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Pure sensory neuralgic amyotrophy in COVID-19 infection

See article on pages E8–E9 in this issue.

We read with great interest the case report on neuralgic amyotrophy following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1]

Respiratory symptoms are the primary manifestations of SARS-Cov-2 infection. Reports of several neurologic manifestations have most commonly involved the central nervous system.[2] In addition to olfactory dysfunction, peripheral nervous system involvement has been reported primarily as Guillain-Barré syndrome.[3] We report pure sensory neuralgic amyotrophy in a patient with coronavirus disease 2019 (COVID-19). An otherwise healthy 52-year-old man was admitted to the hospital for a pneumonia and tested positive for COVID-19 RNA by naso-pharyngeal swab. He was treated with hydroxychloroquine, antibiotics and oxygen and was discharged after 5 days. A week after the discharge, the patient developed excruciating pain in the left wrist and upper limb in the distribution of the lateral antebrachial cutaneous nerve followed shortly thereafter by hypoesthesia and dysesthesia in the same distribution. At onset, the pain was rated by the patient as 10/10 and was treated with acetaminophen with minimal relief. It gradually decreased and eventually resolved after 2 weeks. The patient noted no weakness and no other areas of pain or sensory symptoms. The neurological examination revealed normal strength, normal sensation except as noted, and normal reflexes. Electrodiagnostic testing performed 5 weeks after symptom onset showed a reduced sensory nerve action potential amplitude of the left lateral antebrachial cutaneous nerve. No other abnormalities were detected on nerve conduction study (Table 1). Needle electromyography of the left deltoid, biceps brachii, triceps brachii, brachioradialis, extensor digitorum communis, flexor digitorum superficialis, and first interosseous muscles was normal. Ultrasound evaluations of the left median, ulnar, radial, posterior interosseous, and musculocutaneous nerves were unremarkable along their explorable courses. A diagnosis of pure sensory neuralgic amyotrophy was made. Six weeks after the onset, hypoesthesia and dysesthesias persisted.

Pure sensory involvement is a possible presentation of neuralgic amyotrophy.[4,5] Antecedent or concomitant infections are considered as possible triggers of an immune-mediated pathophysiologic mechanism.[6] Notably, in the present report, diagnosis was delayed because the lockdown measures prevented a timely evaluation. The present report, which adds to the one described by Siepmann et al.[1] broadens the neurological spectrum of COVID-19 infection and suggests that this virus may be among those associated with neuralgic amyotrophy.

CONFLICTS OF INTEREST

None of the authors has any conflict of interest to disclose.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

KEYWORDS

acute, Covid-19, infection, neuralgic amyotrophy, neuropathic pain, parsonage-turner syndrome, Sars-Cov-2

TABLE 1 Nerve conduction studies

Nerve	Stimulation site	DL (ms)	CV (m/s)	Amplitude (cMAP = mV SNAP = μV)	F latency (ms)
L median (m)	Wrist	2.6 (≤3.5)		12 (≥6)	29 (<32)
	Elbow		58 (≥50)	11 (≥6)	
L ulnar (m)	Wrist	2.1 (≤3.1)		8.6 (≥4)	
	BE		66 (≥50)	8 (≥4)	
	AE		79 (≥50)	8 (≥4)	
L Musculo-cutaneous (m)	Axilla	3.1 (≤3.3)		10 (≥8)	
L median (s)	1th finger		55 (≥48)	19.5 (≥15)	
	3rd finger		60 (≥48)	18.7 (≥15)	
L ulnar (s)	5th finger		58 (≥48)	7.8 (≥6)	
L radial (s)	1th finger		54 (≥40)	16.3 (≥10)	
L lateral antebrachial cutaneous (s)	Antecubital fossa	1.7 (≤2)		4.4 (≥6)	
R lateral antebrachial cutaneous (s)	Antecubital fossa	1.5 (≤2)		16.9 (≥6)	

Abbreviations: AE, above elbow; AFH, above fibular head; BE, below elbow; BFH, below fibular head; cMAP, compound motor action potential; CV, conduction velocity; DL, distal latency; L, left; m, motor; NR, no response; R, right; s: sensory; SNAP, sensory nerve action potential.
Note: Normal values in parentheses.

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Variability of symptoms in neuralgic amyotrophy following infection with SARS-CoV-2

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The report of Cacciavillani and colleagues contributes to the discussion of the possibility of peripheral nerve involvement in coronavirus disease 2019 (COVID-19) and adds to our observation of neuralgic amyotrophy following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1,2] Their case viewed in conjunction with a growing body of evidence underscores a relevant pathophysiological problem of the disease. The mechanisms whereby SARS-CoV-2 targets the human organism might extend beyond the known pathway of binding to the angiotensin-converting enzyme 2 receptor, which is expressed in the epithelium of the respiratory tract, the endothelium, the gastrointestinal system, and other organs.[3] In fact, a direct neuroinvasive potential has been suggested by several authors. Supporting this hypothesis is a recent investigation that detected SARS-CoV-2 RNA in 36.4% (8/22) of brain biopsies obtained from fatal COVID-19 cases,[4] but the route whereby the virus invades the nervous system is unclear. Interestingly, research prior to the COVID-19 pandemic showed that earlier coronaviruses, such as hemagglutinating encephalomyelitis virus, may first enter peripheral nerve terminals before traveling to the central nervous system (CNS) via synapse-connected routes.[5,6] Whether this mechanism also applies to SARS-CoV-2 remains to be answered. However, our patient as well the patient reported by Cacciavillani and colleagues presented with symptoms of peripheral nerve involvement without any signs of CNS damage. In fact, peripheral nerve damage might occur in almost 10% of patients hospitalized for SARS-CoV-2 infection.[3] Whether peripheral nervous system complications following COVID-19, such as neuralgic amyotrophy, result from direct neuroinvasion or from an auto-immune post-infectious mechanism needs to be elucidated. Understanding the sequence of events leading to neural damage in patients with COVID-19 might help identify diagnostic and therapeutic targets, highlighting the need for prospective research on patterns of peripheral and central nervous system involvement in patients with COVID-19.

The report of Cacciavillani includes an important observation that differed from our report. Their patient developed neuralgic amyotrophy possibly related to infection with SARS-CoV-2 without any clinical or electrophysiological signs of motor nerve involvement. This observation highlights the possible variability of symptoms in patients with peripheral nervous system involvement of SARS-CoV-2 infection and the importance of detailed assessment of patients with COVID-19 for neurological deficits. Pure sensory involvement in neuralgic amyotrophy not associated with COVID-19 is rather uncommon.[7] However, the reason for sensory nerve fiber sparing in patients with neuralgic amyotrophy is poorly understood, and the neurotropic pathways of SARS-CoV-2 even more so.

Taken together, the first detailed reports of acute involvement of the peripheral nervous system following infection with SARS-CoV-2, viewed in conjunction with hypothesized mechanisms of neurotropism and high frequencies of neurological symptoms in observational studies of COVID-19, substantiate a need for mechanistic and prospective research on the invasion of the nervous system by SARS-CoV-2.

CONFLICTS OF INTEREST

None of the authors has any conflict of interest to disclose.