Abstract

COVID-19 pandemic is ongoing and information on the neurological aspects of this viral infection is being gathered. Neuromuscular manifestations have been reported uncommonly in these early stages of the analysis. This manuscript studies the available information on the neuromuscular manifestations of COVID-19.

Keywords: COVID-19 neurological manifestations, COVID-19 neuromuscular manifestations, guillain barre syndrome, myositis

Introduction

The world is currently grappling with the pandemic caused by the novel coronavirus, severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2). The disease caused by this virus is called coronavirus disease-2019 (COVID-19) by the World Health Organization. Though the predominant manifestations of COVID-19 are fever, cough, and respiratory system involvement; novel features involving the central nervous system and occasionally the peripheral nervous system are being reported. A search using the keywords COVID-19 and brain, COVID-19 and neurology, SARS-CoV2 and neurology, COVID-19 and peripheral nervous system was carried out and the manuscripts were evaluated.

The search revealed very few manuscripts describing neuromuscular manifestations of COVID-19. One concern is the atypical features of some patients having neuromuscular symptoms, as will be seen below. These patients do not show the systemic and respiratory features of COVID-19. This may have led to underreporting as relevant viral tests may not be ordered on such patients.

Virology and putative pathophysiologic mechanisms

SARS-CoV2 belongs to the family of beta coronaviruses. It shares clinical and antigenic similarities to the SARS coronavirus (SARS CoV1) pandemic of 2002–2003. This is a single-stranded positive RNA virus having a large genome (30 kb). The virus has club-shaped spikes that are visible under the electron microscope as a solar corona; hence the name- coronavirus [Figure 1]. It attaches to the angiotensin-converting enzyme 2 receptors (ACE2) via the spike protein to gain entry into cells. ACE2 receptors are found in the lungs, nasopharynx, heart, kidneys, brain, intestines, vascular endothelium, and testicles. In the brain, ACE2 receptors are found especially in the brain stem cardiovascular regulatory areas.

In some affected individuals, the virus may enter the brain or peripheral nervous system as a consequence of the systemic viremia or a direct neurotropic mechanism via the olfactory epithelium through the cribiform plate (not yet established in COVID-19; though was seen with SARS CoV 1). The virus can then cause manifestations due to direct infection, molecular mimicry, or as a result of the systemic inflammatory response.

Peripheral nervous system involvement

As the predominant manifestations of COVID-19 are respiratory; the covert (sometimes overt) neurological manifestations may be overlooked in the mayhem caused by the pandemic. This was also true of the pandemic of SARS in 2002–2003. Li Kai Tsai and colleagues retrospectively described 4 patients (out of a total of 76 patients) with peripheral neuromuscular manifestations during the SARS CoV 1 pandemic in Taiwan. All their patients were critically ill and demonstrated limb weakness 3 weeks after the onset of the viral infection. Two patients had an axonal motor sensory neuropathy, one had a combination of neuropathy with severe myopathy, and one had mild myopathy. However, the authors attributed all of these due to critical illness neuromyopathy due to either the systemic inflammatory response due to the virus or the high-dose steroids used to treat these patients. They also mentioned 2 other infected patients with markedly elevated creatine kinase levels and rhabdomyolysis.
There are few anecdotal reports of peripheral nervous system involvement in COVID-19. The retrospective, observational case series by Mao and colleagues from Wuhan, China [6] described peripheral neurological involvement in COVID-19. Of the 214 consecutive patients with COVID-19, 36.4% (78 patients) had symptoms of the nervous system. They classified neurological manifestations as those involving the central nervous system (dizziness, headaches, stroke, seizures, and altered sensorium), peripheral nervous system (8.9%) (taste/smell impairment, nerve pain), and skeletal muscular injury (10.7%). These authors reported that neurological manifestations were more common in those who were severely affected by the COVID-19. The patients with neurological manifestations were older, more likely to have comorbid conditions (like hypertension, diabetes) and did not reveal the typical COVID-19 features of fever and dry cough. The onset of neurological features was seen early in the disease course (days 1 to 3); alarmingly in some patients, it was the sole presentation of COVID-19. Those with neurological syndromes had elevated C-reactive protein, increased D dimer levels, and reduced lymphocyte counts.

Abnormalities of sense of smell and taste
The olfactory system is composed of a peripheral neuroepithelium in the nose and the central olfactory nerve and its connections. Hypo or anosmia was seen in 5.1% of the Wuhan cohort. [6] Rosario et al. [7] reported sudden hyposmia in 6 Italian subjects with COVID-19. These subjects did not have a fever or upper/lower respiratory tract symptoms or cough before the smell abnormality. Hypogeusia has observed in 5.6% of the Wuhan cohort [6] and all the Italian subjects. Lechien et al. [8] observed 85.6% (357 out of 417 COVID-19 subjects) of infected patients (predominantly Europeans) to have an abnormality of smell (79.6% were anosmic and 20.4% hyposmic). In 33.6% of the subjects, the abnormalities of smell preceded or were associated with the general symptoms of COVID-19. Gustatory abnormalities have been reported in 88.8% of the infected individuals. Besides, in 72.6% of these patients, the smell abnormality improved completely within 8 days of the resolution of other features of the disease. The abnormality of smell and taste seems to be more prevalent in the Europeans than the Chinese.

The abnormality of smell (in the absence of rhinorrhea) in the current pandemic may indicate the presence of COVID-19 disease. Identification of this peculiar feature may help identify and isolate otherwise asymptomatic individuals with COVID-19.

Myositis
Raised creatinine kinase with muscle pain was observed in 10.7% of the subjects with severe COVID-19 in the Wuhan cohort. [6] These subjects were more aged, with comorbid diseases like diabetes and hypertension, lacked typical COVID-19 symptoms, had lymphopenia with raised levels of D dimer and C-reactive protein.

Guillain-Barre Syndrome (GBS)
There is a single case report [9] of a lady who presented with a demyelinating neuropathy suggestive of GBS. Almost 7 days later, she developed features typical of COVID-19 with a positive throat swab. The authors speculate that the GBS was para infectious in nature (as she had thrombocytopenia and lymphopenia on admission with GBS and she had returned from Wuhan—the pandemic center, 4 days before the onset of her symptoms).

Conclusion
This pandemic is still on and the novel symptoms of COVID-19 are still being reported. Some information available at present on the neuromuscular manifestations related to COVID-19 suggests that such involvement is relatively uncommon. It may occur without the classical features of fever or other respiratory accompaniments of COVID-19. Furthermore, when more data are gathered, the true perspectives will become clear. Since this is a viral infection, para and postinfectious involvement of the peripheral nervous system may underscore among the survivors of the COVID-19.

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Conflicts of interest
There are no conflicts of interest.

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