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Letter to the Editor

The pressing questions in multiple sclerosis Care in the era of COVID-19



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The rapidly evolving pandemic of the severe acute respiratory syndrome corona virus type-2 (SARS-CoV-2) commonly referred to as COVID-19 has raised many questions in the neuroimmunology clinic. The implications on MS patients are complex and multifaceted. Patients and providers share similar concerns and are challenged by this unprecedented situation. The Centers for Disease Control and Prevention (CDC) designated immunocompromised patients and those with disabilities as possible COVID-19 high-risk groups [1]. The MS International Federation (MSIF) published a global advice addressing measures to reduce infection risk and implications related to disease modifying therapy (DMT) that were endorsed by the National MS Society (NMSS). Despite these efforts, many questions remain unanswered and MS clinicians are pressured to make critical decisions without clear guidance. In this viewpoint, we will evaluate some of the common questions raised by patients and colleagues. We propose recommendations that balance infection-related risks versus the risk of neurological morbidity.

1. Should MS clinics close during the pandemic?

Some clinicians suggested closing MS clinics to reduce exposure risk and protect immunocompromised patients. This would obviously be problematic to patients who receive their infused DMTs in the MS clinic/center and for those who require baclofen pump or botulinum toxin therapies for severe spasticity. In addition, new MS cases will continue to emerge during the pandemic and will require specialized management at MS clinics/centers. However, it is important to reduce in-person visits especially for routine follow-ups and for high-risk patients with advanced age, cardiopulmonary disease, and/or severe lymphopenia. Routine laboratory and MRI monitoring could be postponed in patients with longstanding stable disease to minimize exposure risk. Utilization of tablet and wearable device technology for remote clinical monitoring should be explored in lieu of traditional monitoring in clinic. For necessary in-person visits, it is important to shorten waiting room time and limit interactions to the most essential team member.

1- Should patients stop their DMTs during the pandemic?

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Since DMTs weaken or modulate the immune system, many patients are wondering if they should stop their DMTs during the pandemic. The MSIF and the NMSS recommend against discontinuation of treatment. Most SARS-CoV-2 infections occurred in healthy individuals and it is unknown if holding DMTs would lower infection risk. Patients who stop their DMTs might be at the additional risk of virally triggered MS relapses if they catch the infection while unprotected [2]. Moreover, a subset of SARS-CoV-2 infected patients develop a hyperinflammatory response that contributes to lung injury, which may suggest potential benefits from immunotherapies [3]. Therefore, it is probably even safe for MS patients with asymptomatic or mild SARS-CoV-2 infection to continue their DMT depending on DMT type and associated laboratory abnormalities if any. Some risk mitigation strategies may need to be implemented to reduce infection-related risks with certain DMTs especially those associated with lymphopenia or hypogammaglobulinemia.

2. Should newly diagnosed patients delay DMT initiation during the pandemic?

One important question is whether we should delay DMT initiation in newly diagnosed patients until the pandemic is ameliorated. One supportive argument is the fact that relapses are usually mild and infrequent. Therefore, the benefits of delaying immunotherapy during the pandemic for a few months possibly outweigh the risk of a second relapse that may or may not occur in the following year. The counter argument is that early DMT initiation may not only help reduce relapses but also help reduce subclinical disease activity and new lesion formation, which can possibly slow disability progression and conversion to secondary progressive MS. [4] Therefore, it is essential to initiate DMT as early as possible even during the pandemic as emphasized by the MSIF and NMSS. However, several factors should be considered when selecting the new DMT including its mechanism of action, idiosyncratic effects on the immune system, associated infection risk, and its potential impact on the future SARS-CoV-2 vaccine. The early immune response against corona viruses relies mainly on T-cells while long-term immunity and prevention of reinfection relies on B-cell-mediated humoral immunity [5]. Both cellular and humoral immunity

are implicated in the immune response against future SARS-CoV-2 vaccines, which include viral protein, viral vector, and live-attenuated vaccine candidates. DMTs that cause prolonged non-selective lymphopenia (alemtuzumab) may potentially increase the susceptibility/severity of the SARS-CoV-2 infection and reduce protective immunity against the future viral protein vaccine. DMTs that cause selective B-cell depletion (ocrelizumab) may not affect the early immune response against the virus significantly but may decrease long-term immunity and negatively impact vaccine response. All cell-depleting DMTs will likely be incompatible with live-attenuated and possibly viral vector vaccines. Some DMTs have proven anti-viral effects (interferons) and some have theoretical beneficial immune-modulating effects (natalizumab and fingolimod) in COVID-19 patients and therefore may be anecdotally preferred during the pandemic [6] [7] [8].

3. Should we avoid treatment of acute relapses during the pandemic?

Since corticosteroids suppress T-cells, they can potentially increase SARS-CoV-2 infection-related risks, and their use is generally not advisable in COVID-19 patients [9]. Corticosteroids can shorten MS relapse duration but they do not typically change the final outcome except for optic neuritis. Therefore, it is perhaps reasonable to avoid treating mild MS relapses during the pandemic. More importantly, it is imperative to differentiate true relapses from pseudorelapses that can be triggered by viral or other infections, and avoid the inappropriate corticosteroid administration in these situations [11]. Severe brainstem, cerebellar, motor, or optic relapses may be treated with corticosteroids to shorten symptom duration after discussing the risks and benefits with the patient. Bioequivalent doses of oral prednisone at home may be preferred over intravenous methylprednisolone (IVMP) to reduce exposure risk (1000 mg of IVMP = 1250 mg of prednisone). Oral taper after pulse therapy is better avoided. Plasmapheresis is an alternative option for severe attacks as it carries less infection-related risks and may be beneficial in viral sepsis [12].

4. Should patients obtain a medical excuse from work during the pandemic?

MS patients should try to work from home. For some patients with special risk factors (severe lymphopenia, old age, etc.), the treating neurologist may provide a medical excuse if work from home is not possible.

Conclusion

Although the broad lines of MS management during the COVID-19 pandemic should not deviate from the standards of care, some risk mitigation strategies may need to be implemented to minimize the impact on SARS-CoV-2- infection-related risks. This letter is an opinion-based advice regarding MS management in this critical time and is not meant to provide treatment guidelines. The shared decision-making model between patients and treating neurologists should continue to

prevail during the pandemic but implications to COVID-19 should be included in the decision-making process. Management of MS during the pandemic may change as more data become available from MS/COVID-19 registries and pharmacovigilance reports.

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