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Case report

Guillain-Barré-Strohl syndrome and COVID-19: Case report and literature review

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Abstract

In recent months, the new beta-coronavirus has caused a pandemic with symptoms affecting mainly the respiratory system. It is established that the virus may play a neurotropic role and in recent months several cases of Guillain-Barré-Strohl syndrome (GBS) have been reported in patients infected with COVID-19. We report the case of a 54-year-old patient with acute demyelinating polyneuropathy during infection by SARS-CoV-2 who progressed clinically to require assisted ventilation. After several weeks of specific symptomatic treatment, the patient had a favorable outcome. In conclusion, despite being a rare complication, we think it is important to consider the possibility of diffuse involvement of the peripheral nervous system in patients with COVID-19 to adjust clinical monitoring and treatment in these cases.

Keywords: Covid-19; Guillain-Barré; SARS-CoV-2.

1. Introduction

Since December 2019, the world is living a pandemic situation caused by SARS-CoV-2 which originated in Wuhan, China. The symptoms caused by SARS-CoV-2 are similar to those of the 2003 coronavirus SARS-CoV and both share the same receptor as gateway to the cell, angiotensin-converting enzyme 2 (ACE2) [1]. Some cases of involvement of the peripheral nervous system have also been described, mainly in the form of myalgia, but also as acute polyneuropathy [2,3].

Guillain-Barré-Strohl Syndrome (GBS) is an acute polyneuropathy with an incidence of 1.11/100,000 inhabitants. The etiopathogenesis of polyneuropathy in GBS is believed to be due to molecular mimicry between epitopes of microorganisms and peripheral nerve glycolipids [4]. In 2/3 of the patients with GBS there is a history of respiratory or gastrointestinal infection in the previous days or weeks. Some viruses have been described as causative agents of GBS (Influenza A, cytomegalovirus, Zika, Chikungunya…) [4]; however, there are hardly data in the literature about GBS by coronavirus. We report the case of a patient with acute demyelinating neuropathy during infection by SARS-CoV-2 who initially had a clinical progression leading to admission to the Intensive Care Unit (ICU) and subsequently had a regressive clinical outcome.

2. Case report

A 54-year-old male with hypertension and obesity presented to the emergency room complaining of hypoesthesia in the left mandibular region, progressing paraparesis of upper limbs and difficulty walking that started the previous day. Febrile syndrome, non-productive cough and myalgia started five days before and were ongoing when he consulted. He was hemodynamically stable. Neurological examination showed the patient to be conscious, oriented, with preserved higher functions. He had no cranial pair involvement. The muscular balance by muscle groups evidenced an asymmetric weakness in both upper limbs obtaining a muscular balance of 2/5 according to the MRC scale (Medical Research Council grading) in the left upper limb globally and 3/5 in the muscles dependent on the right ulnar nerve. He had no axial or lower limb weakness. He had distal hypoesthesia in the fingers of both hands with no sensory level or hypoesthesia of the lower limbs. Deep tendon

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reflexes were globally absent. Laboratory tests evidenced eosinopenia 0.0% with no other disorders in the blood count (no leukocytosis, lymphopenia, or thrombocytopenia), negative procalcitonin, C-reactive protein (CRP) 3.7 mg/dL, lactate dehydrogenase 286 IU/L (lower 250), creatine kinase 578 IU/L (x 2.5), serum electrolytes, normal liver and kidney function. Nasopharyngeal swab for SARS-CoV-2 polymerase chain reaction was positive. Cerebrospinal fluid (CSF) analysis showed mild albuminocytologic dissociation (protein levels 52 mg/dL and absence of leukocytes). The chest X-ray did not show parenchymal condensations. A neurophysiological study was performed at 3 days of the onset of neurological symptoms, which evidenced sensory and motor polyneuropathy, with signs of demyelination (conduction blocks, absence of F waves in the right ulnar nerve and axon potentials in the F response of the right tibial nerve) of diffuse distribution, but mainly affecting the nerves of the upper limbs (see supplementary Table). Furthermore, antiganglioside antibodies were measured in serum, obtaining IgM for GM2 and GD3 and a weak IgG band for GT1b. According to the diagnostic Brighton Collaboration criteria, our patient was diagnosed with acute demyelinating polyneuropathy [5].

Targeted therapy for SARS-CoV-2 was started with azithromycin, hydroxychloroquine and lopinavir/ritonavir. As a specific treatment for GBS he started infusion of human intravenous immunoglobulins (IVIg) at 0.4 g/kg/day for 5 days. After administration of the first dose the patient reported “flushing” and had a presyncopal episode. As it was suspected to be an adverse effect to IVIg, no new doses were administered. The next two days he had respiratory impairment and increase in the laboratory inflammatory parameters, requiring invasive ventilation and support by the ICU. After 14 days he had clinical and laboratory improvement and progressed to extubation. After discharge from the ICU he had severe flaccid tetraparesis of proximal predominance and muscular atrophy. All of this suggested an overadded critical illness myopathy. He also had severe bilateral facial palsy and dysphagia, both probably explained by progression of the GBS rather than overadded critical illness myopathy. The patient underwent rehabilitation and had a good response. Seven weeks later, he was discharged and able to walk independently with support. The patient gave his consent to publish this case report.

