MULTIPLE SCLEROSIS JOURNAL | MSJ

Case Reports

Recovery from COVID-19 in a B-cell-depleted multiple sclerosis patient

Hannah Wurm, Kate Attfield, Astrid KN Iversen, Ralf Gold, Lars Fugger and Aiden Haghikia

Abstract: Approximately 200,000 multiple sclerosis (MS) patients worldwide receive B-cell-depleting immunotherapy with rituximab (anti-CD20), which eliminates the ability to generate an antibody response to new infections. As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–specific antibodies might help viral clearance, these patients could be at risk of severe complications if infected. Here, we report on an MS patient who had received rituximab for ~3 years. The patient was examined 5 days before the onset of coronavirus disease 2019 (COVID-19) symptoms and was admitted to the hospital 2 days after. She recovered 14 days after symptom onset despite having a 0% B lymphocyte count and not developing SARS-CoV-2 immunoglobulin G (IgG) antibodies.

Keywords: Multiple sclerosis (MS), rituximab, B-cell-depleting therapy, COVID-19, SARS-CoV-2 antibodies, cellular immune responses

Date received: 25 May 2020; revised: 19 June 2020; accepted: 22 June 2020.

Introduction

The first cases of coronavirus disease 2019 (COVID-19) were observed in China in December 2019.[1] The causative virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is the result of a zoonotic transmission either directly from bats or via an intermediate host species.[2] The virus has spread globally since January 2020. Morbidity and mortality rates increase with age and specific comorbidities.[3] Disease severity in patients is linked to not only the viral infection but also the host immune response, creating an urgent need to understand the virus–host interplay. Convalescent serum samples have been applied with apparently good clinical results in COVID-19,[1] raising concerns that multiple sclerosis (MS) patients receiving B-cell-depleting treatment might suffer severe complications during primary infection; such concerns are reflected by decisions to delay the use of anti-CD20 drugs in new patients and suggestions to consider extended-interval dosing for those already receiving anti-CD20 therapy, especially in those who are B-cell depleted or have low levels of immunoglobulin G (IgG).[4] This case report suggests that MS patients receiving B-cell-depleting therapy are not necessarily at higher risk and demonstrates that infection can resolve through cellular immune responses alone.

Report of case

The 59-year-old female MS patient was diagnosed in 2016, and rituximab treatment initiated in September 2017; no CD19+ B-cell reconstitution was detected at any follow-up visits during the 3 years of treatment (Figure 1(a)). On 1 April 2020, the patient had a mild paraparesis and paraspasticity and a limited walking distance, unchanged since the last admission in September 2019 (Expanded Disability Status Scale (EDSS) of 6), and a 0% B-cell count. No COVID-19 symptoms were present. Routine laboratory investigations were normal; magnetic resonance imaging (MRI) showed a stable disease course since initiation of rituximab; natural killer (NK), CD4+, and CD8+ T-cell counts were normal; and the CD4/CD8 T-cell ratio inverted, a common consequence of rituximab treatment.[5]

On 5 April 2020, the patient developed a dry cough, which worsened 2 days later with dyspnea, fatigue, headache, and nausea. The nasopharyngeal swab test for SARS-CoV-2 was positive, and the patient was admitted to hospital with a fever of 39°C and low oxygen saturation. A chest X-ray revealed interstitial pneumonia (Figure 1(b)), and prophylactic intravenous antibiotic (ampicillin/sulbactam) treatment was instituted. The dyspnea rapidly improved, CD4+

Multiple Sclerosis Journal

2020, Vol. 26(10) 1261–1264

DOI: 10.1177/1352458520943791

Correspondence to:

L Fugger
Oxford Centre for Neuroinflammation, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Headley Way, Headington, Oxford, OX3 9DU, UK.
lars.fugger@ndcn.ox.ac.uk

A Haghikia
Department of Neurology, St. Josef-Hospital Bochum, Ruhr-University Bochum, 44801 Bochum, Germany.
aiden.haghikia@rub.de

Hannah Wurm
Ralf Gold
Aiden Haghikia
Department of Neurology, St. Josef-Hospital Bochum, Ruhr-University Bochum, Bochum, Germany

Kate Attfield
Astrid KN Iversen
Oxford Centre for Neuroinflammation, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, Oxford, UK

