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CORRESPONDENCE

Transient acute-onset tetraparesis in a COVID-19 patient

This article has been corrected since Advance Online Publication and a correction is also printed in this issue

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To the Editor:

We read with interest the recent letter to the Editor-in-Chief about SARS-CoV-2 [1]. We wanted to highlight in this letter that although SARS-CoV-2 has a preferential pulmonary and gastrointestinal tropism, it also has systemic and possible neurological effects [2]. We describe the case of a COVID-19 patient presenting to our hospital with newly diagnosed acute-onset tetraparesis in an attempt to increase awareness.

A 22-year-old woman, affected by type I diabetes mellitus, presented to our emergency with worsening dyspnea, fever, and loss of consciousness (Glasgow Coma Scale 6). The first blood investigation showed a state of ketoacidosis (pH 7.05), hypocapnia, and hypoxia. Blood glycemia was 744 mg/dL. Table 1 shows blood test trend during patient hospitalization.

A thoracic high-resolution computer tomography (CT) revealed bilateral ground-glass opacity almost completely involving lung parenchyma, highly suggestive for COVID-19 pattern. Brain CT and CT-angiography highlighted a tiny right frontal parenchymal hemorrhage, excluding vascular malformations. Subsequently, a reverse transcriptase polymerase chain reaction (RT-PCR) assays of nasopharyngeal swab and bronchoalveolar lavage resulted positive for SARS-CoV-2 infection.

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The patient, already intubated, was then transferred to the intensive care unit. Supportive, antiviral, and immunomodulatory therapies have been set.

On 8th day after hospitalization, a thoracic CT showed the persistence of the ground-glass parenchyma opacity pattern. On 12th day, given the partial improvement of respiratory dynamics and the stability of gas exchange, the endotracheal tube was removed.

On 15th day, a neurological examination highlighted an acute flaccid tetraparesis, more pronounced in the distal muscles, with hyperelicitable osteo-tendon reflexes, and concomitant fecal and urinary incontinence. Occasional and migrant hypoaesthetic and dysaesthetic manifestations have been reported in the lower limbs. On 18th day, brain and spine gadolinium magnetic resonance imaging were performed; no particular pathological features were noticed, except for a late subacute phase tiny frontal hemorrhage (8 mm of maximum diameter).

A lumbar puncture and serology examination were also performed (Table 1). RT-PCR on CSF sample resulted negative for SARS-CoV-2 infection. Physiokinesitherapy rehabilitation was then performed, and a subsequent mild and progressive improvement of hyposthenia and sphincter incontinence was observed.

On 30th day, due to clinical improvement, the patient was discharged and addressed to a rehabilitation facility to complete physiokinesitherapy program.

Since the main organic, infectious, and immunomediated causes of acute-onset flaccid tetraparesis have been excluded from the anamnestic, neuroradiological, and laboratory data recorded, we can hypothesize that SARS-CoV-2 had a promoter role in the onset of the tetraparetic clinical presentation.

Early evidence in the literature has already highlighted how SARS-CoV-2 presents a neurotrophic and neuroinvasive tendency [3]. In particular, through ACE-2 host receptor expressed on the plasma membrane, SARS-CoV-2 can infect different human cells and tissues. By exploiting the same biomolecular mechanisms, SARS-CoV-2 can interact with nervous cells and endothelial cells of the

Table 1 Patient laboratoristic parameters. This table summarizes patient laboratoristic parameters recorded during hospitalization and subsequent rehabilitation period.

