Stridor Due to Cranial Nerve X Palsy Progressing to Polyneuropathy in a Teenager With COVID-19

Andrea Dean, MD,a Amira Said, MD,a Kavitha Marri, MD,a Daniel Chelius, MDb

The neurologic manifestations of coronavirus disease 2019 (COVID-19) are wide-ranging, including various cranial neuropathies, beyond anosmia and dysgeusia, the exact neuropathological mechanism of which are yet unknown. Acute cranial nerve (CN) X neuritis with vocal cord paralysis has not been reported in COVID-19 and is a rare presentation of neuropathy in general. A girl aged 14 years was admitted with stridor. She was diagnosed with symptomatic COVID-19 8 days before. By presentation, fever had resolved, but she had developed stridor; sore throat with dysphagia; chest, shoulder, and back pain; and generalized weakness. Neurologic examination and laryngoscopy were consistent with isolated left CN X palsy. Steroids were started, but neurologic disease progressed with subjective pain, right lower face numbness, and eye fatigability. Respiratory distress increased, and she was intubated for airway protection. MRI revealed abnormal enhancement of CNs III, V, XII, and X. Cerebrospinal fluid studies were normal. Nasopharyngeal severe acute respiratory syndrome coronavirus 2 polymerase chain reaction test result was positive. She was treated with intravenous immunoglobulin, a total of 2 g/kg, and steroids were continued. She made a full neurologic recovery and was discharged after 9 days of hospitalization. This is a case of a teenager who presented with an acute, life-threatening CN X palsy and development of a progressive polyneuropathy in the setting of COVID-19. Although there was concern for Guillain-Barre syndrome, a definitive diagnosis could not be made, and the unusual features of this case, including presentation with stridor and predominate CN involvement seem to indicate a separate symptomatic COVID-19–associated polyneuritis.
unlike other isolated cranial neuropathies, has not been described in association with COVID-19. She developed progressive focal neurologic symptoms with involvement of multiple CNs on imaging. She was treated for presumed GBS pharyngeal-cervical-brachial (PCB) variant, but a definitive GBS diagnosis could not be made, and a COVID-19–associated polyneuritis was suspected. We discuss her challenging diagnosis, which illustrates the need for further investigation of the neuropathogenic mechanism of SARS-CoV-2 and urges clinicians to remain vigilant as our understanding of COVID-19 morbidities expands.

PRESENTATION
A girl aged 14 years with obesity presented to the emergency center (EC) with difficulty breathing. Eight days before presentation, she developed fever, malaise, myalgias, sore throat, and cough and was diagnosed with COVID-19 by polymerase chain reaction (PCR). On day 4 of illness, she sought care for shortness of breath at a community EC and was treated with albuterol and prednisone 20 mg daily for 3 days without improvement of difficulty breathing. By the day of presentation to the EC, her fever had resolved, but breathing had become more difficult and increasingly noisy. Her sore throat had worsened with swallowing difficulty. She had bilateral shoulder, chest, and upper back pain and reported generalized weakness. She denied ageusia and anosmia, vision changes, sensory deficit, facial asymmetry, or gastrointestinal symptoms.

In the EC, she was afebrile, with oxygen saturation 99% on room air and tachypnea to 26 breaths per minute. Vital signs were otherwise normal. BMI was 35. Her examination was remarkable for biphasic stridor with mild tracheal tugging on each breath, and she was not distractible. Lungs were otherwise clear. Oropharynx revealed mild erythema without exudate. Neck was supple without lymphadenopathy. She had diffuse tenderness to palpitation over the ribs, shoulders, and upper back. Mentation was normal.

Nasopharyngeal SARS-CoV-2 PCR test result was positive. Chest radiograph and electrocardiogram were unremarkable. She showed no improvement after dexamethasone, albuterol, ipratropium, or nebulized epinephrine and was admitted to the Pediatric Hospital Medicine service. Otolaryngology performed bedside flexible nasolaryngoscopy, which revealed a paretic and medialized left vocal fold that only abducted with cough. The right vocal fold seemed normal by comparison but, on post hoc video review, was likely also weaker than normal (Fig 1).