Lars Fugger
Oxford Centre for Neuroinflammation, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, Oxford, UK/MRC Human Immunology Unit, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, Oxford, UK

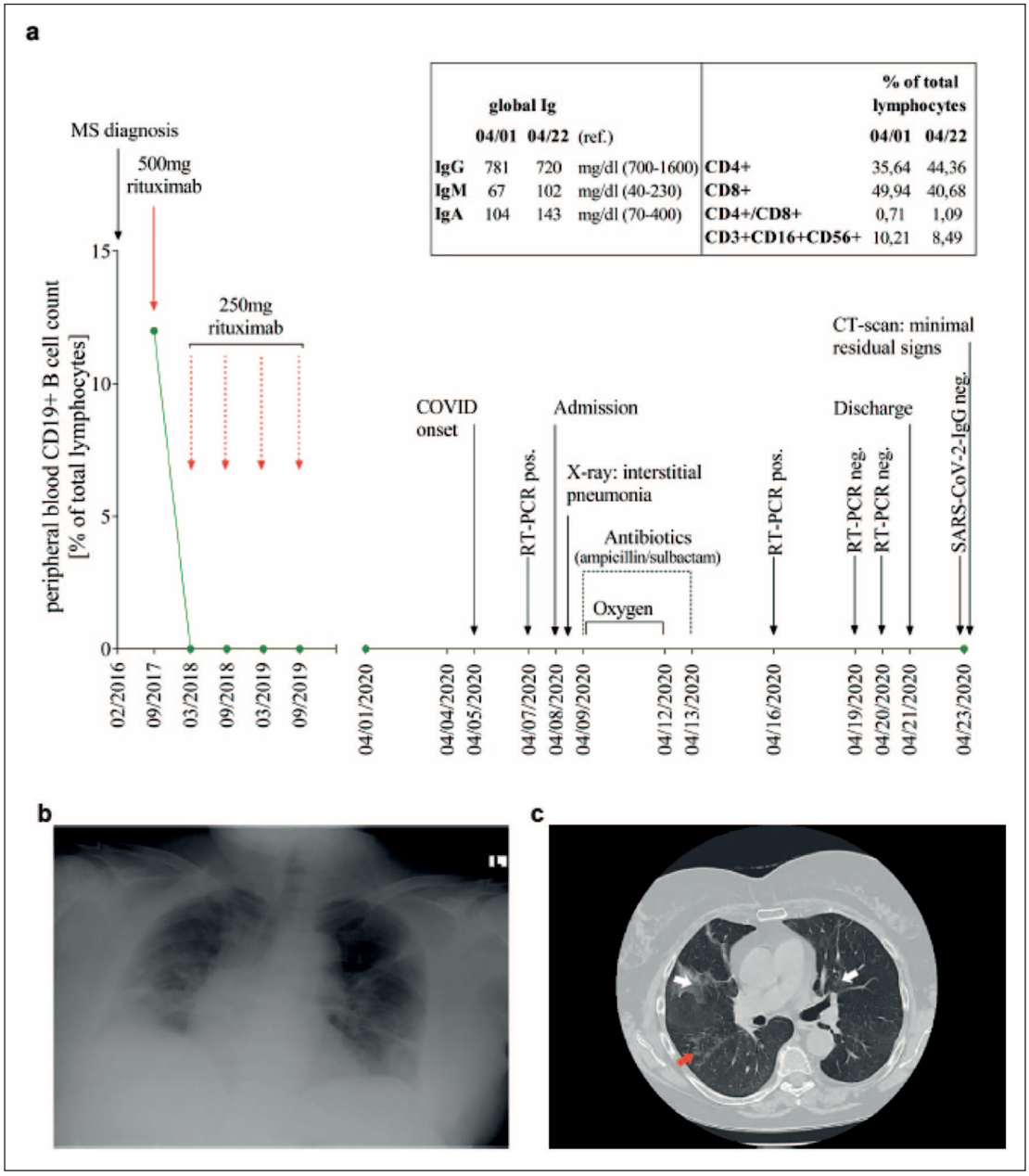

Figure 1. Clinical management of a 59-year-old female patient with progressive multiple sclerosis (MS) infected with SARS-CoV-2. (a) *Disease course.* The patient was diagnosed with MS in February 2016. Rituximab treatment was started in September 2017, and repeat doses were given every 6 months as outlined. Symptoms of COVID-19 developed on 5 April 2020. All symptoms resolved after 14 days. Box shows IgG, IgM, and IgA counts (left), and CD4+ and CD8+ T-cell counts, CD4+/CD8+ ratios, and NK (CD3+, CD16+, CD56+) cell counts (right). Antibody levels and T-cell and NK cell counts were measured on 1 April 2020 (5 days before the onset of COVID-19 symptoms) and on 22 April 2020 (1 day after discharge from hospital and 6 days after the first negative SARS-CoV-2 nasopharyngeal swab test). (b) *Chest X-ray.* The anteroposterior erect chest X-ray was taken on admission, 7 April, showing typical signs of interstitial pneumonia with severely decreased lung volumes and reticulation. (c) *Thoracic high-resolution CT (HRCT) chest scan.* The HRCT scan was performed 1 day after discharge from hospital (22 April) showing residual signs of interstitial pneumonia, that is, dorsobasal dystelectasis (white arrows) and minor honeycombing (red arrow).

T-cell counts increased, the CD4/CD8 ratio normalized, and the NK cell count slightly decreased but was still within the normal range.

On days 14 and 15, after symptom onset, two nasopharyngeal swab test and a cerebrospinal fluid (CSF) sample were negative for SARS-CoV-2 (Figure 1(a)).

All symptoms resolved, and the patient was discharged 13 days after admission. A SARS-CoV-2 IgG antibody test was negative 18 days after symptom onset, and a thoracic chest computed tomography (CT) scan (Figure 1(c)) showed minimal residual signs of interstitial pneumonia (dorsobasal dystelectasis).

Discussion

