Neurologic complications of COVID-19 are not well described. We report 2 patients who were diagnosed with COVID-19 after presenting with diplopia and ophthalmoparesis.

Case 1
A 36-year-old man with a history of infantile strabismus presented with left ptosis, diplopia, and bilateral distal leg paresthesias. He reported subjective fever, cough, and myalgias which had developed 4 days earlier and resolved before presentation. Examination was notable for left mydriasis, mild ptosis, and limited depression and adduction, consistent with a partial left oculomotor palsy. Abduction was limited bilaterally consistent with bilateral abducens palsies (figure, A). Lower extremity hyporeflexia and hypesthesia, and gait ataxia were noted. WBC was 2.9 × 10^3/μL with an absolute lymphocyte count of 0.9 × 10^3/μL. Nasal swab for SARS-CoV-2 PCR was positive. MRI revealed enhancement, T2-hyperintensity, and enlargement of the left oculomotor nerve (figure, B–D). Chest radiograph was unremarkable. The next day, there was worsening left ptosis, complete loss of depression and horizontal eye movements on the left and loss of abduction on the right. The patient received IV immunoglobulin (2g/kg over 3 days) to treat presumed Miller Fisher syndrome and hydroxychloroquine for COVID-19 (600 mg twice a day for 1 day, followed by 400 mg daily for 4 days). Deficits improved partially before discharge 3 days after admission. A ganglioside antibody panel was negative.

Case 2
A 71-year-old woman with hypertension presented with painless diplopia on waking 2 days before and could not abduct her right eye (figure, E). Visual acuity, pupils, and funduscopy were normal. She reported cough and fever for several days. She was sent to the emergency department, where she was febrile and hypoxemic. WBC was 9.2 × 10^3/μL with an absolute lymphocyte count of 0.5 × 10^3/μL. Lumbar puncture was normal with opening pressure of 16 cm H2O. MRI showed enhancement of the optic nerve sheaths and posterior Tenon capsules (figure, F and G). Chest radiograph revealed bilateral airspace opacities (figure H), and nasal PCR for SARS-CoV-2 was positive. Her COVID-19 pneumonia was treated with hydroxychloroquine (dosing as above). Her abduction palsy did not improve significantly before discharge on room air after a 6-day admission. She reported gradual improvement of diplopia when contacted by phone 2 weeks after discharge.

Discussion
We describe 2 patients who developed cranial neuropathies within days of respiratory symptoms related to SARS-CoV-2 infection and were found to have abnormal perineural or cranial nerve findings on MRI. To reduce the risk of transmission, workup was limited to the essential studies needed to determine management.
In a retrospective review of 214 patients with COVID-19 in Wuhan, China, 36.5% had neurologic symptoms, which were more common in patients with severe disease. Most were nonspecific symptoms common in viral infections such as headache and dizziness, but 5.7% presented with acute cerebrovascular disease. The occurrence of hypogeusia and anosmia suggests olfactory bulb involvement, which has been proposed as a mechanism of entry into the nervous system. COVID-19 encephalitis with positive SARS-CoV-2 PCR in the CSF and acute necrotizing brainstem encephalopathy have been reported. CNS manifestations were more prevalent in patients with lymphopenia, as seen in our patients. CNS entry of SARS-CoV-2 may depend on viral interaction with membrane-bound ACE2 receptor, which is expressed not only in nasal and oral mucosa but also in the nervous system, and SARS-CoV-2 appears to have a 10- to 20-fold higher affinity than SARS-CoV for the ACE2 receptor. Notably, neither patient had a history of ACE inhibitor use.

The combination of ophthalmoparesis, leg paresthesia, and areflexia in our first case suggested an acute demyelinating inflammatory polyneuropathy secondary to a virus-mediated immune response, similar to other reports. However, the occurrence of neurologic symptoms within a few days of disease onset led to consideration of direct infection. In our second case, although radiologic evidence of abducens nerve involvement was lacking, the presence of optic nerve sheath enhancement of the involved eye could reflect viral leptomeningeal invasion, although these findings are nonspecific. Given her risk factors and the painless nature of the diplopia, the differential includes an ischemic process. In both cases, neurologic symptoms could be unrelated to SARS-CoV-2 infection. Nonetheless, in the setting of the COVID-19 pandemic, the occurrence of cranial neuropathies should prompt consideration of SARS-CoV-2 infection in patients with even mild symptoms and signs of COVID-19. Hydroxychloroquine was used in both cases per institutional practice, although whether clinical benefit was conferred is not known. Further studies are needed to understand the natural history and prognostic significance of cranial neuropathies in SARS-CoV-2 infection and to determine the best treatment.

**Study funding**

No targeted funding reported.

**Disclosure**

The authors report no relevant disclosures. Go to Neurology.org/N for full disclosures.

**Publication history**

Received by Neurology April 4, 2020. Accepted in final form April 23, 2020.
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COVID-19 presenting with ophthalmoparesis from cranial nerve palsy
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Neurology 2020;95:221-223 Published Online before print May 1, 2020
DOI 10.1212/WNL.0000000000009700

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