The following day, neurologic examination revealed intact cognitive function and language. The patient complained of extremity weakness, but objective tone and strength were normal in all extremities. Reflexes were normal. There was decreased sensation to light touch on the left lower extremity. Coordination was intact. CNs I to IX, XI, and XII were intact.

These findings were most consistent with isolated left CN X palsy. Neurology, otolaryngology, and Pediatric Hospital Medicine agreed on treatment with steroids, and the patient was started on dexamethasone 10 mg orally every 8 hours for 24 hours and, subsequently, switched to methylprednisolone intravenously 80 mg daily.

Over the next 24 hours into hospital day 3, stridor persisted with otherwise stable respiratory status, including negative inspiratory force (NIF) of $-85 \text{ mm Hg}$ and normal oxygen saturations. However, she described increasing weakness of her upper and lower extremities, as well as “shooting” and “stinging” pains mostly in her upper extremities with sensitivity to touch, different from the myalgias she experienced earlier in her COVID-19 illness. She had numbness of right lower face and complained of eye fatigability in which she “lost focus” and had to close her eyes when holding horizontal gaze, although
denied diplopia at the time. She also described a sense of impending doom. As intensified evaluation was underway, she attempted to lay flat in anticipation of an MRI and developed acute respiratory distress with tachypnea and decreased NIF to \(-20 \text{ mm Hg}\). She was sedated and intubated by otolaryngology with direct visualization of her airway, which revealed bilateral medialized vocal folds and no other anatomic obstruction.

Complete blood cell count, complete metabolic panel, sedimentation rate, and C-reactive protein were unremarkable. SARS-CoV-2 antibody panel was immunoglobulin M-positive and immunoglobulin G-negative.

Subsequent brain MRI revealed abnormal enhancement bilaterally in CNs III, V, VII, and X (Fig 2). There was equivocal enhancement of the left olfactory bulb without enlargement. There was mild swelling of the right hippocampal head with abnormal T2 signal. Spinal MRI revealed equivocal faint enhancement of the ventral and dorsal cauda equina nerve roots without thickening and with no additional signal abnormality in the spinal canal (Fig 3).

Cerebrospinal fluid (CSF) examination revealed an opening pressure of 32 cm H2O, likely increased because of sedation and ventilation. CSF was clear, with white blood cell count of 2 (lymphocyte and monocyte), red blood cell count of 1, protein level of 37 mg/dL, albumin level of 18.4 mg/dL, glucose level of 69 mg/dL, and sterile cultures. Viral and bacterial PCR test results were negative, but SARS-CoV-2 testing of CSF was unavailable. CSF demyelinating panel (AQP4 and MOG), autoimmune encephalopathy panel, and CSF antiganglioside antibody panel (GM1, GD1b, and GQ1b) were all negative except mild elevated glutamic acid decarboxylase 65 antibody level of 0.09 mmol/L (normal is <0.02 mmol/L), which was considered insignificant because the finding is prevalent in general population and the profile did not align with her clinical findings.

The patient was continued on methylprednisolone 80 mg daily for acute COVID-19-associated neuritis. Intravenous immunoglobulin (IVIG) was initiated for treatment of GBS, possible PCB variant, which was considered because of development of hyporeflexia in upper extremities after sedation and intubation taken in conjunction with subjective weakness before intubation. Areflexia was never noted throughout her 3-day intubation. Immediately postextubation, she had resolution of her stridor, although laryngoscopy revealed ongoing mild adduction of the left vocal cord. She reported diplopia on horizontal gaze bilaterally and ongoing decreased sensation on lower right face. Neurologic examination did not identify other CN palsy; the remainder of examination was normal, including strength and reflexes.

She completed a 5-day course of IVIG 40 g daily and remained on methylprednisolone 80 mg intravenously daily throughout hospital admission, with an oral prednisone taper at discharge. She was discharged after a 9-day inpatient stay with resolution of focal neurologic symptoms. At outpatient otolaryngology follow-up 10 days after discharge,
nasolaryngoscopy was normal (Fig 4). She reported ongoing fatigability. At 4-week neurology follow-up, she was back to baseline with full recovery.

