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Clinical short communication

Monoclonal antibodies for mild-to-moderate COVID-19 in multiple sclerosis: A case series

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ABSTRACT

We reported on five people with MS, using immunodepleting disease modifying treatments (anti-CD20 monoclonal antibodies and sphingosine-one-phosphate modulators) and with reduced COVID-19 vaccine response, who had mild-to-moderate symptomatic COVID-19, and were treated with anti-SARS-CoV-2 monoclonal antibodies. In particular, we showed the possibility to use monoclonal antibodies to speed-up recovery from COVID-19 in MS, in the absence of any COVID-19 residuals or MS changes (e.g., relapses or disability).

1. Introduction

Multiple sclerosis (MS)-related disability and comorbidities can increase the risk of severe coronavirus disease-2019 (COVID-19) outcomes from severe acute respiratory syndrome–related coronavirus (SARS-CoV-2) infection [1]. Also, some disease-modifying treatments (DMTs), including anti-CD20 monoclonal antibodies and sphingosine-one-phosphate (S1P) modulators, can reduce the response to anti-SARS-CoV-2 vaccination (i.e., reduced seroconversion and/or cellular response) [2–4], and can subsequently be responsible for more severe COVID-19 outcomes, including hospitalizations and intensive care unit admissions [5–7].

There is a wide spectrum of COVID-19 clinical symptoms at presentation, that can be described using the Ordinal Scale for Clinical Improvement (OSCI), a 9-point scale, where 0 corresponds to no infection and 8 to death [8]. Patients with 0–2 OSCI Score have mild-to-moderate disease, characterized by at least one COVID-19 related symptom (e.g., cough, fever, sore throat, rhinorrhoea) in the absence of oxygen therapy or need of hospitalization [8]. From March 2021, Italian regulatory bodies have approved a number of different monoclonal antibodies targeting the spike protein of SARS-CoV-2 (casirivimab+imdevimab 600 + 600 mg, bamlanivimab+etesevimab 1400 + 700 mg, sotrovimab 500 mg), to be administered as one-off intravenous infusion to patients with mild-to-moderate COVID-19 with risk factors of severe disease, including immunodepleting medications. Thus, monoclonal antibodies could be especially relevant to people with MS using DMTs. Indeed, monoclonal antibodies, if early administered, can significantly change the natural history of COVID-19 with faster recovery, and lower rates of hospitalization and death [9].

Hereby, we reported on five people with MS, using immunodepleting DMTs (anti-CD20 monoclonal antibodies and S1P modulators), who had mild-to-moderate symptomatic COVID-19 (OSCI 0–2), and were treated with anti-SARS-CoV-2 monoclonal antibodies.

2. Cases

Demographic, MS and COVID-19 data are presented in Table 1.

2.1. Case 1

A 31-year-old woman on continuous treatment with fingolimod from 1.5 years, in the absence of clinical or MRI signs of disease activity, and with three doses of COVID-19 vaccination, presented with fever, cough, and fatigue on Dec 27, 2021, and, on the following day, tested positive to PCR SARS-CoV-2 nasal swab. On Jan 2, 2022, she received the infusion of bamlanivimab+etesevimab 1400 + 700 mg. Symptoms improved

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after 3 days and nasal swab was negative on Jan 7, 2022. No other medications nor hospital admissions were required. No relapses nor changes in disability were detected.

2.2. Case 2

A 48-year-old man, with past medical history of hepatitis C and Hashimoto's thyroiditis, was on treatment with ocrelizumab for 2.5 years, in the absence of clinical or MRI signs of disease activity. He had two doses of COVID-19 vaccination, but no antibody response. On December 28, 2021, he presented with fever, cough and joint pains. On the same day, he tested positive for SARS-CoV-2 infection, which was later deemed to be Omicron (B.1.1.529) variant. On Jan 1, 2022, he received infusion of sotrovimab 500 mg. His symptoms improved after 3 days, and his nasal swab was negative after 12 days. No other medications nor hospital admissions were required. No relapses nor changes in disability were detected.

