



## LETTER TO THE EDITOR

### Ample evidence suggests SARS-CoV-2 triggers polyradiculitis



### Una amplia evidencia sugiere que el SARS-CoV-2 desencadena la polirradiculitis

Dear Editor:

We eagerly read the review article by Esteban Molina et al. about SARS-CoV-2 associated Guillain–Barre syndrome (GBS).<sup>1</sup> The authors collected 39 patients with SARS-CoV-2 associated GBS reported from 14 countries all over the world between January 2020 and June 2020.<sup>1</sup> Half of the patients were older than 60 years and almost 70% were male.<sup>1</sup> The most common GBS subtypes were acute, inflammatory demyelinating polyneuropathy (AIDP) ( $n=27$ ) and acute, motor and sensory, axonal neuropathy (AMSAN) ( $n=4$ ).<sup>1</sup> One third of these patients required ventilatory support.<sup>1</sup> Most patients profited from immunoglobulins or plasmapheresis.<sup>1</sup> The study is appealing but raises concerns that require discussion.

We do not agree with the question mark at the end of the title. There is ample evidence that not only the virus but also the vaccination can trigger GBS. Arguments for a causal association between SARS-CoV-2 infections and GBS are that as per the end of June 2021 at least 300 cases with SARS-CoV-2 associated GBS have been reported [Finsterer, submitted for publication], that there is a line-safe connexion between the infection and the onset of GBS,<sup>2</sup> that even the vaccination can trigger GBS, and that the cytokine storm, characteristic for the immune response against the virus, can not only be documented in the serum but also in the cerebro-spinal fluid (CSF).<sup>3</sup> We do not agree with the notion that the annual incidence of GBS needs to increase to serve as an argument for a causal relation between infection and GBS. If the population to which the number of GBS cases is related is high, an increase in the number of GBS cases may be hardly comprehensible.

An indirect argument for a causal relation between the virus and GBS is that the prevalence of SARS-CoV-2 associated GBS is most likely underestimated. This is because mild cases can go unrecognised, work-up for suspected GBS is frequently not initiated because of limited resources or restrictions with the application of certain diagnostic tools to infected patients, and because GBS may not be suspected in patients on the intensive care unit (ICU) undergoing mechanical ventilation. Indications for GBS in ICU patients are if weaning from the respirator is not feasible despite absence of pneumonia, if there is muscle weakness and miss-

ing tendon reflexes despite discontinuation of the sedation, and if there are cranial nerve lesions in the absence of a central nervous system lesion.

We partially agree with the results of the index study. In a recent review about the frequency of SARS-CoV-2 associated GBS between the beginning of January 2020 and the end of June 2020, 33 patients, aged 21–84 years, with SARS-CoV-2 associated GBS were collected [Finsterer, submitted for publication]. The male to female ratio was 1.8. In two cases did GBS occur prior to clinical manifestations of the SARS-CoV-2 infection, most likely due to initially subclinical infection with the virus. The latency between onset of COVID-19 and the GBS ranged between –9 and 24 days. Contrary to the index review four patients with acute motor, axonal neuropathy (AMAN) and two with Miller–Fisher syndrome (MFS) were found in addition to 22 patients with AIDP and 2 with AMSAN. Immunoglobulines were given to 27 patients and plasmapheresis was applied in six cases. Nine patients required mechanical ventilation. Complete recovery was achieved in nine patients and partial recovery in 19 cases.

Overall, the review by Esteban Molina rather supports than questions the causal link between infection and GBS. Intensive care doctors and neurologist should be encouraged to initiate work-up for GBS if there is the slightest suspicion as early treatment may shorten rehabilitation and can prevent fatal outcomes.

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## Author contribution

JF: design, literature search, discussion, first draft, critical comments, FS: literature search, discussion, critical comments, final approval.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

1. Esteban Molina A, Mata Martínez M, Sánchez Chueca P, Carrillo López A. SARS-CoV-2, a new causative agent of Guillain–Barré syndrome? *Med Intensiva (Engl Ed)*. 2021;(November), <http://dx.doi.org/10.1016/j.medine.2021.11.014>. S2173-5727(21)00174-0.

2. Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients with COVID-19. *Egypt J Neurol Psychiatr Neurosurg.* 2021;57:55, <http://dx.doi.org/10.1186/s41983-021-00310-7>.
3. Gigli GL, Vogrig A, Nilo A, Fabris M, Biasotto A, Curcio F, et al. HLA and immunological features of SARS-CoV-2-induced Guillain-Barré syndrome. *Neurol Sci.* 2020;41:3391–4, <http://dx.doi.org/10.1007/s10072-020-04787-7>.

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## Reply to ‘‘Ample evidence suggests SARS-CoV-2 triggers polyradiculitis’’



### Respuesta a «Una amplia evidencia sugiere que el SARS-CoV-2 desencadena la polirradiculitis»

Dear Editor:

Firstly, we would like to thank Finsterer and their partners for reading our article<sup>1</sup> with so much interest and dedication. As well as the *Medicina Intensiva* Journal for their kindness allowing us to make the reply that we will develop next.

In June 2020, we published in the online version of this journal, an article<sup>2</sup> showing the clinical case of a 55 year old patient with SARS-CoV-2 infection and neurological symptoms, in which after performing the relevant tests, a sensory-motor polyneuropathy was detected. Being this article, the first Guillain-Barré syndrome (GBS) case reported in Spain, in the course of an infection by the SARS-CoV-2 virus and in addition, supporting the hipótesis spread from China, in January 2020, GBS associated with SARS-CoV-2, chance or coincidence?<sup>3</sup>

Subsequently, such was our concern that we conducted a bibliographic search in the Medline database (PubMed) on published cases of GBS in the worldwide context of SARS-CoV-2 infection. Starting from December 2019 to June 30, 2020, with a total of 39 clinical cases reported. Immediately after the data collection and statistical analysis, we sent a letter to the editor of the *Medicina Intensiva* Journal; available online since September 2020 and titled: SARS-CoV-2, a new causative agent of Guillain-Barré syndrome?<sup>1</sup> Finsterer et al., show their disagreement due to the lack of conviction in our publication about the association of GBS and SARS-CoV-2, and even allude to the fact that vac-

nation can also trigger GBS. From our utmost respect, we would like to emphasize the time difference, more than a year between both publications. Therefore, the experience and the increase in the number of subsequent cases have shown the strength of the SARS-CoV-2 and GBS association. On the whole, the authors, when writing these publications, only suspected this binomial. Furthermore, the process of immunization by the vaccines had not even started.

## References

1. Esteban Molina A, Mata Martínez M, Sánchez Chueca P, Carrillo López A. SARS-CoV-2, A new causative agent of Guillain-Barré syndrome? *Med Intensiva.* 2020, <http://dx.doi.org/10.1016/j.medin.2020.08.009>. S0210-5691(20)30274-6.
2. Esteban Molina A, Mata Martínez M, Sánchez Chueca P, Carrillo López A, Sancho Val I, Sanjuan-Villarreal TA. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *Med Intensiva.* 2020, <http://dx.doi.org/10.1016/j.medin.2020.04.015>. S0210-5691(20)30154-6.
3. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol.* 2020;19:383–4, [http://dx.doi.org/10.1016/S1474-4422\(20\)30109-5](http://dx.doi.org/10.1016/S1474-4422(20)30109-5).

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