	Day 0	Day 3	Day 5	Day 10	Day 15	Day 20	Day 25	Day 30	Day 35
Count $\times 10^9$/L									
White blood cells	28.57 ↑	23.99 ↑	8.62	11.41 ↑	9.68	11.08 ↑	9.63	7.00	
Neutrophil	23.56 ↑	21.92 ↑	6.96 ↑	9.93 ↑	7.25 ↑	4.03	3.85	3.98	
Lymphocyte	3.82	1.46 ↑	1.12 ↑	0.93 ↓	0.88 ↓	0.82 ↓	1.00 ↓	0.94 ↓	
Platelet	365	192	172	313	248	223	260	306	
C-reactive protein mg/L	136.1 ↑	22.6 ↑	10. 2 ↑	1.9	0.7	4.5	2.0	0.9	
D-dimer ug/L	>9000 ↑	3993 ↑	3858 ↑	4169 ↑	2308 ↑	902 ↑	471 ↑	462	
Glucose mg/dL	744 ↑	565 ↑	503 ↑	476 ↑	396 ↑	302 ↑	273 ↑	180 ↑	
Lactate dehydrogenase U/L	729 ↑	618 ↑	567 ↑	434 ↑	360 ↑	338 ↑	348 ↑	222 ↑	
Alanine aminotransferase U/L	38	45 ↑	31	27	40	76 ↑	69 ↑	32	
Aspartate aminotransferase U/L	144 ↑	69 ↑	30	20	28	56 ↑	29	14	
Blood urea nitrogen mg/dL	48	31	33	27	16 ↓	15 ↓	24	28	
Creatinine mg/dL	0.64	0.46	0.33	0.29 ↓	0.28 ↓	0.27↓	0.29 ↓	0.27 ↓	
Cobalamin (B-12) pg/mL						1155			
RT-PCR on nasopharyngeal swab and bronchoalveolar lavage	+				+			−	−
Serology									
Ig Myc Pne					−				
Ig Leg Pne					−				
Ig Chl Pne					−				
Ig HIV 1–2					−				
CSF examination									
Biochemical									
Physical					Clear, colorless, normal pressure				
Glucose					139 mg/dL				
Protein					53 mg/dL				
Protein					0.8 mm^3				
Microscopic									
Bacteria						−			
HSV 1–2 DNA						−			
VZV DNA						−			
Mycobacterium						−			
Borrelia						−			
RT-PCR SARS-CoV-2						−			

+ positive, − negative, ↑ value higher than laboratory reference parameters, ↓ value lower than laboratory reference parameters, *Chle Pne* Chlamydia Pneumoniae, *HIV* human immunodeficiency virus, *HSV* Herpes simplex virus, *Ig* M and G Immunoglobulin classes, *Leg Pne* Legionella Pneumophila, *Myc Pne* Mycoplasma Pneumoniae, *RT-PCR* reverse transcriptase polymerase chain reaction, *VZV* Varicella zoster virus.

central nervous system (CNS) vessels [3]. Once reached the CNS, SARS-CoV-2 can determine the activation of self-reinforcing inflammatory processes through a "cytokine storm", causing irreversible neuronal damage. In addition, the endothelial ruptures in cerebral capillaries, due to the endotheliitis process, can contribute to the pathophysiology of SARS-CoV-2 brain damage [3].

ACE-2 receptor is also expressed on the plasma membrane of spinal cord neurons [2]. A first-reported case of postinfective acute transverse myelitis has been described in the literature [2], suggesting that spinal cord can be the target of SARS-CoV-2 infection. As for other viruses implicated in postinfectious acute myelitis, the nervous tissue damage is not only given by a direct neuroinvasive action of SARS-CoV-2, but also by an indirect injury of the hyperactivated immune system [3].

It must be underlined that in the case here described, despite the CSF RT-PCR resulted negative for SARS-CoV-

2 research, the conjunction between neurological clinic, laboratoristic, and thoracic imaging data may support the possible SARS-CoV-2 CNS involvement, confirming its neuroinvasive and neurotrophic character role. Furthermore, the acute onset of a transient tetraparetic status in the absence of neuroradiological evidence of organic damage leads us to support the probable neuro-irritative and neuro-shocking role of the SARS-CoV-2.

In addition, our patient suffered from type I diabetes mellitus. As known, the high chronic glucose blood levels can injure nerves throughout different biochemical pathways [4]. Therefore, we can deduce that the neuro-shocking and neuro-irritative effect of SARS-CoV-2, in addition to hyperglycemic neuro-stress, can have a promoting and synergistic role in the manifestation of the tetraparetic transient acute clinic.

In summary, while it is well known that SARS-CoV-2 primarily targets pulmonary and gastrointestinal systems, there is now also clear evidence of its systemic involvement. Moreover, early evidence suggests that is may also target the CNS, but we clearly need more data and studies to confirm this. As described in this case, the neuroinvasive and neurotrophic potential of SARS-CoV-2 could have a synergistic and promoter role in determining neuro-irritative and neuro-shocking effects, without necessarily causing neuroimaging evident organic damage. We call on all to be aware of this possibility and to ensure that any cases like this are reported so we can develop a clear picture of all the possible effects of this world-changing virus.

Compliance with ethical standards

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

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