2.3. Case 3

A 44-year-old man was admitted to the Haematology Unit to receive inpatient chemotherapy for a rare cutaneous (panniculitis-like) T-cell lymphoma. He was on treatment with ocrelizumab from 2 years, in the absence of clinical or MRI signs of disease activity, and never vaccinated against COVID-19. Due to contact-tracing procedures, he tested positive to PCR SARS-CoV-2 nasal swab on Jan 13, 2022. On the following day, he presented with fever, headache, and joint pains. On Jan 17, 2022, he received the infusion of casirivimab+imdevimab 600 + 600 mg, followed by remdesivir infusions (200 mg on the first day and 100 mg on the next two days). His symptoms improved after 2 days. No other medications for COVID-19 were required; however, after 20 days, he still tested positive and required admission to COVID-19 ward to receive inpatient lymphoma treatment. He tested negative to COVID-19 on Feb 16, 2022. No relapses nor changes in disability were detected.

2.4. Case 4

A 53-year-old woman was on treatment with ocrelizumab from 3 years, in the absence of clinical or MRI signs of disease activity, and fully vaccinated against COVID-19 (booster dose on Jan 20, 2022), but without antibody response. On January 22, 2022, she presented with fever, cough, fatigue, joint pains, and gastrointestinal symptoms. On the following day, she tested positive to PCR SARS-CoV-2 nasal swab. On Jan 25, 2022, she received infusion of sotrovimab 500 mg. After 4 days, she had clear improvement of symptoms. Her nasal swab was negative after 16 days from symptoms' onset. No other medications nor hospital admissions were required. No relapses nor changes in disability were detected.

2.5. Case 5

A 54-year-old woman was on treatment with fingolimod from 9 months due to clinical and MRI activity during previous treatment with interferon beta1a. She had her third dose of COVID-19 vaccination on Oct 5, 2021, in the absence of antibody response. On Feb 4, 2022, she presented with fever, cough, throat ache, fatigue, headache, and joint pains. On Feb 7, 2022, she tested positive to SARS-CoV-2 on PCR nasal swab. On Feb 10, 2022, she received infusion of sotrovimab 500 mg monoclonal antibodies. After 2 days, she had clear improvement of symptoms, and, after further 2 days, tested negative to SARS-CoV-2 nasal swab. No other medications nor hospital admissions were required. No relapses nor changes in disability were detected.

3. Discussion

Our case series confirmed that MS patients using some DMTs mount low antibody titres after COVID-19 vaccination with subsequent risk of infection and worse outcomes [2,3], but highlighted the possibility to use safely monoclonal antibodies to treat COVID-19.

In particular, in our small case series, we referred to treatment with monoclonal antibodies MS patients with high risk of severe COVID-19

Table 1
Demographics, MS clinical and treatment features, and COVID-19 timeline and treatment.

