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Case report

Cervical spinal cord infarction associated with coronavirus infectious disease (COVID)-19

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ABSTRACT

Coronavirus disease (COVID-19) has a number of emerging neurological manifestations in addition to pneumonia and respiratory distress. In what follows, we describe a case of a previously healthy young man with severe COVID-19 who subsequently developed an acute flaccid paralysis. Work up revealed a lesion in his cervical spinal cord concerning for spinal infarction or transverse myelitis. He received empiric pulsed steroids without improvement. Taken together, we felt his presentation was most consistent with spinal cord infarction in the setting of critical illness with COVID-19. We believe this is a rare case of spinal cord stroke associated with COVID-19.

1. Case report

Coronavirus disease (COVID-19), has variable manifestations in the critical illness phase beyond acute respiratory distress syndrome including neurologic manifestations [1,2] and a marked hypercoagulable state [3]. Clinical manifestations of the hypercoagulable state may include venous thromboembolic disease; thrombosis of arterial monitoring and venous dialysis access catheters; and cerebral infarction [4]. Laboratory evaluation often demonstrates elevated pro-inflammatory biomarkers including serum concentrations of C-reactive protein, D-dimer, fibrinogen, and interleukin-6, among others [5,6]. We report a case of cervical spinal cord infarction and flaccid quadriparesis associated with COVID-19 disease.

A 31 year-old male with no known medical history was admitted to a network inpatient facility with eight days of an acute respiratory illness, which was confirmed by reverse transcriptase polymerized chain reaction of a nasal swab sample to be COVID-19. On hospital day (HD) 6, he was intubated for worsening respiratory failure and transferred to our facility the next day. His vital signs upon admission were T 35.6 °C, HR 126 beats/min, BP 147/93 mm Hg, and RR 18 breaths/min. Neurologic examination revealed spontaneous movement of all four extremities, with no focal findings. There were no other abnormalities on physical examination. Laboratory data are shown in Table 1. Previous undiagnosed diabetes mellitus was identified (hemoglobin A1c, 12.7%). Hypercoagulability was confirmed by rotational thromboelastometry (ROTEM) [7]. Blood cultures and duplex ultrasonography of the lower extremities were normal.

Once admitted to our ICU the patient was started on enoxaparin 80 mg subcutaneously every 12 h for aggressive thromboprophylaxis [8]. Desired anti-coagulation was confirmed by an anti-factor Xa concentration of 0.7 IU/mL (therapeutic range, 0.5–1.0 IU/mL) on HD 9. Over the following four days mechanical ventilation, vasopressor therapy, and sedation were weaned. There was an isolated recorded blood pressure of 60/37 on HD 8, however on detailed chart review this was reversed with increasing vasopressors within moments. Blood pressure was otherwise consistently at target. The patient moved all extremities during daily sedation holidays. On the morning of HD 12 the patient was unable to move his lower extremities and endorsed absent sedation below the nipples. Up to that point, he had maintained oxygen saturation > 90% and was normotensive. Formal neurologic evaluation revealed that cranial nerves were intact except for multirotational nystagmus. Sensation to light touch and pinprick were intact above the nipples, but absent caudally. The sensory level was at the T4 dermatome. Power of the upper extremities was present but

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Table 1
Laboratory Values Reflective of Pro-Inflammatory State. HD, Hospital day; ESR, erythrocyte sedimentation rate.

Parameter (normal value)	HD 7	HD 12
C-reactive protein (<0.9 mg/dL)	1.3	<0.4
D-dimer (0–229 ng/mL)	1,952	619
ESR (0–20 mm/hr)	63	74
Fibrinogen (180–400 mg/dL)	699	348
Interleukin-6 (<5 pg/mL)	916	43
Lactate dehydrogenase (118–230 U/L)	618	356
Partial thromboplastin time (27.6–36.6 sec)	39.2	50.0
Prothrombin time (9.9–12.5 sec)	13.2	11.4
Platelet count (150–450 × 103/mL)	335	265
White blood cell count (3.4–11.2 × 103/mL)	11.5	9.4

diminished bilaterally (bilateral deltoid muscle 2/5, bilateral triceps muscle 2/5, right biceps muscle and wrist extensors 2/5, left biceps muscle and wrist extensors 3/5, bilateral hand grip 1/5). Power of the lower extremities was absent bilaterally (0/5, flaccid paralysis). He was areflexic except for a weak left biceps tendon reflex. Plantar responses were mute. Clonus was absent. Using the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), the upper extremity motor sub-score was 17/50, lower extremity motor sub-score was 0/50, sensory subscores were 44/112, and the American Spinal Injury Association Impairment Scale was A.

