Pearls & Oysters: Facial nerve palsy in COVID-19 infection

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Pearls

- Coronavirus disease 2019 (COVID-19) has been associated with various neurologic manifestations, including anosmia, acute ischemic stroke, Guillain-Barré syndrome, and encephalopathy.
- During the COVID-19 pandemic, physicians seeing patients with these neurologic manifestations should consider COVID-19 as a differential diagnosis to prevent diagnostic delays and further transmission of disease.
- Cranial nerve involvement could potentially be associated with COVID-19.

Oysters

- When a patient presents with isolated facial nerve palsy, a careful neurologic examination is required to rule out concomitant cranial nerve involvement (such as trigeminal nerve or vestibulocochlear nerve palsies) that would suggest alternative localization sites.
- Facial nerve palsy is commonly due to, or associated with, a viral infection and should not be assumed to be idiopathic.
- Investigations such as CSF analysis and MRI can be helpful in evaluating for CNS infection, inflammation, and other secondary causes.

In early March 2020, a previously healthy 27-year-old man was admitted directly to the isolation ward of a tertiary health care center in Singapore with symptoms of myalgia, cough, and fever for 4 days. His symptoms started the day after he returned from Spain. He also complained of a new left-sided throbbing headache with no associated photophobia or neck stiffness. On examination, he had mild bilateral conjunctival injection and respiratory examination was unremarkable. He did not have any focal neurologic deficits. Chest radiography did not show any infiltrates and a nasopharyngeal swab returned positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on real-time reverse transcription PCR (RT-PCR) assay.

On the third day of hospitalization (day 6 of illness), the patient developed left facial weakness, which was preceded by left retro-auricular pain and dysgeusia. Neurologic examination revealed involvement of the left frontalis, orbicularis oculi, buccinator, and orbicularis oris, consistent with a left lower motor neuron type facial nerve palsy. Corneal reflex was present, and there was no hyperacusis. The rest of the neurologic examination was unremarkable and his reflexes were normal. Kernig and Brudzinski signs were negative. There were no associated vesicles in the outer ear nor was there any parotid swelling. HIV screen was negative. CSF analysis did not show any pleocytosis, and glucose and protein levels were normal. CSF PCR for herpes simplex virus (HSV), varicella-zoster virus (VZV), Epstein-Barr virus, and cytomegalovirus and RT-PCR for SARS-CoV-2 were negative. MRI of the brain showed enhancement of the left facial nerve (figure, A). He was started on prednisone and valacyclovir for treatment of Bell palsy.

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Lopinavir/ritonavir was also initiated with the intention of reducing SARS-CoV-2 viral replication. His SARS-CoV-2 viral load was high during the early phase of illness (4–7 days from symptom onset) and decreased rapidly following the administration of lopinavir/ritonavir, becoming undetectable by the end of the second week (figure, B). No significant virologic rebound was observed. On review 1 week later, there was no significant change in the degree of his facial weakness, but his headache and retroauricular pain improved.

Discussion

We are in the exponential phase of learning about COVID-19, an emerging infectious disease, which has caused an ongoing global pandemic. In a cohort of 214 Chinese patients, COVID-19 presents most commonly with fever in 88.7% and cough in 67.8% of patients, 5% of whom required intensive

care monitoring.¹ Neurologic manifestations of COVID-19 have been reported in up to 36.4%.² Thus far, impairment of taste and smell, dizziness, and headache have been reported as common symptoms in COVID-19.²

Recently, reports of significant neurologic associations have emerged, including increased incidences of Guillain-Barré syndrome, encephalopathy, and strokes.^{2–5} In an Italian cohort, Guillain-Barré syndrome has been reported in approximately 0.5% of patients with COVID-19, with the first symptoms of flaccid paralysis and facial diplegia occurring at 5–10 days after onset of acute respiratory symptoms.⁵ In Strasbourg, France, encephalopathic features were commonly seen in patients with severe COVID-19 who had acute respiratory distress syndrome, some of whom had MRI abnormalities including leptomeningeal enhancement, perfusion abnormalities, and ischemic stroke.⁴ A case of acute hemorrhagic necrotizing encephalopathy associated

