



Critical illness neuro-myopathy (CINM) and focal amyotrophy in intensive care unit (ICU) patients with SARS-CoV-2: a case series

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Abstract

We found four patients with some characteristic phenotype in our ICU, characterized by focal hypotrophies of the shoulder girdle and the bilateral peroneal district and underlying critical illness neuro-myopathy. In our opinion, these hypotrophies are secondary to the prone position. Is our intention to start early treatment protocol with electrostimulation to evaluate the effectiveness in the prevention of critical illness and focal hypotrophies in ICU SARS-CoV-2 patients, to increase chances of returning to a preinfection functional status.

Keywords Sars-CoV-2 · COVID-19 · Critical illness neuro-myopathy · Intensive care unit · Pandemic

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a new strain of coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Within a few months of the first report in China, SARS-CoV-2 had spread worldwide, declared a global pandemic on 11 March 2020 by the World Health Organization. The outbreaks of COVID-19 have constituted a public health emergency of international concern. Respiratory distress is the most characteristic symptom, and more than half of patients with dyspnea need intensive care [1]. The estimated average time spent in intensive care unit (ICU) is described to be around 3 weeks. Prone position was recognized for its ability to improve oxygenation used as salvage therapy for refractory hypoxemia in ARDS, but potential complications could be facial pressure

ulcers, facial edema, lip trauma from endotracheal tube, and brachial plexus injury (due to arm extension) [2].

The aim of this communication is to highlight the relevance of neuromuscular involvement and its different clinical features in ICU patients with SARS-CoV-2. The neurotrophism of SARS-CoV-2 has been well demonstrated [3, 4]. Indeed, infected patients could show severe central nervous system involvement, such as necrotizing hemorrhagic encephalopathy, stroke, encephalitis, and epileptic seizures. Moreover, myalgia with elevated creatine kinase, hyposmia, and dysgeusia are well-known to be correlated at the infection [5, 6]. In addition, some cases of acute peripheral nervous system disease [7, 8] are recently reported.

Neuromuscular disorders and critical illness neuromuscular myopathy (CINM) could dramatically reduce the patient chances of returning to a preinfection functional status [8–10] and could have a detrimental role in respiratory failure outcome.

A 74-year-old Caucasian female (patient n. 1), non-smoker, with hypertension and hypercholesterolemia, in home therapy with sartanic and statins, was admitted in our hospital on 25 March 2020 for related COVID-19 respiratory failure. She early started noninvasive ventilation (NIV) in association with prophylactic heparin therapy (4.000 units/day), hydroxychloroquine 200 mg/day, and antiretroviral drug. Ten days later, due to progressive worsening of the respiratory distress, she was admitted to ICU and started invasive ventilation with high peeps and pronation cycles (16 h prone/8

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Table 1 Nerve conduction study parameters

Nerve	Side	Distal latency (msec)	Distal amplitude (mV)	Proximal amplitude (mV)	Velocity (m/sec)
Motor recordings					
Common peroneal	Right	Absent	Absent		
	Left	Absent	Absent		
Tibial	Right	3.1	3.4	3	41
	Left	3.3	1.4	1.5	49.6
Ulnar	Right	2.3	1.1	1.3	60.8
Sensory recordings					
Sural	Right	Absent	Absent		
	Left	Absent	Absent		
Superficial Peroneal	Right	Absent	Absent		
	Left	1.5	8.7		48.7
Ulnar	Right	1.6	6.8		53.8

supine position). On the ninth day, tracheotomy was performed. After 3 days, the curarization was suspended, and a weaning was started by mechanical ventilation.

For bronchoaspirate positivity for *A. baumannii* and *S. aureus* and positive blood cultures for carbapenem-resistant *Klebsiella* and *C. albicans*, she started antibiotic therapy. The patient always remains sleepy, asthenic, and unresponsive, despite the absence of sedation.

A neurological consultation was requested after 1 month in ICU. The examination showed drowsiness, no cranial nerve involvement, tetraplegia with diffuse hypotonia, and hypotrophy, mainly at shoulder girdle and to the peroneal district, without fasciculations. Deep tendon reflexes were absent with normal plantar response. There was no evidence of pyramidal and meningeal signs. Sensitivity was unevaluable due to mental status.

Laboratory results were clinically significant for lymphocytopenia: 0.71 (n.v 1.30–2.90 m/mmc), thrombocytopenia 64 (n.v 140–450 m/mmc), D-dimer 698 (n.v < 350 ng/ml), LDH 191 (n.v 120– U/l), PCR 6.32 (n.v 0.00–0.50 mg/dl), and procalcitonin 3.89 (n.v < 0.5 ng/mL). Cerebrospinal fluid showed 10 white blood cells and normal protein level; PCR for coronavirus-19 was negative. We also researched serum antibodies anti-GM1 IgG-IgM, anti-GQIb IgG-IgM, anti-GM2 IgG-IgM, anti-MAG, anti-sulfatide, anti-GAD, and anti-CASPR2, all negative. The patient underwent

electromyography (EMG): nerve conduction studies showed symmetrical axonal polyneuropathy, and needle study showed chronic neurogenic distal pattern with some proximal myopathic potential on deltoid muscle bilaterally (Table 1). The neurophysiological findings were compatible with CINM.

Due to muscular weakness, she needed continuous ventilation on pressure support (PSV) with gradually decreasing supports, until alternating cPAP and PSV cycles. She performed physiotherapy and cough machine therapy 4 times/day. On 6 May, a worsening of the respiratory function requires to switch back to controlled ventilation. A progressive deterioration of the clinical conditions occurred (related to new superinfection), until death after 3 days.

We also studied three other SARS-CoV-2 patients (patient n. 2, 3, and 4) in ICU (Table 2, Fig. 1) who underwent invasive ventilation and pronation cycles due to respiratory distress. All these patients had similar phenotype, characterized by evident hypotrophy of the peroneal district and/or of the shoulder girdle and underlying CINM at the EMG. The neurophysiological findings did not show nerve conduction blocks (particularly at the peroneal capitellum bilaterally).

Only one patient (patient n. 3), probably due to a younger age, had a positive outcome, even if characterized by slow recovery of motor skills, in particular due to foot flexion deficit, improved after intensive physiotherapy.

Table 2 Features of patient 2, 3, and 4

Patient	Age	Gender	Phenotype*	EMG	Time in ICU	Superinfection	Outcome
2	71 years	M	U - L	CINM	> 3 weeks	+	Deceased
3	60 years	M	U - L	CINM	> 3 weeks	+	Alive
4	73 years	M	L	CINM	> 3 weeks	-	Deceased

M, male; U, upper girdle hypotrophy; L, lower girdle hypotrophy; EMG, electromyography; CINM, critical illness neuro-myopathy; ICU, intensive care unit

Fig. 1 Bilateral severe upper girdle hypotrophy (patient n. 2)



In conclusions, patients with SARS-CoV-2 infection in ICU are particularly predisposed to develop neuromuscular involvement for several modifiable and unmodifiable reasons, such as prolonged bed rest, intercurrent infections, and use of steroid therapy. In our opinion, these findings may be related to the prone position maintained for a long time by patients during the ventilation period and could be facilitated by underlying neuropathy, even further studies will be needed to demonstrate this evidence [9, 10].

It is our intention to start early treatment protocol with electrostimulation to evaluate the effectiveness in the prevention of CINM and focal hypertrophies in ICU SARS-CoV-2 patients, to increase chances of returning to a basal functional status.

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Compliance with ethical standards

Conflict of interests The authors declare that they have no conflict of interest.

Ethics approval Observational case series; ethics approval not required.

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