Additional serum laboratory values included elevated beta-2 microglobulin (2.6 mg/L; normal range, 1.2–2.4 mg/L), normal immunoglobulin A (227 mg/dL; normal range 85–499 mg/dL), normal ganglioside Gm1 antibody (IgG) (5 IU; normal range 0–50 IU) and ganglioside Gm1 antibody (IgM) (16 IU; normal range 0–50 IU); aquaporin-4 IgG and myelin oligodendrocyte glycoprotein (MOG) IgG were undetectable. Magnetic resonance imaging (MRI) of the spinal cord with and without gadolinium (Fig. 1) revealed pronounced T2 hyperintensity and enhancement of the cervical spinal cord spanning C4 through C6 with corresponding restricted diffusion and patchy enhancement mostly within the central gray matter, highly concerning for acute-to-subacute spinal cord infarction. Intramedullary edema surrounded the area of infarction extending from the cervico-medullary junction, predominantly involving the dorsal columns, and extending caudally to T1, where it involved predominantly the central gray matter. Lumbar puncture and MRI of the brain were not performed acutely in the interest of infection control. Despite negative serology, differential diagnosis also included neuromyelitis optica spectrum disorder, MOG antibody associated demyelination, sarcoidosis or a viral transverse myelitis. Given the possibility of a potentially reversible inflammatory process, the patient received methylprednisolone 1 g daily for 5 days, but without improvement. Considering the clinical course, serologies and imaging, we felt the most likely diagnosis was spinal cord infarction. He required tracheostomy for ventilator dependence and gastrostomy for nutritional support.

As in sepsis generally, COVID-19 disease is characterized by interactions between inflammatory and coagulation cascades [5], but the hypercoagulable state associated with COVID-19 disease is distinct from the typical hypocoagulable state of bacterial sepsis, which is associated with thrombocytopenia. Therapeutic anticoagulation has been advocated in view of recent observations of pathologic clotting in COVID-19 [9,10], and a suggestion of a survival benefit for critically ill patients [10]. Neurologic associations with COVID-19 are numerous, including both central and peripheral neurologic symptoms [2–4]. The distribution of cord injury in this case does not conform to classically described vascular distributions of the anterior or posterior spinal arteries, and instead is in central "watershed" areas. This pattern is usually associated with prolonged hypotension in the setting of cardiac arrest [11]. A case series (n = 60) comparing MRI features of spinal infarcts and inflammatory lesions secondary to neuromyelitis optica spectrum disorder suggest that while anterior cord predominance is more consistent with infarct, of the 39 patients with infarcts, 24 had central cord imaging changes on axial slices [12]. Moreover, longitudinally extensive T2 hyperintensity has been observed in the setting of spinal cord infarction, and is attributed to secondary vasogenic edema can be seen in the brain [13]. Of note, the presence of diffusion restriction is not specific for infarct, and it has been seen with inflammatory etiologies [14].

It should be highlighted that because CSF analysis was not performed due to infection control practices at the time, there remained significant clinical uncertainty to justify a trial of high dose steroids. The lack of clinical improvement following steroids is more suggestive of a cord infarct, but not conclusive. Spinal cord pathology associated with the Covid-19 pandemic has included primary spinal epidural abscesses [15], two published case reports of acute myelitis [16,17] - both of which showed neurological improvement with high-dose steroids, and two cases of possible infarction [18].

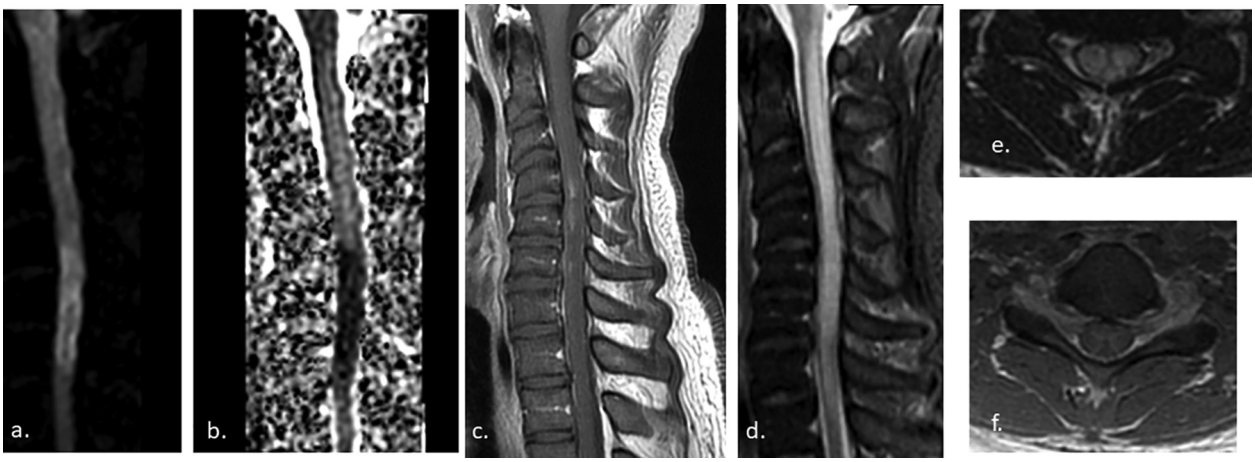

Fig. 1. MRI of the cervical spine. (a) Sagittal DWI and (b) ADC demonstrate restricted diffusion extending from C4 through C6. (c) Sagittal T1-weighted imaging with gadolinium and (f) axial T1-weighted imaging with gadolinium demonstrate corresponding stippled enhancement, predominantly within central gray matter. (d) Sagittal STIR and (e) axial T2-weighted imaging demonstrate T2 hyperintensity extending from the cervicomedullary junction to the level of the T1 vertebral body.

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.

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