

# Mild COVID-19 Infection in a Patient with Multiple Sclerosis, while Taking Fingolimod: A Case Report

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## Abstract

**Background:** Fingolimod, as an immunosuppressive drug, is used in the treatment of patients with Multiple Sclerosis. During recent pandemic, several controversies raised to stop or continue immunosuppressive drugs such as fingolimod in patients who developed coronavirus disease 2019. In this regard, most of consensuses advised to stop the consumption of this drug, but try to re-initiate before 6-8 weeks to prevent the disease's activity or occurrence of rebound phenomenon.

**Case presentation:** we report a 40-year old female patient with Multiple Sclerosis receiving fingolimod. Having peripheral lymphopenia, she developed coronavirus disease 2019 symptoms, tested for polymerase chain reaction of coronavirus, and the result was positive. Afterward, she stayed at home and did not stop fingolimod. However, her symptoms have improved and she did not need hospitalization for the entire course of coronavirus disease 2019 infection.

**Conclusion:** The effects of the treatment with fingolimod on a patient infected by coronavirus disease 2019 are complex. On one hand, fingolimod withdrawal can increase the number of circulating lymphocytes, which consequently improves body defense against viral infections. On the other hand, it can also increase the risk of cytokine storm, which could be harmful. Therefore, further studies needed to find the risks and beneficial effects of fingolimod on coronavirus disease 2019 patients.

**Keywords:** Fingolimod; COVID-19; Multiple Sclerosis; Immunotherapy.

**Abbreviations:** MS: Multiple Sclerosis; COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute rRespiratory Syndrome Coronavirus-2; ARDS: Acute Respiratory Distress Syndrome; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; mrCRP: C-Reactive Protein; PCR: Polymerase Chain Reaction; EDSS: Expanded Disability Status Scale; S1P: Sphingosine-1-Phosphate; ICU: Intensive Care Unit

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## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) induce coronavirus disease 2019 (COVID-19) that can lead to severe acute respiratory distress syndrome (ARDS) [1]. Although immunosuppressive drugs are used to prevent exacerbations of Multiple Sclerosis (MS), in the face of COVID-19 pandemic, there is a concern on the risks of performing immunosuppressive treatments. Fingolimod has been shown to be associated with a mild increase in the risk of infections such as varicella zoster

and herpes simplex during pivotal or post marketing studies [2]. Herein, we reported a patient with MS who developed COVID infection and was then fully recovered while taking this medication.

## Case Report

Our patient is a 40-year old woman who had hypoesthesia of lower limbs in 2016, which spontaneously improved. Thereafter, in October 2017, she developed optic neuritis and again

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hypoesthesia of lower limbs. Her symptoms have been improved with 10grams of methyl prednisolone and plasmapheresis. Moreover, Magnetic resonance imaging (MRI) showed multiple hyperintense lesions in the brain and spinal cord compatible with MS. Fingolimod was started for her in December 2017 and continued with regular clinical and laboratory monitoring until now. She did well on this treatment with no adverse event, except a mild increase in liver enzymes, which was fully recovered after temporary dose reduction. The last Expanded Disability Status Scale (EDSS) was 1.5 on 16 May 2020. In the previous year, her absolute lymphocyte count ranged from 390 to 600 lymphocytes/ $\mu\text{L}$ , and the last MRI in November 2019 showed no new T2 or enhancing lesion, she was also clinically stable. The last test before the admission time showed that absolute lymphocyte count was 370 lymphocytes/ $\mu\text{L}$ .

### COVID-19 history

On July 15, 2020, she presented with severe chills, diarrhea, myalgia, anosmia, dysgeusia, cold sweats, and severe headache. She was tested for COVID-19 polymerase chain reaction (PCR) of a nasopharyngeal swab, which was positive. Therefore, she started treatment with azithromycin by passing 5 days from the initiation of the symptoms with infectious disease's specialist consultation. The patient continued the consumption of fingolimod on her own and did not stop it with the fear of MS exacerbation. However, her symptoms have resolved after 15 days with no need for hospitalization. Unfortunately, no chest CT scan was performed for her, and  $\text{O}_2$  saturation was not given, because she completely stayed home during the isolation for COVID-19. 15 days later, her symptoms have improved and on her PCR test's for COVID became negative. She experienced mild hypoesthesia on the left side of her face during the course of her disease, which has spontaneously recovered.

### Discussion

Our patient had a mild to moderate COVID-19 infection, while taking fingolimod and lymphopenia (grade 3) due to his medication. The patient did not stop her medication without consultation with physicians and she was then fully recovered

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from COVID-19 without any need for hospitalization or any complications. By reviewing the literature, we have found several cases of patients with MS who developed COVID-19 infections while taking fingolimod.

In two cases, both of them stopped the consumption of fingolimod and were then hospitalized in intensive care unit (ICU). However, their symptoms have rapidly improved and both of them were then transferred to wards after few days [3,4]. Moreover, there were no reports of the rebound of MS or the time of restarting the treatment with fingolimod in any of these two cases. We believe that our case did not develop respiratory symptoms and she was totally different from the other cases in the literature that had respiratory problems.

Fingolimod is a sphingosine-1-phosphate (S1P) receptor modulator that can cause functional lymphopenia [5,6]. Fingolimod sequesters T cells in lymph nodes and decreases trafficking of active T cells to central nervous system [7]. However, it shows a limited activity on the innate immune response that is needed for fighting against COVID-19 infection [8,9]. Additionally, COVID-19 patients may experience a condition called cytokine storm that is a severe immune reaction in which so much cytokines are rapidly released into the blood. Although the role of cytokines is important in normal immune responses, the release of such a large amount of them into the body at once can be harmful [10]. In this case, the immunomodulatory function of fingolimod may make the COVID-19 infection slighter.

### Conclusion

Since withdrawal from fingolimod can cause rebound of MS disease with severe disabling and even fatal outcomes, we believe that fingolimod may also have some beneficial effects on treating MS patients infected by mild COVID-19. To the best of our knowledge, a clinical trial with fingolimod has been proposed in COVID-19 patients and this case report supported the continuation of this drug in mild cases. In addition, we believe that this drug could be continued in special cases according to the severity of COVID infection, especially in those without respiratory symptoms.

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