As cross-neutralization of SARS-CoV-2 by antibodies to other coronaviruses is unlikely,[6] this case, suggests that SARS-CoV-2 infection can resolve solely through cellular immune responses. This finding is further supported by a study reporting the successful recovery from SARS-CoV-2 infection in a set of twins who lacked B-cells due to X-linked agammaglobulinemia.[7] These observations shed light on other COVID-19 studies,[6,8] which demonstrated that patients with mild disease symptoms have low antibody levels[6] and those with weak IgG responses clear virus faster than those with strong IgG responses.[8] Collectively, these findings suggest that the best correlate of viral clearance might be obtained by measuring cellular immune responses rather than antibody levels. Furthermore, potentially harmful effects of SARS-CoV-2 antibodies toward the Spike protein are highlighted by experiments with a SARS-CoV-1-spike Modified vaccinia Ankara (MVA) vaccine in rhesus macaques.[9] In this trial, antibody-dependent enhancement (ADE) of infection of alveolar macrophages resulted in a switch from a wound healing to a proinflammatory phenotype. Subsequent interleukin-6 (IL-6), interleukin-8 (IL-8), and monocyte chemoattractant protein-1 (MCP-1/CLL2) secretion ignited a hyperinflammatory reaction, resulting in severe alveolar damage similar to that seen in some COVID-19 patients.[1] Thus, if ADE contributes to COVID-19 pathogenesis,[10] patients receiving rituximab might be less likely to develop alveolar hyperinflammation due to a lack of SARS-CoV-2 antibody production and the absence of effector-memory B-cell-mediated proinflammatory cytokine production.[5]

Data from a cross-sectional questionnaire study ($n = 712$) from Iran found that MS patients on B-cell-depleting therapy had a 2.6-fold increase in the risk of being in the COVID-19-suspect group. This group comprised patients who reported fever and cough or fever and shortness of breath, and those who had a suggestive chest CT ($n = 34$); however, only two COVID-19-suspect patients were hospitalized and neither required intensive care.[11] This study suggests that MS patients as a group have a mild to moderate disease course regardless of the treatment regimen and also that those on B-cell-depleting therapy might be at higher risk of SARS-CoV-2 infection. As none of the patients were tested for SARS-CoV-2, these observations need to be verified in a setting where virus testing is possible.

