



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Anti-CD20 and COVID-19 in multiple sclerosis and related disorders: A case series of 60 patients from Madrid, Spain

Dear Editor,

We have read with great interest the case report of a patient with Multiple Sclerosis (MS) treated with ocrelizumab that developed COVID-19 without serious complications (Novi et al., 2020). The authors suggest a potential protective effect for severe complications of COVID-19 of anti-CD20 drugs. Besides, Prof. Giovannoni's editorial reviews the evidence supporting the hypothesis that immunosuppression of patients with MS on certain disease-modifying therapies may protect of severe COVID-19 infection (Giovannoni, 2020). These data contradict the first assumption that patients with MS on immunosuppressive therapies could be at risk of severe complications of COVID-19.

We aimed to analyze the frequency and severity of COVID-19 in our series of patients treated with anti-CD20 in a tertiary hospital in Madrid, Spain, one of the regions worst affected by the pandemic. All patients were contacted by phone from 28th to 29th April 2020 (Matías-Guiu et al., 2020a), when total confirmed cases in the Region of Madrid accounted for 60,765. At the moment of the beginning of the pandemic, 60 patients were treated with anti-CD20 (54 with rituximab and 6 with ocrelizumab). The mean age was 47.21 ± 9.86 years-old in the whole group, 47.09 ± 9.56 in patients with rituximab, and 48.33 ± 12.16 in patients with ocrelizumab. 32 patients were classified as having relapsing-remitting MS (53.3%), 14 (23.3%) as secondary-progressive, 9 (15.0%) as primary-progressive forms and 5 as optic neuromyelitis (8.3%). COVID-19 infection was reported in 9 (15%) in the whole sample, 7 (12.9%) in patients receiving rituximab, and 2 (33.3%) in patients with ocrelizumab. Main clinical characteristics of COVID-19 are depicted in Table 1. Interestingly, all patients with COVID-19 did not show serious complications, despite that a patient required admission to a hospital.

We also analyzed the time of administration and the frequency of infection by SARS-CoV2, with no apparent relationship. In this regard, 2 (15.38%) of the 13 patients that received treatment in June-August 2019 were infected; 1 (10%) of 10 patients treated in September-October 2019; 2 (13.3%) of the 15 patients that were treated in November-December 2019; and 4 (20%) of 20 patients that received the treatment in January-February 2020. Two patients had received the first dose with the onset of the pandemic, and no one was infected.

We also evaluated the frequency of infection in people living with the patients with MS. On the one hand, 3 of the 7 patients (42%) with rituximab that developed COVID-19 had at least one relative at home suffering the infection. On the other hand, in the 47 patients with rituximab that did not develop symptoms of Covid-19, eight (17.0%) of them had at least one relative at home with COVID-19. In the two patients with ocrelizumab, both had relatives infected at home.

The main limitation of our study was that SARS-CoV2 was not confirmed by RT-PCR in most cases because of an institutional decision of not performing the assay in mild cases not requiring hospital admission. However, all patients had highly suggestive symptoms in an epidemiological scenario of high probability infection, and their primary physicians quarantined them.

Therapeutic management of MS patients during Covid-19 pandemic is one of the most relevant issues (Giovannoni et al., 2020), although other concerns regarding a possible role of white matter lesions as a virus reservoir, like in other coronavirus have risen (Burks et al., 1980; Matías-Guiu et al., 2020b). Our study suggests that anti-CD20 does not seem to have an important role in the risk of infection by SARS-CoV2. In this regard, it was more associated with the infection of other relatives living at home (Chan et al., 2020). These findings support the view that the presence of B cells is not absolutely required for recovery from COVID-19 (Quinti et al., 2020; Soresina et al., 2020). It is worth mentioning that all cases were relatively mild and only one required hospital admission but without complications. This is consistent with the preliminary observations in MS from Italy (Sormani, 2020). However, this apparently lower severity of the infection should be studied specifically. In addition, a substantial proportion of patients lived with a relative suffering the infection, but they did not develop symptoms. Overall, these findings seem to support the hypothesis outlined by Prof. Giovannoni in his editorial.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Table 1

Description of cases with COVID-19 and Anti-CD20.

