COVID-19 and Disease-Modifying Therapies with Immunosuppressive Effects Targeting CD20

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Introduction

It is evident that a minority of COVID-19 patients may progress to severe illness, with risk factors including advanced age and the presence of underlying health conditions such as hypertension, diabetes, obesity, smoking, cardiovascular ailments, and lung disease. Moreover, individuals with compromised immune systems, such as those with multiple sclerosis (MS) undergoing immunosuppressive Disease-Modifying Therapies (DMTs), are believed to be at an elevated risk of experiencing severe COVID-19.

In this context, it is quite reassuring to come across a case report in this issue detailing a patient with primary progressive MS who had previously received treatment with Ocrelizumab, an anti-CD20 monoclonal antibody that depletes B-cells. This patient developed COVID-19 without complications [1]. While it's important to remember that a single instance doesn't establish a pattern, this case report aligns with the anecdotal accounts, primarily found on social media, of other MS patients undergoing immunosuppressive therapies who also had uncomplicated experiences with COVID-19. It's worth noting that the few reported cases of individuals with MS developing severe COVID-19 tend to be unsurprisingly older, have comorbidities, and exhibit more advanced disease progression.

This particular case and online reports provide support for the hypothesis that immunosuppression, or at least moderate immunosuppression linked to Multiple Sclerosis Disease-Modifying Therapies (MS DMTs), might confer a degree of protection against the development of severe COVID-19 infections. This observation aligns with expectations, given that the severe pulmonary complications of COVID-19 infection are consistent with Acute Respiratory Distress Syndrome (ARDS), which seems to have an immunological basis [1-3].

Presently, numerous exploratory trials are underway to investigate various immunosuppressive therapies as potential treatments for COVID-19, including Fingolimod (NCT04280588), an S1P modulator; tocilizumab (NCT04331795), an anti-IL6-receptor antagonist; Anakinra (NCT04341584), an IL1 receptor antagonist; and Emapalumab (NCT04324021), an anti-interferon-gamma monoclonal antibody. All of these are being evaluated for their efficacy in treating COVID-19-associated ARDS [4,5].

In a recent study, the Intensive Care National Audit & Research Centre in the UK compared 2249 patients with severe COVID-19 to 4759 patients with viral pneumonia who were admitted to Intensive Care Units (ITU) in the UK between 2017 and 2019 (Icnarc Website, 2020). The proportion of immunocompromised patients in the COVID-19 cohort was notably lower, about 3.7 times less than that in the viral pneumonia cohort (2.3% vs. 8.5%, $p < 0.00001$; Figure 1) [3]. It's important to acknowledge potential bias in this data, as patients with COVID-19 who are considered too frail and/or disabled may not make it to the ITU, possibly leading to an overrepresentation of immunosuppressed patients. Nevertheless, at least in a non-MS population, this data suggests that immunosuppressive therapies might be associated with improved outcomes in individuals with COVID-19.

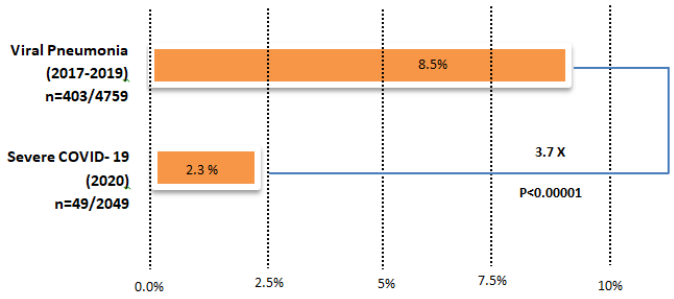

Figure 1. Percentage of individuals with compromised immune systems upon admission.

The initial antiviral responses primarily rely on T-cells, specifically CD8+ cytotoxic T-lymphocytes, and natural killer cells, with a comparatively lesser role played by B-cells. This observation may clarify why patients undergoing anti-CD20 therapies tend to handle viral infections reasonably well. Ocrelizumab and other anti-CD20 therapies have a relatively minor impact on T-cell counts and haven't been linked to severe viral infections [4]. In the clinical trials for ocrelizumab in Multiple Sclerosis (MS), infections were slightly more frequent in patients receiving ocrelizumab compared to those in comparator groups (interferon-beta-1a or placebo) [3,4]. However, these infections were typically mild to moderate in severity. Severe infections, such as pneumonia, urinary tract infections, and cellulitis, were more likely of bacterial origin. Nonetheless, there are exceptional cases, such as a singular report of fulminant hepatitis associated with an uncommon echovirus-25 infection in a patient on ocrelizumab therapy [6].

In light of the case report and supporting data, the Multiple Sclerosis (MS) community may need to reconsider its previous guidance against administering MS Disease-Modifying Therapies (DMTs) during the COVID-19 pandemic, as advocated by Alasdair Coles and the MS Advisory Group in 2020 [7]. For individuals with highly active MS, the potential consequences of delaying treatment or restricting access to high-efficacy therapies must be thoughtfully weighed, especially because the risks of severe COVID-19 in immunosuppressed patients can be mitigated through self-isolation and protective measures. Withholding immunosuppressive therapies in cases of active MS could inadvertently heighten the risk of severe COVID-19. The ongoing collection of real-world data should, hopefully, provide definitive answers to these questions. As it stands, the existing and emerging data suggest that initiating and continuing anti-CD20 therapies during the COVID-19 pandemic is likely to be safe.

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