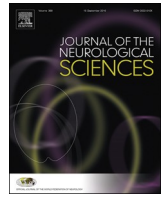




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Response to letter to the Editor

Exacerbation of chronic inflammatory demyelinating polyneuropathy in concomitance with COVID-19



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Dear Editor,

We have read with great interest the article “Myasthenic Crisis in COVID-19” by Delly et al. [1], which described the case of a patient with myasthenic crisis simultaneous with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The authors claimed that, given the possible infection-induced exacerbations of myasthenia gravis (MG) [2] and the shared cytokine hyperactivation state of coronavirus disease 2019 (COVID-19) and MG crisis [1], COVID-19 might have precipitated the MG course.

To support this hypothesis and to widen the spectrum of possible interactions between SARS-CoV-2 infection and neuroimmunological disorders, we present the case of a 69-year-old man with a 6 years-history of chronic inflammatory demyelinating polyneuropathy (CIDP) who developed a clinical exacerbation in concomitance with COVID-19.

The diagnosis of CIDP had been formulated 6 years ago, based on the typical clinical presentation [3], electrophysiological findings [4], and the presence of cerebrospinal fluid (CSF) albuminocytological dissociation [3]. Anti-ganglioside antibodies and serum paraproteins, were absent. The disease course showed a stepwise progressing profile [3], with exacerbations manifesting predominantly with worsening of hypoesthesia and weakness in the four limbs. Additional comorbidities were pemphigus vulgaris and hypothyroidism. The patient benefited from permanent immunosuppressive treatment: prednisolone (variable dose, 5 mg at the time of admission), mycophenolate mofetil (1000 mg b.i.d.), rituximab (1 g × 2, for 11 months due to pemphigus), and intravenous immunoglobulins (IVIG) (0,4 g/kg/day, 5 days every 4–5 weeks). The last exacerbation was reported in February 2020. On that occasion, the neurological examination revealed distal weakness in the upper extremities (MRC 4/5), global areflexia, distal hypoesthesia, and hypopallesthesia in the four limbs and gait ataxia.

In March 2020, the patient was referred to our Department of Neurology complaining of fever [max body core temperature (BcT) 38.5 °C] since two days and sudden occurrence of dysarthria and link facial palsy together with worsening of gait ataxia. The RT-PCR for SARS-CoV-2 RNA with a nasopharyngeal swab was negative. Chest-X-

ray, brain magnetic resonance imaging, and laboratory investigations were unremarkable. The CSF analyses showed no infectious signs with normal leucocyte count (2/μL). The day after, multiple cranial nerve palsies (bilateral ptosis, bilateral facial palsy, anarthria, and dysphagia), severe tetraparesis (2–3 MRC in all limbs) and anesthesia in four limbs occurred, progressing within few hours up to high fever (BcT 40 °C), and dyspnea. Moreover, repeated high levels of creatine kinase (CK) [max. 2701 U/L, normal values (nv) < 171], CK-MB (54 U/L, nv < 25), C-reactive Protein (223 mg/L, nv < 6), procalcitonin (88.9 ng/mL, nv < 0.5), and troponin (2.057 ng/mL, nv < 0.026) were documented.

The patient was transferred to the intensive care unit (ICU). An electroneurographic examination was carried out but no motor and sensitive potentials were evocable. Given the progressive respiratory failure, the patient underwent non-invasive and then invasive mechanical ventilation. At this point, the SARS-CoV-2 RNA by PCR in bronchial secretions by means of bronchoscopy resulted positive. Accordingly, a high-resolution computed tomography of the chest revealed inflammatory infiltrates in the right inferior lung. The patient was diagnosed with COVID-19 pneumonia. Therefore, steroids and mycophenolate were stopped, whereas a therapy with IVIG (1 g/kg/day) was settled for five days. During the ICU hospitalization, the patient was also treated with ritonavir/lopinavir, ribavirin, clarithromycin, meropenem and enoxaparin. Moreover, consecutive investigations disclosed high levels of serum IL-6 (max. 375 – min 10.4 mg/dL, nv < 7), ferritin (812 microg/L, nv 4–665), D-dimer (4.34 mg/fibrinogen equivalent units, nv < 0.5), fibrinogen (5.1 g/dL, nv 1.8–3.5) and LDH (261 U/L, nv < 250). After two weeks of mechanical ventilation, neurological and respiratory status progressively improved. 22 days after hospitalization, the patient was extubated; then, oxygen-therapy was reduced, and the therapy with mycophenolate reintroduced. A chest-X-ray revealed a regression of previous infiltrates. 36 days after admission, given the resolution of symptoms, four negative RT-PCR for SARS-CoV-2 with nasopharyngeal swabs together with two negative tests on bronchial secretions, the patient was discharged to home.

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One month later, a further neurological examination disclosed a full recovery of cranial nerve deficits, with persistence of hypoesthesia, mild proximal weakness in the four limbs (MRC 3–4/5), areflexia, and gait ataxia. A new cycle of IVIG was administered with clinical benefit. An electrophysiological examination revealed pathological findings similar to those described one year before. SARS-CoV-2 IgA and IgG tested positive, while RT-PCR for SARS-CoV-2 RNA with nasopharyngeal swab was negative.

In summary, we describe a patient with CIDP who manifested a clinical exacerbation in association with SARS-CoV-2 infection. In detail, the appearance of neurological symptoms, together with the onset of fever and their simultaneous worsening with emerging of classic COVID-19 manifestations, suggests that SARS-CoV-2 infection may have triggered or at least contributed to the neurological worsening. Indeed, although a specific causal association between SARS-CoV-2 or other human coronaviruses infections and exacerbations in CIDP and MG has been not previously reported, some lines of evidence suggested that virus infections and/or pyrexia may favour a pro-inflammatory state which, in turn, may lead to the amplification of the autoimmunity and, thus, to the deterioration of immune-mediated neurological diseases [2,5,6]. Moreover, human coronavirus 229E and OC43 have been associated with multiple sclerosis (MS), likewise the inoculation of JHMV, a murine coronavirus, induces a MS-like disease in murine models [7,8]. On another issue, in our case report, a significant up-regulation of IL-6 was documented, in accordance with previous data in both CIDP and COVID-19, supporting the view of a possible common immunological pathway [9,10]. Moreover, although, in this case, CIDP was known to show a typical stepwise progressing course, the current manifestations appeared significantly more critical (e.g. severe tetraparesis) and wide (e.g. multiple cranial nerve involvement) compared to previous exacerbations. Thus, the hypothesis of a coincidental occurrence with COVID-19 appeared less probable.

Taking together our and previous findings, the potential association between SARS-CoV-2 infection and exacerbations of neuroimmunological disorders, remains speculative, but probable. If the hypothesis will be confirmed in larger case series, neurologists should be aware that SARS-CoV-2 infection might be a possible precipitating factor for clinical worsening in immune-mediated polyneuropathies.

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Declaration of Competing Interest

None.

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