	#1	#2	#3	#4	#5
Age	31	48	44	53	54
Sex	F	M	M	F	F
Disease duration *(years)*	3	4	22	16	15
Subtype	RR	PP	RR	SP	RR
EDSS	1.5	4.0	5.0	6.5	3.0
DMT	Fingolimod (from Jun 12, 2020)	Ocrelizumab (5 infusions, most recent on Oct 1, 2021)	Ocrelizumab (3 infusions, most recent on Nov 12, 2021)	Ocrelizumab (6 infusions, most recent on Sep 17, 2021)	Fingolimod (from Feb 1, 2015)
Comorbidities	None	Hashimoto's thyroiditis; previous hepatitis C	Panniculitis-like T cell lymphoma	None	None
Smoking	Never	Past	Past	Never	Current
COVID19 vaccination	Comirnaty (3rd dose on Nov 22, 2022)	Comirnaty (2nd dose on Dec 10, 2021)	Unvaccinated	Comirnaty (3rd dose on Jan 20, 2022)	Comirnaty (3rd dose on Oct 5, 2021)
Anti-SARS-CoV-2 (2019-nCoV) IgG after vaccination	Positive (IgG >2080 BAU/mL)	Negative	Negative	Negative	Negative
Pre-COVID19 lymphocytes	950/uL	1330/uL	480/uL	1400/uL	420/uL
COVID19 onset	Dec 27, 2021	Dec 28, 2021	Jan 14, 2022	Jan 22, 2022	Feb 4, 2022
COVID19 positive swab	Dec 28, 2021	Dec 28, 2021	Jan 13, 2022	Jan 23, 2022	Feb 7, 2022
COVID19 symptoms	Fever, cough, fatigue, throat ache, headache, joint pains	Fever, cough, joint pains	Fever, headache, joint pains, gastrointestinal symptoms	Fever, cough, fatigue, headache, joint pains, gastrointestinal symptoms	Fever, cough, fatigue, throat ache, headache, joint pains
Monoclonal antibody treatment	Bamlanivimab+etesevimab (Jan 2, 2022)	Sotrovimab (Jan 1, 2022)	Casirivimab+imdevimab (Jan 17, 2022)	Sotrovimab (Jan 25, 2022)	Sotrovimab (Feb 10, 2022)
COVID19 negative swab	Jan 7, 2022	Jan 12, 2022	Feb 16, 2022	Feb 7, 2022	Feb 14, 2022

outcomes, as a consequence of low vaccination response (using ocrelizumab and fingolimod) or absence of vaccination [2,3], concomitant disease and treatment (e.g., chemotherapy for lymphoma), and high disability [1,5–7]. As such, while we included a pool of at-risk patients, we showed that, following the use of monoclonal antibodies for COVID-19, all of them fully recovered, in the absence of COVID-19 long-term symptoms, monoclonal antibodies' side effects, or MS changes in terms of relapses or disability. Of note, no patient developed respiratory symptoms, nor required additional tests (e.g., chest imaging) and treatments (e.g., anti-inflammatory drugs), nor required hospitalization for COVID-19, thus suggesting that monoclonal antibodies achieved their expected effect, as in the general population [9], in the absence of safety concerns.

Our case series is limited by the small sample size, though comprehensive of MS patients at risk of worse COVID-19 outcomes due to a variety of reasons. In particular, looking at vaccine response, in line with previous studies [10], our case series confirmed the lack of serological response to vaccination in ocrelizumab-treated patients also after booster dose, while we did not assess T-cell responses [11–14]. In the current scenario of endemic COVID-19 and continuous treatment with immunosuppressive DMTs affecting both humoral and cellular immunity [15], passive immunization with monoclonal antibodies will likely be a cornerstone in preventing severe COVID-19 in this category of patients.

This is the first study describing safety and efficacy of monoclonal antibodies for COVID-19 in MS patients using immunosuppressant DMTs. Omicron variant was detected in Italy in Nov 2021, and became prevalent (>80%) in Jan 2022 [16,17]. Considering that casirivimab+imdevimab and bamlanivimab+etesevimab resulted poorly effective against Omicron BA.1 variant [9,18–23], from Jan 2022, we preferred sotrovimab. However, more recently, in vitro data showed that Omicron BA.2 variant may be poorly controlled by sotrovimab [17,18,21], and, thus, in the future, we shall consider the use of antivirals (such as remdesivir, molnupinavir, nirmatrelvir/ritonavir), also combined to monoclonal antibodies, as we already did in case 3. People with MS using DMTs and not mounting vaccination immunity may especially benefit from combination therapy with monoclonal antibodies and antivirals, which target two different SARS CoV-2 antigens (spike protein and polymerase, respectively), to overcome the risk of variant escape [17].

MS neurologists should be aware that MS patients more-at-risk of worse COVID-19 outcomes should be referred to treatment with monoclonal antibodies as early as possible. In the meanwhile, additional evidence should come from larger cohorts, also accounting for differences between DMTs and other MS (e.g., disability, disease duration) and clinical variables (e.g., age, comorbidities), in order to provide detailed guidance on the use of monoclonal antibodies in specific subcategories of MS patients.

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