DISCUSSION

This is a case of a progressive polyneuritis involving CNs in a teenager with acute SARS-CoV-2 infection. Early in her illness, CN X palsy, causing stridor, appeared to be isolated. Cranial neuropathies during COVID-19 infection are common, most notably, anosmia and dysgeusia, which can occur in otherwise asymptomatic persons. Isolated optic neuritis, acute sensorineural hearing loss, vestibular neuritis, CN III palsy, and CN VI palsy, as well as postmortem CN X involvement, have been reported. Despite these reports, there was little guidance on treatment of this patient’s potentially life-threatening CN X palsy, which is rare outside of direct disturbance of the nerve. Methylprednisolone dosing was derived from case reports of COVID-19-associated cranial neuropathies and recommendations for Bell’s palsy, a common but incompletely understood neuropathy of CN VII presumed to have a viral trigger. However, it should be noted that the patient worsened despite steroid treatment.

After an initial period of stability, she complained of worsening symptoms, which, despite a lack of objective findings, were concerning in the setting of her life-threatening neuropathy of poorly understood etiology. Neuroimaging revealed involvement of the oculomotor, trigeminal, and vagus nerves, which was consistent with eye fatigability and eventual diplopia, facial numbness, stridor, and dysphagia. She did not have facial weakness or anosmia corresponding with facial nerve or olfactory bulb enhancement. CN enhancement in the absence of corresponding symptoms has been described in children with suspected COVID-19.

The extent of peripheral nerve involvement in our patient’s process remains unclear. Her decreased NIF was thought to reflect upper airway obstruction and decreased effort secondary to anxiety, as opposed to weakness of inspiratory muscles. However, hyperalgesia suggestive of
neuropathic pain, as well as her weakness and hyporeflexia, may point to early peripheral nerve involvement. However, weakness was not objective, and her hyporeflexia was seen only after sedation.

The patient’s imaging, in conjunction with reported upper-extremity weakness and hyporeflexia, triggered concern for GBS PCB variant. PCB is characterized by acute weakness of the oropharyngeal, neck, and shoulder muscles with swallowing dysfunction, and presentations can be atypical.33-36 However, in retrospect, her constellation of signs and symptoms were not consistent with GBS, including polyneuritis cranialis or overlapping variants.37,38 Notably, she did not have cytoalbuminoligic dissociation or antiganglioside antibodies in her CSF, although these findings can be absent, especially early in the disease course,39 such as when our patient’s investigation took place. Her diagnosis may have been delineated by electrodiagnostic studies, and this case study is limited by their absence. Ultimately, at the time of respiratory failure, GBS could not be excluded and triggered treatment with IVIG. However, steroids, which play no role in the treatment of GBS, were continued throughout her illness.

Although the tendency for SARS-CoV-2 to affect a variety of CNs is now recognized, this patient’s unusual presentation with stridor due to CN X palsy represents a previously undescribed neurologic manifestation of COVID-19. Although variants of GBS deserve consideration, a non-GBS polyneuritis is more likely and is consistent with other reports of COVID-19–associated cranial neuropathies.6,9 This case, including her ultimately imprecise diagnosis, illustrates the lack of understanding of the pathogenic mechanisms of SARS-CoV-2 neurologic dysfunction. Importantly, her acute presentation with isolated, symptomatic CN X palsy, which is rare and required life-saving interventions even after a period of stability, serves as reminder that clinicians must remain vigilant for unique manifestations and unpredictable illness progression of COVID-19.

ACKNOWLEDGMENT
We thank Brandon Tran, MD, Department of Radiology, Baylor College of Medicine.

ABBREVIATIONS
CN: cranial nerve
COVID-19: coronavirus disease 2019
CSF: cerebrospinal fluid
EC: emergency center
GBS: Guillain-Barre syndrome
IVIG: intravenous immunoglobulin
NIF: negative inspiratory force
PCB: pharyngeal-cervical-brachial
PCR: polymerase chain reaction
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

REFERENCES
16. Greer CE, Bhatt JM, Oliveira CA, Dinkin MJ. Isolated cranial nerve 6 palsy in 6


