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LETTER TO THE EDITOR

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SARS-CoV-2 myopathy

To the Editor,

Since the occurrence of the first infection with SARS-CoV-2 in December 2019, increasing evidence accumulated that not only the lung but also other organs, including the central nervous system and the peripheral nervous system (PNS), can be involved in the infection. Involvement of the PNS in SARS-CoV-2-infected patients includes Guillain-Barre syndrome,[1,2] myasthenia gravis (MG),[3,4] myositis,[5] myalgia,[6] rhabdomyolysis,[7–9] muscle wasting, and critical-ill myopathy.[10] Here we summarize and discuss recent findings concerning the involvement of the striated muscle in the infection.

Muscle involvement was first described in a retrospective study of 214 Chinese patients. In this study, 23 of 214 (10.7%) of the patients were reported with "skeletal muscle injury." No specific investigations were carried out to further specify the type and pathophysiology of muscle injury, why the cause remained unclear. In a study of 41 infected Chinese patients, 18 (44%) patients reported myalgia and fatigue. In all these patients myalgia was present already at onset of the infection. Seven patients required ICU care and eleven did not. In a study of 138 infected Chinese patients, myalgia was reported by 48 (34.8%) patients. Creatine-kinase (CK) was normal in most of these patients. In a retrospective European study of 1420 infected patients, myalgia was found in 887 (62.5%) patients. In a study of 1099 Chinese patients myalgia and fatigue were reported in 164 (14.9%) participants. However, CK-elevation more than 200 U/L was detected in only 90 of 657 (13.7%) tested patients. In an US study on 1150 SARS-CoV-2-infected patients, 67 (26%) complained about myalgia. CK-elevation was noted in some patients, without reporting the exact number. In a study of 27 pediatric patients with multisystem SARS-CoV-2 infection, four developed muscle weakness of whom three had a myogenic electromyography (EMG). All these studies did not mention how often muscle symptoms had been recognized already before the infection and none of these patients was prospectively investigated for primary or secondary muscle disease.

TABLE 1 SARS-CoV-2-infected patients with muscle involvement so far reported

NOP	Age	Sex	Symptoms	Signs	CK, U/L	MG	EMG	MB	Reference
887	NR	NR	Myalgia	NR	NR	NR	NR	NR	[Lechien]
164	NR	NR	Myalgia, fatigue	NR	>200 in 90	NR	NR	NR	[Guan]
67	NR	NR	Myalgia	NR	NR	NR	NR	NR	[Cummings]
48	NR	NR	Myalgia	NR	Normal	NR	NR	NR	[Wang]
23	NR	NR	Muscle injury	NR	NR	NR	NR	NR	[Mao]
18	NR	NR	Myalgia, fatigue	NR	NR	NR	NR	NR	[Huang]
11	NR	NR	Myalgia	NR	NR	NR	NR	NR	[Chen]
10	NR	NR	NR	NR	NR	NR	NR	Myositis	[Duarte-Beto]
5	NR	NR	Myalgia	NR	NR	NR	NR	NR	[Zhong]
4	8–15	2M, 2F	Weakness	NR	NR	NR	Myogenic	NR	[Abdel-Mannan]
1	60	M	Weakness	Tenderness	11,842	>12,000	NR	NR	[Jin]
1	58	F	Weakness	PT, DTR	700	NR	Fibrillations	Myositis	[Zhang]
1	36	F	Weakness	PT	NR	NR	NR	NR	[Singh]
1	42	F	Weakness, DV, DP	Weakness	NR	NR	NR	NR	[Anand]
1	71	M	Weakness, myalgia	None	8720	2079	NR	NR	[Valente-Acosta]
1	16	M	Myalgia, fatigue	Tenderness	427,656	45 mcg/L	NR	NR	[Gefen]
1	38	M	Myalgia	Normal	42,670	NR	NR	NR	[Zhang]
1	NR	M	Myalgia, weakness	Weakness	25,384	NR	NR	NR	[Beydon]

Abbreviations: CK, creatine-kinase; DP, dysphagia; DTR, diminished tendon reflexes; DV, double vision; EMG, electromyography; MB, muscle biopsy; MG, myoglobin; NOP, number of patients; NR, not reported; PT, ptosis.

Specific myopathies have been particularly reported in single patients (Table 1). In a 58-year-old female with limb weakness and ptosis, CK-elevation, and fibrillations on EMG, myositis was diagnosed upon muscle biopsy. Myositis was also reported in two other patients. Rhabdomyolysis was reported in three patients. In one of these patients CK-elevation reached a value of more than 400,000 (Table 1). In a 38-year-old Chinese male with myalgia SARS-CoV-2-associated myositis with rhabdomyolysis was diagnosed. SARS-CoV-2-associated myositis and rhabdomyolysis was also reported in another male based upon muscle magnetic resonance imaging. In all three patients did pulmonary manifestations occur simultaneously or precede the onset of muscle symptoms. Exacerbation of MG was reported in two patients. In a single patient with previously diagnosed, seronegative MG, weakness of limb muscles and extraocular muscles increased upon the infection with SARS-CoV-2. In another patient with previously stable MG the infection caused exacerbation of MG as well. A new symptom reported was myalgia in this patient. In a case series of 10 SARS-CoV-2-infected patients from Brasil, minimal invasive, ultrasound-guided, postmortem studies revealed that 60% of the patients had features of myositis and 80% displayed necrotic muscle fibers on autopsy.

The causes of muscle damage in SARS-CoV-2-infected patients are quite heterogeneous. Myopathy could be explained by infection with the virus (myositis), by immune mechanisms (immune myositis), by electrolyte disturbances, critical ill myopathy, drugs, or hypoxia. Myalgia in infected patients is presumably due to immune-mediated myositis. In a recent review it was concluded that myopathy in SARS-CoV-2-infected patients is rather related to damage via immune mechanisms due to massive cytokine release than direct invasion of the virus into muscle tissue. Whether the infection only unmasks previously unrecognized NMD or truly induced a previously nonexistent NMD remains speculative but there are indications that SARS-CoV-2 truly damages the skeletal muscle in many patients. Aggravation of preexistent muscle disease is conceivable, particularly if respiratory muscles are involved or if muscle disease is immune-mediated.

Overall, the striated muscles are frequently affected in patients with SARS-CoV-2 infection but, in the majority of the cases, muscle involvement is nonspecific, manifesting as myalgia (11%–62% of cases), fatigue, weakness, or wasting. Only rarely a specific muscle disease, such as myositis, MG, or rhabdomyolysis is diagnosed. Work-up of muscle involvement in the infection is usually incomplete why the causes of muscle disease remain unsolved in the majority of the cases. However, muscle damage in SARS-CoV-2-infected patients is presumably more likely immune-mediated, due to electrolyte-disturbances, a complication of sepsis, bed-rest, or due to hypoxia than the consequence of a direct viral attack on myocytes. More in-depth studies of muscle disease associated with SARS-CoV-2 infection are warranted.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

KEYWORDS

coronavirus, myalgia, myopathy, myositis, rhabdomyolysis

Josef Finsterer MD, PhD[1]
Fulvio A. Scorza MD[2]

[1]*Klinikum Landstrasse, Messerli Institute, Vienna, Austria*
[2]*Disciplina de Neurociência. Escola Paulista de Medicine/Universidade Federal de São Paulo (EPM/UNIFESP), São Paulo, Brasil*

Correspondence
Josef Finsterer, MD, PhD, Klinikum Landstasse, Messerli Institute, Postfach 20, 1180 Vienna, Austria.
Email: fifigs1@yahoo.de

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