Acute Worsening of Atypical Parkinson's Syndrome After Receiving Second Dose of Moderna COVID-19 Vaccine

Rachel Russell, MD; Brian Quinn, MD

ABSTRACT

Introduction: Atypical Parkinson's syndromes are a rare set of neurodegenerative conditions in which a patient experiences the typical symptoms of Parkinson's disease, in addition to various other unrelated issues.

Case Presentation: We present the case of a 71-year-old White man with a 1-year history of weakness and upper extremity tremors that, per patient report, rapidly worsened after receiving the second dose of the Moderna COVID-19 vaccine. His symptoms were consistent with an asymmetric atypical Parkinson's disease, with electromyogram results indicating chronic motor neuron involvement.

Discussion: There have been multiple reports of deterioration in patients with Parkinson's disease and atypical Parkinson's syndromes in response to contracting COVID-19. However, there are few, if any, case reports that describe an acute change in Parkinson-related symptoms in association with the COVID-19 vaccines.

Conclusions: As the pandemic continues, we must continue to remain vigilant as we learn more about the long-lasting effects of the virus and vaccines.

INTRODUCTION

More than 6 million people in the world have Parkinson's disease, making it the second most common neurodegenerative disease.[1] Considered to be primarily a movement disorder, Parkinson's disease is clinically diagnosed based on the presence of the "characteristic" symptoms, which include tremors, bradykinesia, cogwheel rigidity, and postural instability.[2] There are other conditions that share similar symptoms with different underlying causes known as atypical Parkinson's syndromes. The most common of these include multiple system atrophy, progressive supranuclear palsy, and Lewy body dementia. However, many other entities that qualify as atypical Parkinson's syndromes exist that are not well explained.[3]

Similar to Parkinson's disease, atypical Parkinson's syndromes often present with 1 or more of the "characteristic" symptoms. However, they are differentiated by the presence of other atypical symptoms, including early presence of postural instability, early autonomic failure, vertical supranuclear gaze palsy, signs of pyramidal or cerebellar dysfunction, and apraxia.[4] As with Parkinson's disease, the diagnosis of these conditions is established clinically based on symptoms, although additional testing, such as electromyography (EMG) and magnetic resonance imaging (MRI), can provide additional information and diagnostic support.[5] Another unique aspect of atypical syndromes is that they tend to be more severe and progress at a faster rate than Parkinson's disease, with significant worsening of symptoms within 3 to 5 years.[1,3] Additionally, while one of the major defining features of Parkinson's disease is the symptomatic response to dopamine therapy, this same response is not typically seen in atypical Parkinson's syndromes. There are no well-supported treatments available for any of the atypical disorders. Despite this, most clinicians opt to use similar treatments as those used in classical Parkinson's disease.[6] With the emergence of COVID-19, there has been significant interest on the effect the virus may have on various neurodegenerative disorders, including Parkinson's. There have been reports of acute worsening of Parkinson's following a COVID-19 infection, as well as the devel-

• • •

Author Affiliations: Medical College of Wisconsin, Milwaukee, Wisconsin (Russell); Department of Internal Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin (Quinn).

Corresponding Author: Rachel Russell, MD, Medical College of Wisconsin, 8701 W Watertown Plank Rd, Wauwatosa, WI 53226, phone 608.658.7791; email russellrachel25@gmail.com.

opment of "post-infectious Parkinsonism" in neurologically normal patients.[7] While there have not been many specific reports demonstrating the effect of COVID-19 on atypical Parkinson's syndromes, the response is expected to be similar.[8] There are no conclusive reports detailing the exact mechanism in which COVID-19 worsens Parkinson's symptoms. However, it has been hypothesized that the COVID-19 virus may have the ability to gain access to the central nervous system as evidenced by the reported symptoms of hyposmia/anosmia and dysgeusia by those infected.[9] If COVID-19 can access the central nervous system, it could explain the variety of neurological symptoms observed in those currently and previously infected with the virus.[9] Many clinicians believed that the COVID-19 vaccine offered significant promise to those suffering from Parkinson's and Parkinson-like syndromes, as it would provide protection with little risk of significant side effects.[8]

We present the rare case of a 71-year-old White man with no significant past medical history who presented with significant weakness that reportedly worsened shortly after receiving his second dose of the Moderna COVID-19 vaccine. He was subsequently found to have an asymmetric atypical Parkinson's syndrome.

