Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

Immunosuppression during the COVID-19 pandemic in neuromyelitis optica spectrum disorders patients: A new challenge

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On March 11, 2020, the World Health Organization (WHO) declared the COrona VIrus Disease-2019 (COVID-19) as a pandemic. As of March 31, 2020, the outbreak of the COVID-19 has been confirmed in around 200 countries (World Health Organization). So far, COVID-19 has infected more than 800,000 people worldwide and caused more than 37,000 deaths. In this context, the most severely affected countries are the United States of America (USA), Italy, Spain and China. As vaccines and approved targeted drugs for treatment of the COVID-19 are still unknown, the current management of COVID-19 is supportive (World Health Organization, 2020).

COVID-19 morbidity and mortality has been associated with respiratory failure due to acute respiratory distress syndrome (ARDS) (World Health Organization, 2020; Chen et al., 2020). In addition, COVID-19 complications have also been related to elderly age and comorbidities such as heart diseases, diabetes mellitus, cancer, smoking habit and lung disease such as asthma or chronic obstructive pulmonary disease, among others (World Health Organization, 2020). In this context, there is concern as to whether immunosuppressant (IST) treatment increases the risk of severe COVID-19. Currently, there is no evidence that patients on IST treatments or recently transplanted patients have a higher risk of COVID-19 complications, and therefore there is no evidence they are a more vulnerable population.

COVID-19 may trigger a dysregulation in the balance between Th1 and Th2 lymphocytes, but it should be demonstrated. COVID-19 may primarily involve T lymphocytes, particularly diminishing CD8+ T and CD4+ T cells (Chen et al., 2020). Additionally, B cells levels were significantly high in severe cases (Chen et al., 2020). However, it was recently published that some patients with severe COVID-19 may experience a cytokine storm syndrome (CSS) as a hyperinflammatory response to the virus, mainly related to the monocyte-macrophage system activation (Mehta et al., 2020). Typically, this hyperactivation has been described in a context of T cell-directed IST treatment (Chen et al., 2020; Mehta et al., 2020). It was recently reported that increased interleukin (IL)−6 levels and pneumonia were risk factors for mortality in a Chinese cohort (n = 150) infected with COVID-19 (Chinese Clinical Trial Registry, 2020). An elevated concentration of CCR6+ Th17 and CD8 T cells have been associated with an overactivation of T cells that could contribute to severe COVID-19 complications (Xu et al., 2020). Other elevated proinflammatory cytokines such as IL-2R, IL-10 and TNF-α were also described in severe cases and other biomarkers such as D-dimer or ferritin were associated with severity (Mehta et al., 2020) .

Neuromyelitis optica spectrum disorder (NMOSD) is defined as an astrocytopathy often characterized by devastating neurological sequelae, including persistent paraplegia and blindness (Palace et al., 2019). Does NMOSD increase the risk of COVID-19? At present the time, there is no evidence to suggest that having NMOSD increases the risk of COVID-19 nor developing severe COVID-19. Would COVID-19 increase the risk of having an NMOSD relapse? Although it is well-known that infections may trigger relapses (particularly viral infections), there is no evidence that COVID-19 causes exacerbations in NMOSD patients. If a relapse is confirmed, what if the patients need steroid treatment? The use of steroids in the COVID-19 infected patients remains controversial (World Health Organization, 2020). However, a new clinical trial recently initiated that compare IV methylprednisolone (1–2 mg/kg/day for 3 days) versus a control group without steroids, in patients with severe novel coronavirus pneumonia, will help to response some of our questions in the near future (ClinicalTrials.gov, Identifier: ChiCTR2000029386).

Since disability in NMOSD is relapse-related (Palace et al., 2019), long-term relapse prevention treatment should be recommended for all aquaporin-4 (AQP4-ab)-positive and negative patients who are diagnosed with NMOSD. Azathioprine, mycophenolate mofetil and rituximab are the most widely used drugs to treat NMOSD (Collongues et al.,). Recently, placebo-controlled trials for NMOSD treatment have been published (Pittock et al., 2019; Cree et al., 2019; Tahara et al., 2020). Monoclonal antibodies such as eculizumab (anti complement protein C5) (Pittock et al., 2019), inebilizumab (anti-CD19) (Cree et al., 2019), rituximab (anti-CD20) (Tahara et al., 2020) and satralizumab (anti-IL6 receptor) (Yamamura et al., 2019) have been shown to reduce the risk of new relapses compared with placebo. Additionally, a randomized, open-label, head-to-head study (TANGO) (Zhang et al., 2019) comparing intravenous tocilizumab (an IL-6 inhibitor) versus azathioprine showed that tocilizumab significantly reduced relapses and stabilized NMOSD patients. Should we continue treating NMOSD patients with

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IST therapies during the COVID-19 pandemic? There is no evidence that stopping IST treatment decreases the risk of COVID-19 or severe COVID-19. As previously mentioned, severe COVID-19 may be associated with a CSS and strikingly, two drugs used to treat NMOSD are being currently evaluated in confirmed COVID-19 infected patients: 1) intravenous (IV) tocilizumab (a randomized, double-blind, placebo-controlled phase III clinical trial to evaluate the safety and efficacy) plus standard of care in hospitalized adult patients with severe COVID-19 pneumonia (ClinicalTrials.gov, Identifier: NCT04317092), and 2) eculizumab in confirmed COVID-19 infected patients with ARDS and ICU patient (ClinicalTrials.gov, Identifier: NCT04288713). Are any prophylactic or therapeutic measures recommended? Immunizations, particularly influenza vaccine, pneumococcal vaccine and varicella zoster virus vaccine included in the vaccination schedule, are important. In addition, general recommendations such as hygiene, quitting smoking and social distancing among others are the best practices to mitigate the risk of infection (World Health Organization, 2020). Although we have no evidence-based data at the present time, tocilizumab, eculizumab or rituximab may be used in highly active NMOSD, but individual cases will need a risks/benefit assessment. Additionally, there is no data on the COVID-19 course in NMOSD patients receiving IST treatment and no recommendation exists to stop treatments used in NMOSD patients so far.

As the COVID-19 pandemic unfolds worldwide, the demand for data on the impact of the novel coronavirus on NMOSD patients will grow rapidly. This information will be crucial for patients and clinicians to make evidence-based decisions on how we should manage their disease during the pandemic, or in case of acquiring COVID-19. Guidelines for clinicians managing and treating NMOSD patients are needed.

Conflicts of Interest

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