Recovery from COVID-19 has previously been reported in one MS patient with hepatitis B infection who was treated for a year with the B-cell-depleting drug ocrelizumab and the antiviral drug lamivudine (3TC).[12] Whereas recovery from COVID-19 in this patient could potentially be facilitated by lamivudine, our report highlights that B-cell-depleted MS patients can clear the virus without the aid of antiviral therapy. These observations are in line with the lack of fatalities reported by an international pharmacovigilance case series of 30 ocrelizumab-treated MS patients infected by SARS-CoV-2.[13]

It is unknown whether the patient described here, or any patient who has recovered from SARS-CoV-2 infection in the absence of B-cells, is at higher risk of reinfection. However, this case suggests that MS patients receiving B-cell-depleting therapy are not at higher risk of severe complications from primary SARS-CoV-2 infection, and demonstrates that viral clearance is possible without B-cell involvement and antiviral therapy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Patient consent

Written consent has been obtained from the patient.

References

1. Tay MZ, Poh CM, Renia L, et al. The trinity of COVID-19: Immunity, inflammation and intervention. *Nat Rev Immunol* 2020; 20: 363–374.
2. Andersen KG, Rambaut A, Lipkin WI, et al. The proximal origin of SARS-CoV-2. *Nat Med* 2020; 26(4): 450–452.
3. Wu Z and McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323: 1239–1242.

4. Brownlee W, Bourdette D, Broadley S, et al. Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic. *Neurology* 2020; 94: 949–952.

5. Lund FE. Cytokine-producing B lymphocytes-key regulators of immunity. *Curr Opin Immunol* 2008; 20(3): 332–338.

6. Okba NMA, Muller MA, Li W, et al. Severe acute respiratory syndrome coronavirus 2-specific antibody responses in coronavirus disease patients. *Emerg Infect Dis* 2020; 26(7): 1478–1488.

7. Soresina A, Moratto D, Chiarini M, et al. Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover. *Pediatr Allergy Immunol* 2020; 6736: 19.

8. Tan W, Lu Y, Zhang J, et al. Viral kinetics and antibody responses in patients with COVID-19. *MedRxiv*. Epub ahead of print 26 March 2020. DOI: 10.1101/2020.03.24.20042382.

9. Liu L, Wei Q, Lin Q, et al. Anti-spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. *JCI Insight* 2019; 4(4): e123158.

10. Iwasaki A and Yang Y. The potential danger of suboptimal antibody responses in COVID-19. *Nat Rev Immunol* 2020; 20: 339–341.

11. Safavi F, Nourbakhsh B and Azimi AR. B-cell depleting therapies may affect susceptibility to acute respiratory illness among patients with multiple sclerosis during the early COVID-19 epidemic in Iran. *Mult Scler Relat Disord* 2020; 43: 102195.

12. Novi G, Mikulska M, Briano F, et al. COVID-19 in a MS patient treated with ocrelizumab: Does immunosuppression have a protective role? *Mult Scler Relat Disord* 2020; 42: 102120.

13. Hughes R, Pedotti R and Koendgen H. COVID-19 in persons with multiple sclerosis treated with ocrelizumab—A pharmacovigilance case series. *Mult Scler Relat Disord* 2020; 42: 102192.

Multiple Sclerosis Journal

2020, Vol. 26(10) 1264–1266

DOI: 10.1177/1352458520943783

Correspondence to:
R Dersch
Clinic of Neurology and Neurophysiology, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Breisacher Str. 64, 79106 Freiburg, Germany.
Rick.Dersch@uniklinik-freiburg.de

Rick Dersch
Thomas Wehrum
Sebastian Rauer
Benjamin Berger
Clinic of Neurology and Neurophysiology, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

Sebastian Fähndrich
Medical Department—Pneumology, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

Monika Engelhardt
Medical Department—Hematology, Oncology & Stem Cell Transplantation Clinical Cancer Research Group, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

COVID-19 pneumonia in a multiple sclerosis patient with severe lymphopenia due to recent cladribine treatment

Rick Dersch, Thomas Wehrum, Sebastian Fähndrich, Monika Engelhardt, Sebastian Rauer and Benjamin Berger

Abstract

Background: Most cases of COVID-19 are considered mild, but patients with immunosuppressant treatment might be prone to severe courses of disease. Expert panels advise to delay treatment with cell-depleting MS therapies during the COVID-19 pandemic.

