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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COVID-19 in a multiple sclerosis (MS) patient treated with alemtuzumab: Insight to the immune response after COVID

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ABSTRACT

Background: The severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is a novel disease that has spread abruptly over the world, allowing the development of countermeasures an urgent global priority. It has been speculated that elder people and patient with comorbidities may be at risk of developing complication. On the other hand, it has been seen that immunosuppressed patients could develop a mild presentation of the disease. Based on this hypothesis, several immunosuppressant agents are currently being tested as potential treatment for coronavirus 2019 (COVID-19).

Methods: report a patient treated with alemtuzumab (Humanized monoclonal antibody against the lymphocyte and monocyte surface antigen CD52, which depletes B and T cells) (Thompson et al., 2018) for recurrent remittent multiple sclerosis (RRMS) who developed mild COVID-19.

Results: Despite complete B and T cell depletion, patient symptoms abated few days with no need for hospitalization due to COVID-19 and no clinical evidence of disease activation regarding her MS.

Discussion: This report shows that MS patients with mild depletion of B and T cells can mount an antiviral response against COVID-19 and produce IgG.

Main text

The severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is a new disease that was first described in Wuhan China (Zhou et al., 2020) and it´s abrupt spread has made the development of countermeasures an urgent global priority (Chandrashekar et al., 2020). Clinical manifestation typically includes fever, dry cough, fatigue and often pulmonary involvement but these symptoms appears to be mild in the majority of patients. However, about 15% of affected individuals can develop a severe disease with respiratory insufficiency that may require intensive care management (Guan et al., 2020). Elderly and patient with comorbidities may be at risk of developing complication (Wu et al., 2020).

The understanding of its immunopathogenesis is, till now, limited. There is a study on macaques that had shown that coronavirus disease 2019 (COVID-19) induced humoral and cellular immune responses and provided protective immunity against SARS-CoV-2 after 1 month of the initial infection (Chandrashekar et al., 2020). At the beginning of the pandemic, different postulated about immunosuppressed patients were made, in one hand it was believed that patients under immunosuppression might be more susceptible to COVID-19 complications. On the other hand, it was proposed that immunosuppression might play a protective role by preventing the overly active immune response that, in some cases, might drive clinical deterioration (Mehta, 2020). Currently, there is evidence on patients with multiple sclerosis (MS) using ocrelizumab who were infected with SARS-CoV-2 and had a similar behavior as general population (Novi et al., 2020). The big doubt was if the patients could produce IgG and memory response if their MS treatment was based on depletion of B cells (Heidt et al., 2012, Baker, 2017)

We report a case of COVID-19 in a patient with multiple sclerosis treated with Alemtuzumab (humanized anti-CD52 monoclonal antibody).

She is a 24-years old Chilean female, left-handed, who works as engineer, her father had multiple sclerosis. In December of 2018 she developed subacute onset of vertigo, diplopia and ataxic syndrome. Brain MRI study was performed and showed multiple demyelinating lesions in the brain and spinal cord that fulfilled criteria of dissemination in time and space with positive oligoclonal bands. Patient was diagnosed with remittent recurrent multiple sclerosis (RRMS) and categorized as highly active disease. She was treated with five days of intravenous methylprednisolone and started her first cycle of Alemtuzumab in January 2019.

During April 2019 she had a mild relapse that was also treated with intravenous steroids. At this time, she was diagnosed with mild to moderate depression and started antidepressants. After that, she kept improving physically and mentally.

August 2019, eight months after the first cycle of alemtuzumab she had her neurological appointment, her EDSS was cero (0) and the brain and spinal cord MRI showed no new lesions neither enhancing ones.

On February 4th, 2020 she had her second cycle of alemtuzumab, well tolerated, no infusion reactions.

On May 26th, 2020, the patient developed cough, sore throat and myalgia, she was remitted to the emergency department (ED) to be tested for COVID-19. She lives with her mother, who received the visit of her partner who was COVID-19 positive one week before. At this time she was having her regular blood test for Alemtuzumab that showed normal leucocyte count and grade 1 lymphopenia (4.5 × 10^3/ul, normal range 4.5-11 × 10^3/ul and 0.93 × 10^3/ul range 1-4.8 ×

Informed consent was obtained from patient.

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10^3/ul respectively), with a normal urine test. PCR for COVID-19 was performed by nasal swab and tested positive in one sample. Patient was discharged from the emergency department to home-quarantine with symptomatic therapy of acetaminophen and levodropropizine for cough with resolution of symptoms in seven to eight days. No fever, dyspnea, diarrhea rash or other complication of this disease was presented. After her quarantine, she was tested for COVID-19 antibodies (qualitative test, immunochromatography) that showed negative IgM and positive IgG.

In this report we describe the first case of a Chilean patient under treatment with alemtuzumab that developed COVID-19, without serious complications. We speculate that immunosuppression played a favorable role in this patient, especially because she experienced COVID-19 only 3 months after her second cycle of alemtuzumab, in a period where we know she can be starting to reconstitute the lymphocyte B population (Baker, 2017), which are mainly naïve B cells, whereas the remaining T cell compartment should be memory cells with a regulatory profile (McCarthy, 2013). From the pivotal alemtuzumab studies against interferon, infections were not the main concern thus the autoimmune phenomenon; especially respiratory and urinary infections were mild to moderate (Fernandez, 2014). Also, when challenged for vaccines, the study done by McCarthy and her group (McCarthy, 2013) demonstrated that the circulating B and T cell pool had immunologic memory to common viruses in the form of IgG titers and normal responses to vaccination (T cell dependent and T cell independent recall antigens and a novel antigen) with a lack of evaluation of the T cell response to vaccine and immune response to live vaccines with the bias of the limited number of patients studied. It is important to notice that in this study a patient with “seroprotective” antibodies to varicella zoster developed meningitis despite protective IgG levels. Another lesson that we have to consider from the ocrelizumab trial (even though it is another type of treatment that only affects B cells) that patients with reduced population of B cells have a blunted humoral response to vaccines and neoantigen (Stokmaier et al., 2018).

In conclusion, we can say that the patient treated with alemtuzumab can produce IgG against COVID-19. In theory, and based on the studies done on macaques (Chandrashekar et al., 2020, Bao et al., 2020), these patients can deal with coronavirus if they are rechallenged after 1 month but it is uncertain how they will respond if they are rechallenged after 3 months or if they with have an adequate response to the COVID-19 vaccine depending of the type of immune response that this vaccine will need (T cell dependent or T cell independent)

Declaration of Competing Interest

None.

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