

Editorial



Transition of COVID-19 to endemic phase and emergence of COVID-19 related neuropathic pain

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Coronavirus disease 2019 (COVID-19) has caused several million deaths since it was first reported in December 2019 [1]. From the beginning of the COVID-19 pandemic, the main concern has been related to its acute respiratory involvement which may need ICU hospitalization and could lead to death. Since peaking in January 2022, new cases have continued to decline around the world. Gradually, extrapulmonary manifestations and post-COVID-19 syndrome have attracted more attention [2]. One of these is pain, one of the most common symptoms in the acute phase even after recovery from COVID-19.

Acute pain during COVID-19 does not seem significantly different from most viral diseases, and myalgia and headache are the main symptoms, while anosmia and ageusia occurs more frequently [3]. Many of these have been managed with symptomatic treatments such as painkillers and anti-inflammatory drugs, but some patients suffer from pain that lasts more than four weeks, which is regarded as one of the post-COVID-19 syndromes [4]. In fact, symptoms in the acute phase, such as headache, anosmia and ageusia, could be recognized as a neurological manifestation.

Much evidence supports the possibility that acute as well as chronic pain in COVID-19 patients could be attributed at least in part to the neurotropic nature of SARS-CoV-2, which causes neuroinflammatory responses in the peripheral and central nervous system [5-8]. Several mechanisms for COVID-19 pain have been suggested, including invasion via the angiotensin-converting enzyme isoform 2 (ACE2) receptor in spinal neurons and microglia, immune-mediated inflammation, and direct viral damage. Moreover, similar to other viral disease with neurological complications, both the peripheral and central nervous system could be affected by COVID-19, causing a wide spectrum of neurological conditions including encephalopathy, ischemic stroke, Guillain-Barre syndrome, and peripheral neuropathies which have a potential for neuropathic pain [6,9].

It was also found that almost 25% of patients with post-COVID pain showed neuropathic symptoms [10]. In another study, half of patients who survived critical COVID-19 illness reported new onset pain, and 30% of them suffered from neuropathic pain [11], although some of these could be related with the patient's ICU stay, the post-intensive

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care syndrome (PICU). While cases with CRPS-like feature after severe COVID-19 were reported [12,13], several cases with no ICU stay or mild to moderate morbidity also showed profound neuropathic pain during and after the infection [14–16]. In addition, despite a certain possibility of nervous system involvement by COVID-19, little is known about the impact of COVID-19 on the severity or characteristics of preexisting neuropathic pain [17]. Based on the results of these studies, a large-scale cohort study is underway to investigate the incidence and severity of neuropathic pain in COVID-19 patients [18].

It seems likely that even if the global epidemic of COVID-19 is converted to an endemic disease in the near future chronic neuropathic pain related to COVID-19 infection may not easily disappear. Although little is still known about the mechanisms, characteristics, and natural history of COVID-19-related pain, many of the above studies show that the importance of awareness of neuropathic pain should be emphasized for early diagnosis and treatment of COVID-19 patients.

DATA AVAILABILITY

Data sharing is not applicable to this article as no datasets were generated or analyzed for this paper.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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