Methods: We report a case of a patient with relapsing-remitting multiple sclerosis who developed COVID-19 pneumonia 2 weeks after the first week of cladribine therapy.

Results: Despite a severe lymphopenia (absolute lymphocyte count 240/µL), the patient had a moderate course of COVID-19.

Conclusion: Apart from maximal supportive treatment, this could be due to cladribine reducing inflammatory response, which probably contributes considerably to severe courses of COVID-19 pneumonia.

Keywords: Multiple sclerosis, cladribine, COVID-19, prognosis

Date received: 17 May 2020; revised: 18 June 2020; accepted: 22 June 2020.

Most cases of COVID-19 are considered mild, but particularly patients with pre-existing conditions are prone to severe courses of disease.[1] Data on patients with autoimmune disorders requiring immunosuppressive therapies are currently scarce.

We report a case of a patient with relapsing-remitting multiple sclerosis (RRMS) who developed COVID-19 pneumonia accompanied by distinct lymphopenia (common toxicity criteria (CTC) grade 3) due to cladribine treatment 2 weeks earlier.

Table 1. Laboratory data during course of COVID-19 pneumonia (normal reference: range in brackets).

Laboratory parameters	Clinical course over time as inpatient treatment				
	Baseline	2–5 days	14–21 days	22–26 days	Discharge
ALC (/µL) (1100–3200)	240	530	370	340	660
CRP (mg/L) (<5)	<5	11.1	250.9	209.9	17.2
PCT (ng/mL) (<0.05)	n.a.	0.06	0.13	0.17	0.06
D-dimer (mg/L) (<0.5)	n.a.	n.a.	0.81	1.05	n.a.
Interleukin-6 (pg/mL) (<7)	n.a.	9.1	127.0	76.5	7.5
LDH (U/L) (135–225)	n.a.	231	424	376	314
Ferritin (ng/mL) (30–400)	n.a.	n.a.	1714	1923	n.a.

ALC: absolute lymphocyte count; CRP: C-reactive protein; PCT: procalcitonin; LDH: lactate dehydrogenase.

Case report

The patient had been diagnosed with multiple sclerosis (MS) in 2016 at the age of 55 years and had since then been on disease-modifying treatment with dimethyl fumarate. Lymphocyte counts were constantly normal, and he was free from disease activity for several years.

In November 2019, a relapse with paresis of the right leg occurred. Magnetic resonance imaging (MRI) scan revealed multiple new cerebral and spinal cord lesions, which were in part gadolinium-enhancing. The treating neurologist decided to escalate treatment to cladribine, which was started with a dose of 90 mg/cycle on 10 March 2020. There was no washout period between discontinuation of dimethyl fumarate and initiation of cladribine, since absolute lymphocyte count (ALC) at this time was normal (1250/µL).

Fourteen days after the first week of cladribine therapy, the patient developed fever and malaise. SARS-CoV-2 was tested as the symptoms of the patient developed during the COVID-19 pandemic. An oropharyngeal swab was positive for SARS-CoV-2-RNA. At this time, the patient showed CTC grade 3 lymphopenia (ALC = 240/µL). However, since his symptoms were rather mild, hospital admission at that time was not necessary.

Due to persistent fever (39.5°C) and progressive respiratory symptoms with thoracic pain, he presented to our emergency department another 12 days later. Bacterial superinfection was suspected as C-reactive protein (CRP) and procalcitonin had substantially increased (122 mg/L and 0.13 ng/mL, respectively). Lung ultrasound showed suspicious findings compatible with pulmonary consolidation. The patient was hospitalized for clinical monitoring, and intravenous (i.v.) antibiotic therapy with ampicillin/sulbactam was started. ALC and other laboratory data are shown in Table 1. Antibiotic treatment was escalated to piperacillin/tazobactam 5 days later due to increased need of nasal oxygen supply and increasing inflammatory markers. In addition, hydroxychloroquine was administered for 5 days and inhalative treatment with aviptadil (vasoactive intestinal peptide (VIP)) was initiated. VIP has potentially anti-inflammatory effects by expanding regulatory T-cells known to be required for limiting pulmonary damage.[2] Apart from nasal oxygen supply, he did not need ventilatory support.

