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Case Report

Critical illness myopathy after COVID-19

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ABSTRACT

This paper describes a patient who developed diffuse and symmetrical muscle weakness after a long stay in the intensive care unit (ICU) due to coronavirus disease 2019 (COVID-19). The patient underwent a neurophysiological protocol, including nerve conduction studies, concentric needle electromyography (EMG) of the proximal and distal muscles, and direct muscle stimulation (DMS). Nerve conduction studies showed normal sensory conduction and low-amplitude compound muscle action potentials (CMAPs). EMG revealed signs of myopathy, which were more pronounced in the lower limbs. The post-DMS CMAP was absent in the quadriceps and of reduced amplitude in the tibialis anterior muscle. Based on these clinical and neurophysiological findings, a diagnosis of critical illness myopathy was made according to the current diagnostic criteria. Given the large number of patients with COVID-19 who require long ICU stays, many are very likely to develop ICU-acquired weakness, as did the patient described here. Health systems must plan to provide adequate access to rehabilitative facilities for both pulmonary and motor rehabilitative treatment after COVID-19.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), which reached pandemic-level diffusion in March 2020. Patients with COVID-19 frequently experience muscular symptoms, such as myalgia, but myopathic changes have not been fully evaluated in this population. A recent review of the neurological complications of COVID-19 included 25 studies with data on skeletal muscle problems, but no study examining the use of electromyography or another diagnostic test to detect myopathic changes (Pinzon et al., 2020). Notably, large numbers of patients with COVID-19 require intensive care unit (ICU) admission and long stays (Lewnard et al., 2020). Critically ill patients are likely to develop muscular complications, such as critical illness myopathy (CIM), which adversely affect short-term and long-term outcomes (Vanhorebeek et al., 2020). This report describes neurophysiological findings from a patient who developed severe muscular weakness, likely due to CIM, after hospitalisation for COVID-19.

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Case description

A 62-year-old woman with a history of hypertension developed fever, cough, myalgia, and diarrhoea at the beginning of March 2020. After a few days of treatment with levofloxacin, which resulted in no clinical improvement, she went to the emergency room of a COVID hospital in Palermo, Italy, where SARS-CoV-2 infection was diagnosed by chest computed tomography (CT) and nasopharyngeal swab testing for SARS-CoV-2 RNA. Seven days after clinical onset, the patient was admitted to an infectious disease unit, where she was treated with lopinavir/ritonavir, hydroxychloroquine and tocilizumab. Nine days after onset, her respiratory function worsened, necessitating transfer to an ICU, where she underwent endotracheal intubation and mechanical ventilation. The ICU stay was complicated by *Staphylococcus aureus* and *Candida tropicalis* bloodstream infections. During her ICU stay, the patient received therapy with neuromuscular blocking agents, antibiotics, antifungal drugs, and corticosteroids. After 28 days, she was moved to an infectious disease unit for 4 days, but respiratory worsening necessitated another transfer to the ICU, where she stayed for a further 2 days. The patient was then moved to a COVID pulmonology unit. In the first days of this stay, she presented psychomotor agitation and temporospatial disorientation; a brain CT examination was normal and, after neurological and psychiatric evaluations, she was treated with olanzapine for about 3 weeks,

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which resulted in progressive improvement of her cognitive function.

Sixty-eight days post-onset, and with SARS-CoV-2 negativity on three consecutive nasopharyngeal swab tests, the patient was moved to a rehabilitation unit. At the beginning of rehabilitative treatment, she required a 40% fraction of inspired oxygen and presented dyspnoea after mild effort. She had muscle atrophy in her lower limbs. Segmental muscle strength evaluation showed diffuse and symmetrical muscle weakness, ranging from 3/5 to 4/5 on the Medical Research Council scale for muscle strength assessment, which was greater in her lower limbs and proximal muscles. The patient was able to walk a few steps with assistance. Deep tendon reflexes were reduced in her lower limbs. Her serum creatine kinase level was normal.

Eighty days post-onset, the patient underwent a thorough neurophysiological protocol, including conventional nerve conduction studies (of the ulnar, peroneal, tibial, and sural nerves), concentric needle electromyography (EMG) of the proximal and distal muscles, and direct muscle stimulation (DMS). The neurophysiological study was performed bedside using a Micromed System Plus Evolution electromyograph (Mogliano Veneto, Italy). DMS was performed in the right quadriceps and tibialis anterior muscles using two monopolar needle electrodes (Rich et al., 1997), and the evoked compound muscle action potential (CMAP) was recorded with two monopolar needle electrodes placed about 1.5 cm distal to the midpoint of a line connecting the two stimulating electrodes. The ratio of the amplitudes of the CMAPs evoked by motor nerve stimulation and DMS was calculated. This ratio aids discrimination between neuropathic and myopathic processes during overall neurophysiological evaluation: values <0.5 are indicative of neuropathy and those near 1 are indicative of myopathy (Rich et al., 1997; Trojaborg et al., 2001). The normal limits were defined as means ± two standard deviations from normative data from the laboratory (standard age-matched data for the electroneurographic studies; obtained from 14 subjects for the DMS study) (Bagnato et al., 2011).

