

Improvement in Parkinson Disease Symptoms After Treatment for COVID-19 with Monoclonal Antibodies

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ABSTRACT

BACKGROUND: Parkinson disease (PD) is a neurodegenerative disease characterized by motor symptoms, such as bradykinesia, and non-motor symptoms, such as fatigue, which can be a particularly disabling feature of the disease.

METHODS: We conducted a retrospective chart review on a patient who reported improvement in baseline PD symptoms after COVID-19 treatment.

RESULTS: The patient is a 76-year-old male with a six-year history of PD who developed a COVID-19 infection, underwent treatment with COVID-19 monoclonal antibodies, and experienced a remarkable improvement in his pre-COVID PD symptoms, most notably his gait and fatigue. Prior to COVID, he rated his fatigue as '9 out of 10,' which worsened to 10 out of 10 during his COVID infection, and post-COVID treatment, his fatigue improved to '3 out of 10'.

PRINCIPAL CONCLUSIONS: We described an unexpected improvement in baseline PD symptoms for a patient treated with COVID-19 monoclonal antibodies. Further investigation will be essential to understand the mechanisms underlying this phenomenon.

KEYWORDS: Parkinson disease; COVID-19; monoclonal antibodies; fatigue

ABBREVIATIONS:

PD: Parkinson disease

COVID-19: Coronavirus disease 2019

IL-6: Interleukin-6

TNF- α : Tumor necrosis factor- α

UPDRS: Unified Parkinson Disease Rating Scale

fatigue for approximately one month following an infusion of monoclonal antibodies for treatment of COVID-19 (coronavirus disease 2019) infection.

MATERIALS AND METHODS

We conducted a retrospective chart review of a patient who reported improvement in baseline PD symptoms after COVID-19 treatment.

RESULTS

The patient is a 76-year-old male with a six-year history of PD, presenting as stiffness, slowness, stooped posture, decreased arm swing, dream enactment, and fatigue. His exam revealed bradykinesia, rigidity, and a Unified Parkinson Disease Rating Scale (UPDRS) motor score of 18, consistent with PD. His pharmacologic regimen included carbidopa/levodopa 25/100mg 1 1/2 tabs thrice daily. His baseline fatigue was severe and disabling, and described as an "overwhelming exhaustion" that caused him to feel like he was "hit by a train." His fatigue was treated – albeit sub-optimally – with methylphenidate 10mg twice daily. He developed a COVID-19 infection which was heralded by a mild cough, fever and body aches, and overall worsening of his PD symptoms. He underwent treatment with a single infusion of casirimivab/imdevimab 600mg/600mg (without steroids) in the outpatient setting. Over the course of a week, his COVID-19 symptoms resolved. He and his wife noticed a remarkable improvement in his PD symptoms, most notably his gait and fatigue. To the amazement of the patient and his wife, his improvement was above and beyond his pre-COVID baseline. He rated his pre-COVID fatigue as '9 out of 10,' which worsened with COVID to 10 out of 10, and improved to '3 out of 10' after the treatment, with the improvement lasting nearly 4 weeks, after which his fatigue returned to pre-COVID levels. His wife commented that after treatment, he appeared like "he didn't have Parkinson's." The improvement was so drastic that the couple went on a 2-week trip to Italy, a previously unthinkable task. This episode occurred between his routine neurology clinic visits, so a clinical exam during the improvement phase was not available.

INTRODUCTION

Parkinson disease (PD) is a neurodegenerative disease characterized by motor symptoms, such as bradykinesia, and non-motor symptoms, such as fatigue, which can be a particularly disabling feature of the disease affecting approximately half of those with PD.¹ We report a case of a man with PD who experienced robust improvement in pre-existing

DISCUSSION

Fatigue is a disabling non-motor symptom which affects approximately half of those with PD.² Patients affected by PD fatigue feel drained and exhausted, even without physical exertion. No approved therapy for fatigue in PD has shown to be effective, but in extreme cases, off-label use of stimulants, such as methylphenidate, can be tried.

In this report, we present a case of a patient treated for COVID-19 with an infusion of casirivimab/imdevimab, a monoclonal antibody targeting the spike protein of SARS-CoV-2, with a subsequent improvement in his baseline PD fatigue. To our knowledge, only one other similar case has been reported, in which the patient experienced a marked improvement in gait and speech post-COVID treatment and lasted for about 40 days. This supporting case gives credence to the effect we observed; however, we report a substantial and novel observation of PD-related fatigue improvement.³ Further evidence to implicate casirivimab/imdevimab in PD improvement in this patient are the half-lives of these two medications, 30.2 and 26.5 days respectively,⁴ mirroring the month-long reprieve of symptoms in our patient. Placebo effect is possible but unlikely given that the patient had no expectations from receiving the infusion except for treatment for his COVID-19 infection. Returning to his pre-COVID baseline was expected but improvement above and beyond his baseline made this incident noteworthy.

The lack of a clinical exam weakens the association between symptom improvement and the COVID treatment. However, certain aspects of improvement are undeniable: the patient's own perception of feeling less tired and walking with more ease; his wife's observation of the same; their spontaneous plan to take an international trip which was previously unfathomable; and return of PD symptoms back to pre-COVID baseline after approximately 4 weeks of benefit. Mechanisms of PD-related fatigue are unclear, but there has been growing evidence of neuroinflammation as a key mediator. In broader literature, fatigue has been associated with a heightened inflammatory response and an activated cytokine network. Notably, pro-inflammatory cytokines have been implicated in PD, mediating dopaminergic cell death.^{5,6} Additionally, levels of inflammatory markers, such as C-reactive protein, are significantly higher in PD patients compared to healthy controls.⁷ It is possible that these neutralizing antibodies may reduce an inflammatory cytokine cascade, a shared feature of both COVID-19 infection and PD.⁸ Studies have shown that the SARS-CoV-2 spike protein directly induces production of inflammatory cytokines, such as IL-6 and TNF- α ,⁹ and it is plausible that spike protein-directed monoclonal antibodies attenuate this process. Other evidence includes a significant reduction in C-reactive protein following treatment of COVID-19 patients with convalescent plasma, a cocktail of donor neutralizing antibodies with similar action.¹⁰ Further investigation will be required to understand the mechanism for this improvement of PD symptoms following COVID-19 monoclonal antibody treatment.

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Disclosures

The authors report no conflicts of interest.

Consent

Written informed consent was obtained from the patient to publish this case report.

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