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Multiple Sclerosis in a COVID-19 Pandemic Scenario

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Abstract

The world COVID-19 pandemic has shocked the humanity in the last year. Most physicians have been involved in the management of this new infection, even in patients with other diseases including Multiple Sclerosis (MS). Three big questions remain open: how does this new infection manifest itself in the MS patients who are already treated with immunomodulatory or immunosuppressive drugs? Do the COVID vaccines work in the same way in these patients? How to best manage MS patients during a pandemic?

Keywords

Multiple Sclerosis, COVID-19, Vaccines, Disease Modifying treatments

Description

Since the end of 2019, the world has been affected by one of the most shocking events of the recent decades: the pandemic by a new SARS-Cov-2 responsible of COVID-19. As a respiratory infection, pneumonia is the main complication, with worse prognosis especially in frail, aged, comorbid or immunosuppressed patients [1]. Multiple Sclerosis (MS) is a chronic autoimmune inflammatory disease of Central Nervous System (CNS) [2] characterized by myelin inflammatory

attack, causing recurrent neurological symptoms. MS patients are treated with several therapies to reduce inflammatory attacks by regulating the immune system. Disease Modifying Therapies (DMTs) act on the immunological regulation with different mechanisms: by sequestering (fingolimod or natalizumab), by depleting in a selective or non-selective way the lymphocytes (cladribine, alemtuzumab or ocrelizumab) or by immunomodulating through different pathways (interferons, glatiramer acetate, teriflunomide and dimethylfumarate).

For these reasons, MS patients could be considered a population at risk for COVID-19 complications. So far, we still lack of conclusive scientific evidences about this topic. COVID-19 infection has a lot of immunological implications: it seems that lymphopenia and especially the reduction of CD4+ and CD8+ T cells, B cells, and Natural Killer (NK) cells, negatively affect prognosis in severe Sars-Cov-2 infection [3]. On the other hand, lymphocytes Th 17 effector, increasing serum concentrations of some cytokines as TNF-a, IL-6 and IL-10, lead to inflammatory reaction to Sars-Cov-2 with destruction of virally infected cells but also destruction of the lung epithelial tissue causing an Acute Respiratory Distress Syndromes (ARDS) and a, sometimes fatal, pneumonia [4].

One of the first open questions that need to be answered regards the relationship between this new infection and MS: in particular, one of the most concerning issues is related to the increased risk of becoming infected or having pulmonary complications in patients affected by MS and treated with several DMTs. it is well known that some DMTs could increase the risk of infections, mainly in patients treated with depletive and immunosuppressant agents. Nevertheless, several reports confirmed that poor outcome for Sars-Cov-2 infection is found in aged and progressive MS patients but also in patients treated with anti-CD20 therapies [5]. Anti-CD20 therapies acting on B cells, could reduce the antigen presenting cells to T lymphocytes and impact on immunoglobulins production, at the same time, could also favorably reduce IL-6 producing B lymphocytes protecting from secondary hyperinflammation syndrome.

Therefore, the exact role of this therapy should be clarified. It is a matter of debate whether other DMTs may even be protective. Indeed, treatments with interferon-beta as well as Fingolimod are currently under investigation as a potential treatment for COVID-19 infection. The second relevant question concerns the efficacy of anti-COVID-19 vaccination under DMTs treatment. As we know, some immunosuppressing or immunomodulating treatments could reduce the immunological response to vaccination. The efficacy of long-term protection of vaccination is driven by the adaptative immune system, trough B cells (responsible for humoral immunity) and T cells (responsible for cell-mediated immunity). Immunomodulatory and immunosuppressive DMTs could impact the vaccine efficacy at various levels; the DMTs acting on adaptive immune system may decrease the efficacy of vaccines by impairing the development of long-term memory [6]. In the VELOCE study, B-cells-depleted ocrelizumab mounted an attenuated response to vaccine antigen [7].

Furthermore, in other trial, patients treated with Fingolimod had lower response rates, and seroconversion were reduced against novel and recall antigens [8,9]. It is still unknown if the humoral response could be masked by the reduction of B lymphocytes while the cell-mediate immunity is preserved. In light of these observations, it could be appropriate to schedule vaccinations at the onset of disease before starting any treatment, but, in the case of the anti-COVID-19 vaccine during DMTs, it would be necessary to find the most favorable window to guarantee the most optimal immunological response to the patient. The perfect window would be before the initiation of any therapy, or alternatively after lymphocyte repopulation for depletive therapies such as alemtuzumab and cladribine, or before reinfusions in anti-CD20 treatments.

The third open discussion concerns the treatment approach to MS during the pandemic. There

has been discussion about extending the dose of some drugs such as Natalizumab or Ocrelizumab during peak phases, to limit hospital access to patients, or limiting the prescription of highly effective immunodepleting drugs such as alemtuzumab or cladribine. Otherwise, to preserve the safety of the patients, we don't know the consequences of underdosing some drugs or choosing the inappropriate drug on future disability for MS patients. In addition, access to rehabilitative or symptomatic therapies has become more difficult, leading to a worsening of the physical state and quality of life of several MS patients during the last year.

Conclusion

In conclusion, in the last years, there have been relevant developments in terms of personalized treatment in MS and increasing attention has been paid to symptomatic treatments, but probably, focusing on COVID-19 pandemic, in the future we could lose sight of the centrality and importance of always treating the right patient with the right therapies.

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