Figure Neuroimaging and viral load of a patient with coronavirus 2019 with facial nerve palsy

(A) Contrast-enhanced MRI of the brain showing enhancement of the left facial nerve (arrow). (B) Severe acute respiratory syndrome coronavirus 2 viral load correlated with clinical course and treatment. RT-PCR = real-time reverse transcription PCR.

with COVID-19 infection has also been reported in Detroit, Michigan, and postulated to be due to intracranial cytokine storm, with MRI showing T2 fluid-attenuated inversion recovery hyperintensities within the thalami and bilateral medial temporal lobes with rim enhancement post contrast.³ The incidence of stroke was 5.7% in patients with COVID-19 with more severe respiratory symptoms in Wuhan, China.² A case series from Spain described cranial nerve manifestations associated with COVID-19 in 2 patients, 1 of whom had Miller Fisher syndrome and the other presenting with polyneuritis cranialis.⁶ To our knowledge, isolated cranial neuropathies have yet to be described.

Facial nerve palsy can be associated with infections, most commonly HSV, as well as VZV and HIV, Lyme disease, and *Mycobacterium tuberculosis*. Noninfectious causes include sarcoidosis and neoplasms. The exact pathogenesis of acute facial nerve palsy remains unclear, but in association with neurotropic herpesviruses (HSV and VZV), it is thought to be related to axonal spread and viral replication leading to inflammation and demyelination.⁷

Coronaviruses are known to have a neuroinvasive propensity. Animal models show that severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus could potentially have a transcribrial route to the brain, causing CNS manifestations.⁸ The mechanism underlying neurologic symptoms in COVID-19 has yet to be clearly elucidated. Similar to the patients with Miller Fisher syndrome and perineuritis cranialis described in Spain and those with Guillain-Barré syndrome described in Italy, our patient developed an isolated facial nerve palsy during the early phase of his illness, on day 6.^{5,6} This may suggest a parainfectious phenomenon. Serum GD1b immunoglobulin G antibodies were also detected in the patient with Miller Fisher syndrome. In all of these cases with Guillain-Barré syndrome and Miller Fisher syndrome, SARS-CoV-2 was not detected in the CSF. As such, cranial neuropathies may be related to immune-mediated injury from proinflammatory cytokines rather than direct viral neurophism.⁶

Studies of viral dynamics show that viral loads are highest 1–2 days prior to symptom onset, and decrease in a monotonic pattern with prolonged viral shedding hovering near the level of detection, resulting in RT-PCR results that vacillate between positive and negative.⁹ Lopinavir/ritonavir is a protease inhibitor combination approved for use in HIV-1 and has demonstrated in vitro activity against SARS-CoV-2. A recent randomized trial conducted in China on patients with COVID-19 with severe respiratory symptoms compared lopinavir/ritonavir, in addition to standard care, to standard care alone, and found no significant decrease in viral load or clinical benefit with lopinavir/ritonavir.¹⁰ However, in this study, the frequency of RT-PCR testing was only every 4–7 days, and it has been

proposed that daily sampling following antiviral treatment may have provided more detailed characterization of the viral load kinetics. More studies are needed to determine if there is a direct effect of lopinavir/ritonavir on viral load, an indirect effect on the immune response, or no effect on the natural course of the disease process. In our patient, we observed a declining trend in SARS-CoV-2 viral load (which is inversely related to the cycle threshold or Ct value) determined by daily nasopharyngeal swab samples after lopinavir/ritonavir was initiated.

This case report only suggests a possible association between isolated cranial neuropathies and COVID-19. More cases are required to support causality. We are reporting this case to inform and alert physicians of the possibility of cranial nerve involvement in the presentation of patients with COVID-19.

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Disclosure

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