CASE REPORT

The patient was admitted to our hospital after falling the previous night due to extreme weakness that began hours after receiving the second dose of the COVID-19 vaccine. He did not have a well-known past medical history as he had not seen a physician in the past 20 years. While he had not sought prior medical advice, he did admit that he had noticed changes within his health in the year preceding this admission. Specifically, he recalled a 1-year history of a tremor in his hands (right side more than the left), which occurred while at rest or performing actions. Around the same time, he noticed a decline in fine motor skills—particularly with his handwriting, which became more unsteady and difficult to read. A few months after that, he began to experience changes in his gait that continued to progress and had become more prominent in the last 6 months. He described these changes as a mixture of "weakness" and "unsteadiness" in which his legs would "freeze" and he would lose his balance, often falling. Concerned about his fall risk, he had started to use a walker 1 to 2 months prior to admission. He did, however, emphasize that he continued to remain capable of caring for himself and performing all daily activities. Similarly, the patient's wife had noticed these symptoms, adding that he required additional time and effort to perform small tasks, such as buttoning his shirts, tying his shoes, and writing a check. She said that her primary concern was his change in gait, which had resulted in multiple falls at home. She had encouraged him to seek medical care; however, she believed that because he was still able to care for himself, his condition was not life-threatening.

Table. Patient's Complete Lab Findings

Test	Results	Normal Range	Units
Basic metabolic panel			
Blood urea nitrogen	13	6–23	mg/dL
Sodium	138	136–145	mmol/L
Potassium	4	3.4–5.1	mmol/L
Chloride	101	96–105	mmol/L
Bicarbonate	24	22–29	mmol/L
Anion gap	13	10–18	mmol/L
Glucose	113	65–99	mg/dL
Creatinine	1.02	0.70–1.03	mg/dL
Calcium	10.2	8.6–10.2	mg/dL
Complete blood cell count			
White blood cell count	9.4	3.9–11.2	103/µL
Red blood cell count	5.5	4.4–5.9	106/µL
Hemoglobin	16	13.7–17.5	g/dL
Hematocrit	48	40–51	%
Mean corpuscular volume	88	79–98	fL
Platelet count	241	165–366	103/µL
Serum protein electrophoresis			
Total protein	6.7	6.1–8.2	g/dL
Albumin fraction	3.84	2.90–5.10	g/dL
Alpha 1 fraction	0.33	0.10–0.40	g/dL
Alpha 2 fraction	0.74	0.50–1.10	g/dL
Beta fraction	0.87	0.70–1.60	g/dL
Gamma fraction	0.92	0.60–2.00	g/dL
Antinuclear antibody (ANA) profile			
ANA	Positive	–	–
Anti-double stranded DNA screen	<1	<4	IU/mL
SSB antibody screen	<0.2	0.0–0.9	AI
Centromere antibody, IgG	<0.2	0.0–0.9	AI
Smith antibody screen	<0.2	0.0–0.9	AI
Smith and RNP antibody	<0.2	0.0–0.9	AI
Antichromatin antibody IgG	<0.2	0.0–0.9	AI
Ribosomal P antibody	<0.2	0.0–0.9	AI
Scl 70 antibody screen	2.6	0.0–0.9	AI
Anti-Jo-1	<0.2	0.0–0.9	AI
SSA antibody screen	<0.2	0.0–0.9	AI
RNP antibody screen	<0.2	0.0–0.9	AI
Other labs			
COVID-19	Asymptomatic	–	–
Creatine kinase	93	<190	Unit/L
Thyroid stimulating hormone	2.780	0.270–4.200	µIU/mL
Vitamin B12	278	232–1245	pg/mL
Vitamin B6	27.4	20.0–125.0	nmol/L
Vitamin B1	96	70–180	nmol/L
Vitamin E	5.8	5.5–18	mg/L
Copper	116.3	70.0–140.0	µg/dL
Rapid plasma reagin	nonreactive	–	–
Erythrocyte sedimentation rate	15	0–32	mm/hr
C-reactive protein	2.07	0.00–0.50	mg/dL
Rheumatoid factor	<10	<13	IU/mL