Sex / Age (years-old)	Clinical form	Clinical presentation.	Duration of symptoms (days)	RT-PCR	Anti-CD20
Woman / 41	RR	Fever, cough, ageusia, fatigue	7	Not performed	Rituximab
Woman / 46	RR	Fever, odynophagia, myalgias, anosmia	10	Not performed	Rituximab
Woman / 41	NMO	Fever, fatigue, ageusia, chest pain	15	Negative	Rituximab
Man / 42	PP	odynophagia, cough	7	Not performed	Rituximab
Woman / 43	RR	Fever, cough, gastrointestinal alterations	15	Positive	Rituximab
Woman / 43	PP	Ageusia, Anosmia	15	Positive	Ocrelizumab
Man / 52	PP	Fever, gastrointestinal alterations, dyspnea	7	Negative (positive serological test)	Rituximab
Woman / 46	RR	Fever, gastrointestinal alterations, pneumonia	15	Negative	Rituximab
Woman / 55	SP	Fever, cough, dyspnea, pneumonia, fatigue, Anosmia	21	Negative; Positive in bronchial exudate	Ocrelizumab

References

- Burks J, S, DeVald B, L, Jankovsky L, D, Gerdes J, C, 1980. Two coronaviruses isolated from central nervous system tissue of two multiple sclerosis patients. *Science* 209, 933–934.
- Chan, JFW, Yuan, S, Kok, KH, To, KK, Chu, H, Yang, J, et al., 2020. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 395, 514–523. [https://doi.org/10.1016/S0140-6736\(20\)30154-9](https://doi.org/10.1016/S0140-6736(20)30154-9).
- Giovannoni, G, 2020. Anti-CD20 immunosuppressive disease-modifying therapies and COVID-19. *Mult. Scler. Relat. Disord.* 41, 102135. <https://doi.org/10.1016/j.msard.2020.102135>.
- Giovannoni, G, Hawkes, C, Lechner-Scott, J, Levy, M, Waubant, E, Gold, J, 2020. The COVID-19 pandemic and the use of MS disease-modifying therapies. *Mult. Scler. Relat. Disord.* 39, 102073.
- Matías-Guiu, J, Porta-Etessam, J, Lopez-Valdes, E, Garcia-Morales, I, Guerrero-Solá, A, Matias-Guiu, JA, 2020a. Management of neurological care during the COVID-19 pandemic. *Neurologia*. <https://doi.org/10.1016/j.nrl.2020.04.001>.
- Matías-Guiu, J, Gomez-Pinedo, U, Montero-Escribano, P, Gomez-Iglesias, P, Porta-Etessam, J, Matias-Guiu, JA, 2020b. Should we expect neurological symptoms in the SARS-CoV-2 epidemic? *Neurologia* 35, 170–175. <https://doi.org/10.1016/j.nrl.2020.03.001>.
- Novi, G, Mikulska, M, Briano, F, Toscanini, F, Tazza, F, Uccelli, A, et al., 2020. COVID-19 in a MS patient treated with ocrelizumab: does immunosuppression have a protective role? *Mult. Scler. Relat. Disord.* 42, 102120. <https://doi.org/10.1016/j.msard.2020.102120>.
- Quinti, I, Lougharis, V, Milito, C, Cinetto, F, Pecoraro, A, Mezzaroma, I, et al., 2020. A possible role for B cells in COVID-19? Lesson from patients with agammaglobulinemia. *J. Allergy Clin. Immunol.* <https://doi.org/10.1016/j.jaci.2020.04.013>.
- Soresina, A, Moratto, D, Chiarini, M, Paolillo, C, Baresi, G, Focà, E, et al., 2020. Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover. *Pediatr. Allergy Immunol.* <https://doi.org/10.1111/pai.13263>.
- Sormani, MP, Italian Study Group on COVID-19 Infection in Multiple Sclerosis, 2020. An Italian programme for COVID-19 infection in multiple sclerosis. *Lancet Neurol.* [https://doi.org/10.1016/S1474-4422\(20\)30147-2](https://doi.org/10.1016/S1474-4422(20)30147-2).

Paloma Montero-Escribano, Jorge Matías-Guiu,
 Patricia Gómez-Iglesias, Jesús Porta-Etessam, Vanesa Pytel,
 Jordi A. Matias-Guiu*

Department of Neurology, San Carlos Health Research Institute, Universidad
 Complutense. 28040 Madrid, Spain

E-mail address: jordimatiaguiu@hotmail.com (J.A. Matias-Guiu).

* Corresponding author.