A bacterial pathogen could not be identified. A repeated oropharyngeal swab 28 days after onset of the infection was still positive for SARS-CoV-2-RNA. The patient was discharged after 16 days because respiratory symptoms and fever had ceased and inflammatory markers had declined. During COVID-19 pneumonia, neurological symptoms remained stable, and due to the infection, the second cladribine cycle has thus far been postponed.

Written informed consent was obtained from the patient to report his individual cases.

Discussion

Despite immunosuppressive therapy with cladribine and severe lymphopenia, our case of an RRMS patient

showed a fairly moderate,[1] albeit prolonged course of COVID-19 pneumonia with need of nasal oxygen supply and bacterial superinfection requiring i.v. antibiotic treatment. The patient recovered without any sequelae.

In line with our report, a milder course of COVID-19 infection in an ocrelizumab-treated MS patient was reported recently.[3] Expert panels advise to delay the treatment with cell-depleting MS therapies during the COVID-19 pandemic and consider alternatives, or to postpone subsequent cycles if a patient was already on treatment.[4] With regard to cladribine, these concerns are based on the sustained B- and T-lymphocyte reduction following treatment, which predisposes patients to infections. However, cladribine has only limited effects on innate immunity. It remains unclear why those two immunosuppressed MS patients showed rather mild to moderate courses of COVID-19 infection. Nevertheless, in a recently published MS cohort (none on cladribine treatment),[5] and in cancer patients, mild-to-moderate courses of disease have also been observed.[6] It has been suggested that not a direct effect of the pathogen, but the host response characterized by hyperinflammation with cytokine release determines severity of COVID-19 infections.[7] Novi et al.[3] speculated that reduced interleukin (IL)-6 release due to ocrelizumab treatment might have exhibited a protective role in their patient. Even though cladribine also potentially leads to reduced levels of various pro-inflammatory cytokines,[8] IL-6 levels rose markedly in our case. Therefore, the reason why our patient showed a moderate course of COVID-19 infection could not finally be clarified, but was probably in part due to the maximal supportive care.

In summary, the first case report of an MS patient developing COVID-19 infection with severe lymphopenia while under immunosuppressive therapy with cladribine is reassuring because the patient did not develop a fatal disease course and recovered without any sequelae. However, larger case series are necessary before more reliable conclusions can be drawn.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: R.D. reports receiving lecture fees by Roche and travel grants by Biogen. T.W. declared having none related to this case and topic. S.F. declared having none related to this case and topic. M.E. declared having none related to this case and topic. B.B. received travel grants and/or training expenses from Bayer Vital GmbH, Ipsen Pharma GmbH, Novartis, Biogen GmbH, Merck Serono GmbH, and Genzyme, as well as lecture fees from Ipsen Pharma GmbH, Alexion Pharma Germany GmbH, Merck Serono GmbH, Sanofi Genzyme, and Roche Pharma AG. S.R. reports receiving consulting and lecture fees, and grant and research support from Baxter, Bayer Vital GmbH, Biogen Idec, Genzyme, Merck Serono, Novartis, Sanofi-Aventis, and Teva. Furthermore, SR is a founding executive board member of ravo Diagnostika GmbH, which sells in-vitro diagnostic medical devices for the detection of infectious diseases and paraneoplastic autoantibodies. None of the authors have any financial or personal relationships with individuals or organizations that could inappropriately influence this publication.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Gandhi RT, Lynch JB and del Rio C. Mild or moderate COVID-19 (ed CG Solomon). *N Engl J Med*. Epub ahead of print 24 April 2020. DOI: 10.1056/NEJMcp2009249.
2. Prasse A, Zissel G, Lützen N, et al. Inhaled vasoactive intestinal peptide exerts immunoregulatory effects in sarcoidosis. *Am J Respir Crit Care Med* 2010; 182(4): 540–548.
3. Novi G, Mikulska M, Briano F, et al. COVID-19 in a MS patient treated with ocrelizumab: does immunosuppression have a protective role. *Mult Scler Relat Disord* 2020; 42: 102120
4. Brownlee W, Bourdette D, Broadley S, et al. Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic. *Neurology* 2020; 94: 949–952.
5. Sormani MP and Italian Study Group on COVID-19 infection in multiple sclerosis. An Italian programme for COVID-19 infection in multiple sclerosis. *Lancet Neurol* 2020; 19: 481–482.
6. Mian H, Grant SJ, Engelhardt M, et al. Caring for older adults with multiple myeloma during the COVID-19 pandemic: perspective from the international forum for optimizing care of older adults with myeloma. *J Geriatr Oncol* 2020; 11(5): 764–768.
7. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020; 395(10229): 1033–1034.
8. Laugel B, Borlat F, Galibert L, et al. Cladribine inhibits cytokine secretion by T cells independently of deoxycytidine kinase activity. *J Neuroimmunol* 2011; 240–241: 52–57.

