms were reported in 45.5% of the patients with severe infection.⁵ As compared with patients who had milder illness, the patients with severe illness were older and more likely to have underlying disorders such as hypertension; they also had fewer typical symptoms of Covid-19, such as fever or cough, but were more likely to have multiorgan involvement such as liver-function abnormalities, impaired renal function, or elevated creatine kinase levels.⁵ In this series, impaired consciousness was present in 14.8% of the patients with severe Covid-19 and stroke in 5.7%.⁵

In a series of 58 consecutive patients with Covid-19 and acute respiratory distress syndrome in France, 14% had neurologic findings on admission, but 67% had neurologic findings when sedation and neuromuscular blockade were discontinued; findings included agitation, delirium, and corticospinal tract signs such as hyperreflexia, clonus, and extensor plantar reflexes.⁶ A dysexecutive syndrome was present in 33% of the patients at discharge.

Vascular dysfunction is prominent in severe Covid-19, as evidenced by elevated levels of D-dimer

and procoagulant factors. Thromboembolic complications, including stroke, are common.⁵⁷

There are case reports of additional clinically significant neurologic presentations in Covid-19, including a case of meningoencephalitis associated with Covid-19 (with the detection of SARS-CoV-2 nucleic acids in the CSF),⁴⁶ a case of acute necrotizing encephalopathy,⁴⁵ and two case reports of myelitis.^{41,47}

Putative mechanisms of neurologic dysfunction in severe Covid-19 include direct neuroinvasion, endothelial dysfunction, and a neurotoxic effect from exuberant inflammation and cytokine release. Unfortunately, neuropathological confirmation of any of those mechanisms is currently lacking.

DISCUSSION OF PATHOPHYSIOLOGY

Dr. Shibani S. Mukerji: Human coronaviruses are large, positive-sense, single-stranded RNA viruses, of which the betacoronavirus genus has been responsible for human disease outbreaks during the past 20 years.⁵⁸ Although betacoronaviruses are known to cause neurologic illness in some people, there is limited understanding about the breadth of neurologic effects associated with SARS-CoV-2 and the potential entry of the virus into the CNS. In SARS-CoV infections, autopsy specimens of the brain show the presence of the SARS-CoV nucleocapsid protein in the cytoplasm of neurons in the hypothalamus and cortex on immunohistochemical analysis,⁵⁹ and viral particles are seen on electron microscopy.⁶⁰ Low levels of SARS-CoV-2 RNA were recovered from brains in two autopsy case series, although the presence of SARS-CoV-2 has not yet been identified in neuronal, glial, or endothelial cells in the CNS.^{32,33}

SARS-CoV is structurally most similar to SARS-CoV-2, and both use the ACE2 receptor to gain entry into cells.⁵⁸ In animal models, ACE2 protein is expressed in multiple tissue types, including that of the lung, gastrointestinal tract, and lymph nodes, as well as in endothelial and smooth-muscle cells. In murine brain tissue, basal ACE2 protein expression is widespread, and the highest levels of expression are found in the primary and secondary motor cortex, caudate nuclei, medullary nuclei, and circumventricular organs.⁶¹ Although ACE2 messenger RNA (mRNA) expression is low in the human brain relative to

renal, gastrointestinal, and cardiovascular tissues, expression can be seen in the cerebellum, hippocampus, cortex, hypothalamus, substantia nigra, and medullary nuclei. Interestingly, mRNA has been identified in the choroid plexus and middle cerebral artery,⁶² and in an autopsy series of three cases in humans, ACE2 protein expression was limited to the endothelium and vascular smooth-muscle cells.⁶³ Although SARS-CoV-2 uses the surface protease TMPRSS2 as a coreceptor for spike protein priming, TMPRSS2 has minimal expression in the brain.⁶⁴ Given our limited understanding of SARS-CoV-2 in the CNS, including the mechanisms of neuronal infection, there is a critical need for integrating brain and spinal-cord autopsy findings with comprehensive clinical details to improve our understanding of virus–host interactions.

DISCUSSION OF MANAGEMENT

Dr. Singhal: This patient had relative contraindications to treatment with intravenous tissue plasminogen activator and to mechanical thrombectomy (including mild deficit 10 hours after she was last seen well, and the potential for infection-related stroke). Because of her mild, stable symptoms and the challenges with performing imaging in the context of Covid-19, urgent computed tomography of the head was deferred and MRI of the head was performed within 2 hours after presentation. Once infarction was confirmed, treatment with clopidogrel was added to her current aspirin regimen on the basis of evidence that short-term dual antiplatelet treatment is beneficial in patients with minor stroke.⁶⁵

Atorvastatin was initiated for stroke prevention. Despite theoretical concerns about the safety of ACE inhibitors in patients with Covid-19, treatment with lisinopril was continued in accordance with recent guidance.⁶⁶ Risperidone treatment was continued, since the benefit outweighed known risks in patients who have had a stroke, and low-molecular-weight heparin was administered to prevent deep-vein thrombosis.

FOLLOW-UP

Dr. Baggett: On hospital day 5, tachypnea and fever developed in the patient. A chest radiograph showed bilateral multifocal patchy hazy

and patchy consolidative opacities with peripheral predominance in the middle and lower lung zones. Ceftriaxone and azithromycin were administered. Supplemental oxygen was not initiated. The patient's hospital course was further complicated by delirium, and she was treated with olanzapine and quetiapine. Her condition improved, and she was discharged to a rehabilitation facility on hospital day 14.

FINAL DIAGNOSIS

Brief psychosis and small-vessel cerebral infarction, probably related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

This case was presented virtually at Neurology Grand Rounds during the Covid-19 pandemic.

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

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