The neurophysiological findings are summarised in Table 1. Nerve conduction studies showed normal sensory conduction and low-amplitude CMAPs in the peroneal and tibial nerves. EMG indicated myopathy in the proximal muscles of the upper limbs and in the proximal and distal muscles of the lower limbs. The post-DMS CMAP was absent in the quadriceps, and of reduced amplitude in the tibialis anterior muscle. The ratio of the CMAP amplitudes evoked by peroneal nerve stimulation and DMS of the tibialis anterior was 0.96.

Her stay in the rehabilitation unit lasted 60 days, during which time she received a rehabilitation program 3 h a day for 6 days a week. At discharge, she did not require oxygen supplementation, had a mild weakness in her lower limb proximal muscles and was able to walk without assistance.

Discussion

This patient had a myopathy, with greater involvement of the proximal muscles in her lower limbs, probably reflecting ICU-acquired weakness. The patient met the clinical and neurophysiological criteria for CIM (Stevens et al., 2009). The pathophysiology of CIM is complex and not fully understood, but it probably involves microcirculatory changes, metabolic alterations, electrical muscle alterations with abnormal excitation-contraction coupling, and energetic failure with mitochondrial dysfunction (Zhou et al., 2014). A recent metanalysis identified several risk factors significantly associated with ICU-acquired weakness (including CIM and/or critical illness polyneuropathy) (Yang et al., 2018); among them, being female, having sepsis and hyperglycaemia, using neuromuscular blocking agents, lengthy mechanical ventilation and ICU stay were present in this case. Preventive and supportive measures–such as glycaemic control, nutritional intervention, early mobilisation, and physical therapy, but no specific therapy–have been shown to be beneficial in CIM management (Zhou et al., 2014; Vanhorebeek et al., 2020). How COVID-19 makes patients susceptible to muscle damage is an open question. In the previous coronavirus outbreak, causing the severe acute respiratory syndrome in 2002–2004, a post-mortem study showed a spectrum of myopathic changes, suggesting a common occurrence of CIM in patients who did not survive (Leung et al., 2005).

In conclusion, increasing evidence shows that patients with SARS-CoV-2 infection may develop various neurological complications as a direct or indirect viral action (Pinzon et al., 2020). In addition, ICU-acquired weakness should be suspected and properly diagnosed in all patients who develop symmetrical

Table 1
Neurophysiological findings.

	SNAP amplitude (μV)	Sensory conduction velocity (m/s)	CMAP amplitude (mV)	Motor conduction velocity (m/s)	MUAPs
NCS					
Right ulnar	21.6	57.1	7.1	54.2	
Left ulnar	20.1	59.5	9.0	56.4	
Right peroneal	8.0	46.2	**0.7**	44.3	
Left peroneal	10.8	44.8	**0.1**	43.1	
Right tibial			**5.7**	44.2	
Left tibial			**2.6**	44.3	
Right sural	24.3	50			
DMS					
Right quadriceps			**Muscle inexcitability**		
Right tibialis anterior			**2.4 (0.96)**[a]		
EMG					
Right and left FDI					Normal
Right and left deltoid, quadriceps and tibialis anterior					**Short-duration and low-amplitude with early full recruitment, more evident in the quadriceps**

The bold text indicates abnormal values.
Abbreviations: SNAP, sensory nerve action potential; CMAP, compound muscle action potential; MUAP, motor unit action potential; NCS, nerve conduction studies; DMS, direct muscle stimulation; EMG, electromyography; FDI, first dorsal interosseous.
[a] The ratio of the amplitudes of the CMAPs evoked by peroneal nerve stimulation and DMS is reported in parentheses.

weakness after hospitalisation for COVID-19. In light of the large number of patients with COVID-19 who require lengthy ICU stays, many are very likely to develop ICU-acquired weakness, as did the patient described here, in the coming months. Since rehabilitation programs can be effective to reverse muscle weakness caused by CIM, health systems must plan to provide adequate access to rehabilitative facilities for patients requiring both pulmonary and motor rehabilitative treatment after COVID-19.

Study funding

None declared.

Conflict of interest

None declared.

Ethical statement

Because this report just reviewed clinical data, there was no need of a specific ethical approval. Informed consent was signed by the patient for the publication of this report.

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