COVID-19 and high-efficacy multiple sclerosis therapies: Time for business as usual?

Wallace J Brownlee

Multiple Sclerosis Journal
2020, Vol. 26(10) 1267
DOI: 10.1177/1352458520948211

During the Coronavirus-19 (COVID-19) pandemic, many neurologists have adopted a cautious approach to treating multiple sclerosis (MS) by delaying lymphocyte-depleting therapies (Cladribine, Alemtuzumab, anti-CD20 agents), due to concerns that treatment may increase the risk and/or severity of COVID-19 infection.[1]

In this issue of *Multiple Sclerosis Journal*, two patients are reported who received treatment with Cladribine[2] or Rituximab[3] during the escalating COVID-19 pandemic in Europe. Both patients were hospitalized within a month of treatment with confirmed COVID-19 infection. Remarkably, despite severe lymphopenia due to recent Cladribine or undetectable B-lymphocyte counts from long-term Rituximab therapy, both patients only developed moderate COVID-19 pneumonia with good recovery. These new cases add to an increasing number of reports of favourable outcomes in MS patients receiving high-efficacy, lymphocyte-depleting therapies who have developed COVID-19 infection.[4,5]

In the vast majority of people with MS, COVID-19 produces a mild illness.[6] Preliminary data suggest that older age, comorbidities and more advanced physical disability are more strongly associated with poor outcomes in people with MS with COVID-19 than disease-modifying therapy use.[6] With falling rates of new COVID-19 infections in most countries, and reassuring reports of mild COVID-19 infection even in our most immunosuppressed patients, are we now ready for business as usual when treating MS? The answer is probably yes, and in many otherwise healthy, young adults with MS, the risks of disability worsening from delayed initiation or re-treatment with a high-efficacy treatment (or opting for a less effective treatment) will outweigh the potential risks of severe COVID-19 infection.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: Dr W.J.B. has received honoraria for educational activities and/or participated in advisory boards for Biogen, Celgene, Merck, Mylan, Novartis, Roche and Sanofi.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

Correspondence to:
WJ Brownlee
National Hospital for Neurology and Neurosurgery, Queen Square, Box 83, London WC1N 3BG, UK.
w.brownlee@ucl.ac.uk

Wallace J Brownlee
Department of Neuroinflammation, Queen Square Multiple Sclerosis Centre, UCL Queen Square Institute of Neurology, London, UK/National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

References

1. Brownlee W, Bourdette D, Broadley S, et al. Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic. *Neurology* 2020; 94: 949–952.
2. Dersch R, Wehrum T, Fähndrich S, et al. COVID-19 pneumonia in a multiple sclerosis patient with severe lymphopenia due to recent cladribine treatment. *Mult Scler* 2020; 26(10): 1264–1266.
3. Wurm H, Attfield K, Iversen A, et al. Recovery from COVID-19 in a B cell-depleted multiple sclerosis patient. *Mult Scler* 2020; 26(10): 1261–1264.
4. Meca-Lallana V, Aguirre C, Beatrizdel R, et al. COVID-19 in 7 multiple sclerosis patients in treatment with ANTI-CD20 therapies. *Mult Scler Relat Disord* 2020; 44: 102306–102306.
5. Carandini T, Pietroboni AM, Sacchi L, et al. Alemtuzumab in multiple sclerosis during the COVID-19 pandemic: A mild uncomplicated infection despite intense immunosuppression. *Mult Scler* 2020; 26(10): 1268–1269.
6. Sormani MP. An Italian programme for COVID-19 infection in multiple sclerosis. *Lancet Neurol* 2020; 19(6): 481–482.