Abbreviations: RNP, ribonucleoprotein; SSA, Sjögren's syndrome-related antigen A

On the day of admission, the patient reported having felt at his baseline the previous day. However, a few hours after receiving the second dose of his COVID-19 vaccine, his weakness began with increased "unsteadiness" and difficulty ambulating. That evening, when he tried to get into bed, he fell and was unable to get up. His family found him the next morning and brought him to the hospital for further workup.

Upon examination, it was noted that he had a resting tremor, severe rigidity, and bradykinesia with the right side significantly more affected than the left. Notably, he was found to have a moderate degree of osteoarthritis to his right shoulder, possibly contributing to more limited range of motion on this extremity. Neurology was consulted and reported that his clinical picture indicated likely asymmetric atypical Parkinson's syndrome.

A full workup was performed, including a brain MRI, a spine MRI, and an EMG. The only significant findings were those of the EMG, which demonstrated evidence of a mild, diffuse, chronic lower motor neuron process affecting the right cervical, thoracic, and lumbosacral regions. This finding, indicating a low-grade neuropathy, suggested that the patient could have had some underlying motor neuron disease contributing to his condition. However, the EMG abnormalities noted were mild and did not meet criteria for the diagnosis of an official motor neuron disease, such as amyotrophic lateral sclerosis (ALS). Therefore, the interpretation of this finding was that the patient had an atypical Parkinson's syndrome with motor neuron involvement. Numerous labs also were drawn and are described in the Table. The only notable lab abnormalities included a positive antinuclear antibody screen with elevated topoisomerase antibodies (SCL-70) and an elevated C-reactive protein (a well-known inflammatory marker).

With high suspicion for an asymmetric atypical Parkinson's syndrome given the patient's symptoms and clinical condition, he was started on 1 carbidopa/levodopa 25/100 tablet 3 times daily, with plans to slowly increase the dose until reaching the final goal dose of 2 tablets 3 times a day. He also was given 10 mg baclofen to be taken 3 times a day. He was discharged from the hospital to a rehabilitation center for continued strength and conditioning. Unfortunately, minimal improvement occurred, despite continued treatment with medication and physical therapy. Approximately 5 months after the initial discharge, he was hospitalized for continued worsening of his symptoms with a profound weakness and inability to ambulate, as well as failure to thrive. Two months after this hospitalization, he passed away.

DISCUSSION

Atypical Parkinson's syndromes are a set of neurodegenerative conditions defined by the presence of classical Parkinson's disease symptoms (bradykinesia, tremors, rigidity, and postural instability), in addition to various other to other signs of upper and lower motor neuron dysfunction.[2,3] As previously mentioned, deteriorations in Parkinson's disease have been well-documented within the context of a COVID-19 infection; however, these same interactions have not been recorded with the administration of the vaccine.[8]

There have been many reported side effects of the Moderna COVID-19 vaccine, the most common being fever, headache, chills, nausea, muscle pain, and injection site pain, swelling, or redness.[10,11] According to the Michael J. Fox Foundation, there have been a few subjective reports of community members who experienced brief periods of worsened symptoms after receiving a COVID-19 vaccination.[12] However, to our knowledge, there have been no official case reports presenting an acute change in Parkinson-related symptoms after receiving any of the COVID-19 vaccines.

It was readily apparent that our patient had underlying signs of an atypical Parkinson's syndrome before obtaining the vaccine. We suspect that his acceleration of symptoms may have been due to the body's immune response to the inoculation. While atypical Parkinson's syndromes are known for rapid progression, the progression is typically seen within the context of a few years.[3] In contrast, this patient saw an abrupt worsening of symptoms that occurred within hours of receiving the vaccine. This sudden deterioration is likely due to 1 of 2 underlying reasons: (1) he was experiencing merely a flareup of his condition as defined by brief worsening of symptoms in response to a trigger or (2) he had experienced a rapid progression of his disease, the latter of which is particularly difficult to prove.