3. Discussion

The association between GBS and SARS-CoV-2 is still theoretical. A study performed in Italy compares the incidence of GBS in its region in the year 2020 vs 2017–2019 and reports a 5.41 times increase [6]. Some cases of polyneuropathy caused by other types of coronavirus have been published in the literature [7,8] and some authors support a potential neurotropic role of the virus during the active infection [9]. In the past months a substantial number of case reports of polyneuropathies consistent with GBS during or after infection by COVID-19 have been published [3,10,11-23] (see supplementary Table 1 and all case report references in the supplementary appendix). To note, the great majority of the cases reported (86.5%) were older than 50 years with a male predominance. Only the 29.7% had anosmia and/or ageusia during the COVID-19 infection. There is probably no direct root infection as the virus was not detected in the CSF of 23 patients.

A viral infection can cause neuromuscular damage through different mechanisms: direct damage as neuritis or myositis in the context of an active infection, as part of a systemic inflammatory response syndrome or by cross-immunity. The inflammation caused by some coronaviruses can trigger immune dysfunction with release of several proinflammatory immune factors that, besides damaging the lungs, could damage other organs and/or nerves. Recently, it has been described a systemic hyperinflammation in patients with COVID-19 with macrophage activation syndrome. Also, some cases of GBS by Zika virus have led to hypothesize this possible parainfectious pathogenesis [24]. It must be noted that in our case and several cases of GBS by COVID-19 reported to date, neurological dysfunction starts a few days after infection by SARS-CoV-2 and/or overlaps COVID-19 symptoms. Besides that, some authors found a higher prevalence of axonal variant of GBS in this group [3]. This leads to think that the peripheral nervous system injury could be due to the acute inflammatory response. In our case, interleukin-6 levels are not available, but other inflammatory parameters such as ferritin or CRP were high. On the other hand, the diffuse distribution of polyneuropathy, the demyelinating findings in the neurographic study and the presence of antiganglioside antibodies would support an immune-mediated origin. Additionally, a postinfectious origin can not be excluded because Sars-CoV-2 infection can have a long incubation period. Some of the cases published to date, were probably caused by a postinfectious and molecular mimicry, as the onset of polyneuropathy occurred more than two weeks after the infection, the nasopharyngeal swab for SARS-CoV-2 polymerase chain reaction had become negative during the GBS in some of them and had a good response to IVIg [11,12,14,15,17]. To remark, a recent study has shown that the spike protein of SARS-CoV-2 binds also to sialic acid–containing glycoproteins and gangliosides on cell surfaces [25]. Therefore, a cross-reaction between epitopes within the SARS-CoV-2 spike saccharides and gangliosides of peripheral nerve is a feasible possibility. Despite this, there is a lack of scientific evidence for this association at the moment. We consider this is important in order to take precautions both in the indications of a future vaccine and in treating patients with the transfer of IgG from other reconvalescent COVID-19 patients.

As limitations we would highlight that in our patient there is no screening available which rules out concomitant infection by other microorganisms associated with GBS. In two of the published cases, GBS occurred after coinfection by SARS-CoV-2 and *Campylobacter jejuni* [16,18]. However, due to the absence of an epidemiological history of symptoms suggesting other infections and the temporal relationship

with SARS-CoV-2 infection, we think this possibility is very unlikely.

In conclusion, the SARS-CoV-2 is a virus of recent diagnosis that has also been shown to affect the peripheral nervous system, although its mechanism remains unclear. Although GBS due to SARS-CoV-2 is a rare complication, we think it is important to consider this possibility in patients with COVID-19 concomitantly or even after weeks following infection by SARS-CoV-2 because this involves a different prognosis and a specific treatment associated with conventional treatment.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.nmd.2020.08.354.

References

[1] Zhou P, Lou Yang X, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579:270–3. https://doi.org/10.1038/s41586-020-2012-7.

[2] Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China 2020. https://doi.org/10.1001/jamaneurol.2020.1127.

[3] Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain–Barré syndrome associated with SARS-CoV-2. N Engl J Med 2020. https://doi.org/10.1056/nejmc2009191.

[4] Van Den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, Van Doorn PA. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol 2014;10:469–82. https://doi.org/10.1038/nrneurol.2014.121.

[5] Sejvar JJ, Kohl KS, Gidudu J, Amato A, Bakshi N, Baxter R, et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2011;29:599–612. https://doi.org/10.1016/j.vaccine.2010.06.003.

[6] Gigli GL, Bax F, Marini A, Pellitteri G, Scalise A, Surcinelli A, et al. Guillain-Barré syndrome in the COVID-19 era: just an occasional cluster? J Neurol 2020. https://doi.org/10.1007/s00415-020-09911-3.

