Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Reply to "Comprehensive work-up is warranted for patients with severe COVID-19 and muscle weakness including respiratory muscles"

We read with great interest and a certain degree of surprise the letter by Finsterer (2021) about our description of a series of COVID-19 patients with intensive care unit related weakness (ICUAW) (Cabañes-Martínez et al., 2020). Our first thought after reading the letter was that there must have been some confusion about the content of our paper. It was never our intention to elaborate a list of the theoretical causes of weakness on any given patient, regardless of their clinical situation, signs and symptom, but to describe the neurophysiological findings (and in some cases, the muscle biopsy findings) in a group of patients with ICUAW. We have no doubt about the diagnosis of our patients, as they were all critically ill and presented symmetric, generalized weakness affecting limb and respiratory muscles, with sparing of facial muscles. The main objective of our study was to neurophysiologically determine the presence of myopathy or neuropathy in these patients, which we did in 11 of the 12 patients of our study.

However, we feel that some points need to be clarified:

We reviewed the individual history (and family history) of each patient included in the study, but to provide the whole records of the 12 patients seems unnecessary for the purpose of our study. As stated, none of our patients had a previous neuromuscular disorder (NMD) that we were aware of. Obviously, we have to admit the remote possibility of a non-diagnosed subclinical neuromuscular disease.

Finsterer argues that myasthenia gravis (MG) was not completely excluded without performing single fiber EMG (SFEMG), citing the work by Restivo (Restivo et al., 2020). Curiously enough, the diagnosis of the neuromuscular transmission disorder in this study is based on a pathological decrement in the repetitive nerve stimulation (RNS) test. RNS was normal in our patients. Given the high sensitivity of RNS in moderate-severe generalized MG when using proximal muscles, we believe that we reasonably ruled out the diagnosis of myasthenia. Also, the diagnosis of MG in the study by Restivo was suspected by the clinical symptoms (diplopia and muscular fatigability), symptoms which our patients did not present. Finsterer also argues that high-frequency RNS should have been performed to rule out myasthenic syndrome and to support this argument he cites the report of a patient with chloroquine-induced myasthenic syndrome (Koc et al., 2020). In this report, the patient presented diplopia with fatigability. MG was suspected because of these symptoms, and the diagnosis was confirmed through SFEMG. RNS was not even performed in this case.

Regarding the possibility of a Guillain-Barré syndrome (GBS), we evaluated the proximal segments of the peripheral nerves with the F-responses, which were present in all patients except two (patients 3 and 9). In patient 3, nerve conduction studies (NCS) show decreased amplitude and increased duration of the CMAPs without increased temporal dispersion in some nerves with preservation of the sensory nerve action potentials, findings described in critical illness myopathy (CIM) (Kramer et al., 2018). Patient 9 did not present signs of myopathy or polyneuropathy and was diagnosed of a bilateral peroneal nerve injury. The absence of F-waves on both patients was attributed to decreased motor neuron excitability due to a prolonged period of reduced mobility.

As GBS was not suspected in light of the NCS results, performing cerebrospinal fluid investigations seemed unnecessary at the time of the diagnosis. Cranial nerve function was preserved in our patients, otherwise we would have mentioned it in the article.

We believe that the investigation of possible central nervous system (CNS) causes of respiratory failure in our patients is outside the scope of our study, and does not affect our results.

In relation to the possible presence of dermatomyositis, only patient 1 presented dermatological symptoms, and a complete myositis antibody spectrum examination with autoantibodies, including anti-Ro52 antibodies, was negative. Myalgias are not rare in COVID infection (around 15%, Guan et al., 2020). We do not believe that systematic determination of anti-Ro52 antibodies in the rest of our patients was justified. In his very interesting case report, Cao (Cao et al., 2020) presented a case of amyopathic dermatomyositis that was misdiagnosed with COVID-19 infection, despite three negative tests for COVID-19. Zhang (Zhang et al., 2020) described a case of myositis with bulbar involvement and a compatible muscle biopsy in a COVID-19 patient. Although the tree biopsies in our study showed no signs of inflammation, the possibility of a direct muscular damage caused by the SARS-CoV-2 has been accepted in the discussion of our article.

Finsterer also reports the potential myotoxicity of some drugs used to treat our patients. We acknowledged this possibility in our paper. Nevertheless, CIM defines an ICU-acquired weakness in critically ill patients which is not caused by a single etiological factor, but by different factors, including several drugs commonly used in the ICU setting.

Finally, we appreciate the interest and comments by Finsterer, and we hope that our response will clarify some of his concerns.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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