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Letter to the Editor

Neuralgic amyotrophy associated with COVID-19 infection: the broken bough

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TO THE EDITOR

Neurological manifestations of coronavirus disease 2019 (COVID-19) have been previously discussed in various articles [1,2]. Neuralgic amyotrophy (NA), also known as idiopathic brachial plexopathy, is a rare condition characterized by acute onset of upper extremity pain followed by progressive neurological deficits. Although its etiopathogenesis is complicated and not entirely understood; an infectious or immune-related process seems to be the most sensible cause, due to the high incidence of antecedent infections and immunization in the disease course [3]. In this context, the probable relationship between COVID-19 and NA would not be unsound. To the best of our knowledge, there are only a few cases of NA following COVID-19 infection without any prolonged prone positioning [4-7]. Likewise, presenting another patient with NA shortly after COVID-19 infection, we aim to briefly review the pertinent literature.

A 27-year-old male nurse (with no significant past medical history) had been diagnosed with COVID-19 infection one month ago (a COVID-19 polymerase chain reaction test was positive). On the 7th day of quarantine, in addition to his initial complaints of subfebrile fever, arthralgia, myalgia, and headache; he had experienced gradual right upper limb pain and weakness, aggravated by shoulder and elbow extensions. Hyperesthesia and paresthesia predominantly involving the right thumb and index fingers had also accompanied these symptoms. As having mild respiratory manifestations and a normal chest radiograph, he had been quarantined for two weeks only with favipiravir treatment.

His current physical examination showed limited right elbow extension as well as weakness in shoulder abduction, elbow flexion/extension, wrist extension, and finger abduction on the right upper limb. Hyperesthesia and allodynia were present especially on the lateral antebrachial cutaneous nerve distribution. Reflexes were normal bilaterally. Ultrasonography revealed painful sonopalpation of the median nerve at the arm without any brachial plexus abnormalities (*e.g.*, edema, enlarged nerve fascicles, atrophy, and fatty infiltration of the surround-

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Table 1. Quantitative measurements (kg) using Jamar® dynamometer and pinchmeter

Measurement	Affected hand		Unaffected hand	Normal values [8]
	1st exam	2nd exam		
Grip strength	13.0	23	30.0	54.8
Palmar pinch/3-Jaw (Chuck-thumb, index, and middle fingers)	3.75	5.0	6.75	11.8
Tip-pinch (thumb and index fingers)	2.8	3.75	5.5	8.3
Lateral/key pinch (thumb pad and lateral aspect of index finger)	3.0	7.6	7.0	12.1

Table 2. Clinical features of previously described cases of neuralgic amyotrophy following COVID-19

Reference	Sex	Age	Symptoms	Imaging	EMG	Treatment
Siepmann et al. [4]	M	52	Motor - sensory	US, MRI	+	Oral CS
Mitry et al. [5]	F	17	Motor	MRI	–	Oral CS
Cacciavillani et al. [6]	M	52	Sensory	US	+	N/A
Ismail et al. [7]	M	32	Motor - sensory	MRI	+	IV CS, IVIg
Current case	M	27	Motor - sensory	US, MRI	+	Pregabalin

EMG: electromyography, US: ultrasound, MRI: magnetic resonance imaging, CS: corticosteroid, N/A: not available, IV: intravenous, IVIg: intravenous immunoglobulins.

ing muscles). Magnetic resonance imaging of the brachial plexus or cervical radiographs were not contributory either. Electrodiagnostic evaluations on the 4th week were normal except for insufficient electrical activity in the 1st dorsal interosseous, flexor carpi ulnaris, and flexor pollicis longus muscles. Laboratory findings including serum inflammatory markers, antinuclear, and antineutrophil cytoplasmic antibodies were all normal. Vaccination had not yet started at the time of reporting this case. Therefore, the patient was not vaccinated.

In light of all the above quoted evaluations, we started to follow the patient with the diagnosis of mild demyelination pan-plexopathy after COVID-19. Pregabalin was given initially with 75 mg/day and gradually increased to 300 mg/day. After the 2nd week, the patient reported significant pain relief but only partial improvement in muscle strength. Starting from the 3rd week of follow-up, quantitative measurements were also performed using a Jamar® dynamometer and pinchmeter, which objectively showed the muscle weakness improvement with home-based strengthening exercises (**Table 1**). The normal values in addition to the unaffected hand are shown in the table [8].

COVID-19 primarily affects the respiratory system, but many studies have also reported the potential neurotropism related to the infection [1,2,8]. COVID-19 patients experience complaints like headache, myalgia, hyposmia/anosmia, and clouding of consciousness that suggest involvement of the nervous system. Of note, neurological complications are of great/additional importance as regards worsening of the respiratory symptoms and poor disease prognosis [1,2]. In the formation of the poor prognosis, it is suggested that the medullary cardiorespiratory center, which is considered as a potential target of the virus, is affected as well as the local involvement of the respiratory muscles due to myalgia and neuropathy. Additionally, loss of consciousness and other accompanying central nervous system involvements have an effect on the respiratory system and directly on poor prognosis [1].

To the best notice of the authors, only four cases of NA have been reported in the COVID-19 literature [4-7]. **Table 2** summarizes the comparison of clinical characteristics among the aforementioned cases of post-COVID-19 NA. The patients seem to have been followed by different physicians and different diagnostic methods. Taking into account the fact that the diagnosis of NA is primarily made through clinical history/symptoms and physical exam findings, the diversity in this table is certainly understandable during the current extraordinary pandemic conditions. Herein, the common point is that although there are no obvious initiating factors (*e.g.*, long-term intensive care admission, prone position, *etc.*), the scenario of motor and/or sensory complaints in the upper extremities appears to have ensued after COVID 19 infection. We would like to draw attention to the fact that other cases reported in the literature include a history of hospitalization in the intensive care unit and possibly facilitating factors such as being kept in the prone position. There are many immunological and pharmacological predisposing factors that can lead to neuropathy in addition to general condition disorder in patients requiring intensive care unit admission [9]. In addition, keeping patients in the prone position to increase saturation due to respiratory failure is frequently preferred during the pandemic process [10]. Mechanical and positional compression has been an accepted factor in the etiology of neuropathy for many years.

Without ignoring this effect, there are articles on COVID 19 and NA which include intensive care and the prone position, which argue that immune mechanisms originating from viral infection may also be effective [9,10]. According to some studies, coronaviridae—such as the hemagglutinating encephalomyelitis virus—can enter the peripheral nerve terminals prior to peregrinating to the central nervous system [1,11]. Although the affinity of those viruses to the nervous system is known, there is no clear involvement of the central nervous system in the previously reported four cases. At this point, although we cannot exclude neuro-invasion models to explain COVID-19 neurological manifestations [1,2,11]; we rather underscore the autoimmune post-infectious mechanisms for NA in COVID-19.

In conclusion, apart from the detrimental respiratory manifestations the patients are trying to survive, physicians should also keep in mind the various/possible neurological involvement patterns associated with COVID-19 infection. This holistic approach will definitely help patients/physicians and provide better life quality (with less disability) in the long run after "the game is won".

CONFLICT OF INTEREST

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

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