[7] Kim JE, Heo JH, Kim HO, Song SH, Park SS, Park TH, et al. Neurological complications during treatment of middle east respiratory syndrome. J Clin Neurol 2017;13:227–33. https://doi.org/10.3988/jcn.2017.13.3.227.

[8] Sharma K, Tengsupakul S, Sanchez O, Phaltas R, Maertens P. Guillain–Barré syndrome with unilateral peripheral facial and bulbar palsy in a child: a case report. SAGE Open Med Case Reports 2019;7. 2050313X1983875 https://doi.org/10.1177/2050313x19838750 .

[9] Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the cns: tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. ACS Chem Neurosci 2020;11:995–8. https://doi.org/10.1021/acschemneuro.0c00122.

[10] Alberti P, Beretta S, Piatti M, Karantzoulis A, Piatti ML, Santoro P, et al. Guillain-Barré syndrome related to COVID-19 infection. Neurol Neuroimmunol Neuroinflamm 2020;7:1–4. https://doi.org/10.1212/NXI.0000000000000741.

[11] Andrea A, Luana B, Silvia DM, Erika S, Massimo DS. New clinical manifestation of COVID-19 related Guillain-Barrè syndrome highly responsive to intravenous immunoglobulins: two Italian cases. Neurol Sci 2020. https://doi.org/10.1007/s10072-020-04484-5.

[12] Camdessanche JP, Morel J, Pozzetto B, Paul S, Tholance Y, Botelho-Nevers E. COVID-19 may induce Guillain–Barré syndrome. Rev Neurol (Paris) 2020. https://doi.org/10.1016/j.neurol.2020.04.003.

[13] Gutiérrez-Ortiz C, Méndez A, Rodrigo-Rey S, San E, Murillo P, Bermejo-Guerrero L, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19 2020. https://doi.org/10.1212/WNL.0000000000009619.

[14] Lascano AM, Epiney J, Coen M, Serratrice J, Bernard-Valnet R, Lalive PH, et al. SARS-CoV-2 and Guillain-Barré syndrome: AIDP variant with favorable outcome. Eur J Neurol 2020. ene.14368.https://doi.org/10.1111/ene.14368.

[15] Padroni M, Mastrangelo V, Asioli GM, Pavolucci L, Abu-Rumeileh S, Piscaglia MG, et al. Guillain-Barré syndrome following COVID-19: new infection, old complication? J Neurol 2020:1. https://doi.org/10.1007/s00415-020-09849-6.

[16] Rana S, Lima AA, Chandra R, Valeriano J, Desai T, Freiberg W, et al. Novel coronavirus (COVID-19)-associated Guillain-Barré syndrome: case report. J Clin Neuromuscul Dis 2020;21:240–2. https://doi.org/10.1097/CND.0000000000000309.

[17] Scheidl E, Canseco DD, Hadji-Naumov A, Bereznai B. Guillain-Barre syndrome during SARS-CoV-2 pandemic: a case report and review of recent literature. J Peripher Nerv Syst 2020. https://doi.org/10.1111/jns.12382.

[18] Virani A, Rabold E, Hanson T, Haag A, Elrufay R, Cheema T, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection. IDCases 2020;20. https://doi.org/10.1016/j.idcr.2020.e00771.

[19] Zhao H, Shen D, Zhou H, Liu J, Chen S. Correspondence. Lancet Glob Heal 2020;4422:2–3. https://doi.org/10.1016/S1474-4422(20)30109-5.

[20] Oguz-Akarsu E, Ozpar R, Mirzayev H, Acet-Ozturk NA, Hakyemez B, Ediger D, et al. Guillain–Barré syndrome in a patient with minimal symptoms of COVID-19 infection. Muscle Nerve 2020. https://doi.org/10.1002/mus.26992.

[21] Helbok R, Beer R, Löscher W, Boesch S, Reindl M, Hornung R, et al. Guillain-Barré syndrome in a patient with antibodies against SARS-COV-2. Eur J Neurol 2020. ene.14388 https://doi.org/10.1111/ene.14388 .

[22] Bigaut K, Mallaret M, Baloglu S, Nemoz B, Morand P, Baicry F, et al. Guillain-Barré syndrome related to SARS-CoV-2 infection. Neurol Neuroimmunol Neuroinflamm 2020;7:2–5. https://doi.org/10.1212/NXI.0000000000000785.

[23] Ottaviani D, Boso F, Tranquillini E, Gapeni I, Pedrotti G, Cozzio S, et al. Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. Neurol Sci 2016:1–4. https://doi.org/10.1007/s10072-020-04449-8.

[24] Parra B, Lizarazo J, Jiménez-Arango JA, Zea-Vera AF, González-Manrique G, Vargas J, et al. Guillain-Barré syndrome associated with Zika virus infection in Colombia. N Engl J Med 2016;375:1513–23. https://doi.org/10.1056/NEJMoa1605564.

[25] Fantini J, Di Scala C, Chahinian H, Yahi N. Structural and molecular modelling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection. Int J Antimicrob Agents 2020;55:105960. https://doi.org/10.1016/j.ijantimicag.2020.105960.