There is evidence that indicates that illness and infection are among the top 10 most common causes of sudden flareup of symptoms in patients with Parkinson's syndrome.[13] Similar to an illness, vaccinations are designed to activate the immune system—although they do so at a much slower and limited rate, thus not causing the disease.[14] Therefore, it is plausible that a vaccine could serve as a trigger for disease flareup. As previously stated, there is limited information regarding vaccination effects on those with Parkinson's disease and atypical Parkinson's syndromes, although there have been case reports of vaccinations—including those for COVID-19—causing flareups in various other chronic diseases.[15-17] Had this phenomenon been due to a flare in symptoms, it would be expected that the patient would fully recover and return to baseline.[13] But given his lack of prior medical care, it is not possible to identify the exact baseline from which we could expect him to return. Therefore, while it is impossible to definitively prove that the vaccine caused a rapid progression of his disease, there is an undoubted correlation between the vaccine administration and the patient's change in symptoms, which continued to significantly change his life.

It is interesting that the patient's response was seen only after obtaining the second dose of the vaccine. In fact, the only adverse side effect he experienced with the first dose of the Moderna vaccine was 24 hours of injection site pain. We assume that this is most likely because the body mounts a stronger immune response to the second vaccine dose.[18] Most people obtaining the COVID-19 vaccine (Pfizer or Moderna) feel significantly more side effects with the second dose.[11,19]

It is important to note that despite our patient's presentation, clinicians continue to recommend that all patients with classical and atypical Parkinson's disease receive the COVID-19 vaccine,

as infection with the virus has been linked with significantly worse outcomes.[8]

CONCLUSIONS

We report the case of an atypical response to the second dose of the COVID-19 vaccine, such that a previously independent individual with signs of an underlying atypical Parkinson's syndrome experienced a rapidly progressive worsening of his condition. While case reports exist acknowledging the association between worsening classical and atypical Parkinson's symptoms and a COVID-19 infection, to our knowledge, there have been few case reports indicating worsening of symptoms in response to vaccination.[8]

As we begin to recover from the COVID-19 pandemic, we are continually learning more about the long-lasting effects of the virus and vaccine safety profiles. It is unknown what the enduring impact will be regarding chronic conditions such as neurodegenerative disorders. Therefore, it is important that we continue to monitor and assess our patients' outcomes.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Tolosa E, Garrido A, Scholz SW, Poewe W. Challenges in the diagnosis of Parkinson's disease. *Lancet Neurol.* 2021;20(5):385-397. doi:10.1016/S1474-4422(21)00030-2

2. Sveinbjornsdottir S. The clinical symptoms of Parkinson's disease. *J Neurochem.* 2016;139(Supp 1):318-324. doi:10.1111/jnc.13691

3. McFarland NR, Hess CW. Recognizing atypical parkinsonisms: red flags and therapeutic approaches. *Semin Neurol.* 2017;37(2):215-227. doi:10.1055/s-0037-1602422

4. Litvan I. What is an atypical parkinsonian disorder? In: Litvan I, ed. *Atypical Parkinsonian Disorders: Clinical and Research Aspects*. Humana Press; 2005:1-9.

5. McFarland NR. Diagnostic approach to atypical parkinsonian syndromes. *Continuum (Minneap Minn).* 2016;22(4 Movement Disorders):1117-1142. doi:10.1212/CON.0000000000000348

6. Levin J, Kurz A, Arzberger T, Giese A, Höglinger GU. The differential diagnosis and treatment of atypical parkinsonism. *Dtsch Arztebl Int.* 2016;113(5):61-69. doi:10.3238/arztebl.2016.0061

7. Gonzalez-Latapi P, Fearon C, Fasano A, Lang AE. Parkinson's disease and COVID-19: do we need to be more patient? *Mov Disord.* 2021;36(2):277. doi:10.1002/mds.28469

8. Bloem BR, Trenkwalder C, Sanchez-Ferro A, et al. COVID-19 vaccination for persons with Parkinson's disease: light at the end of the tunnel? *J Parkinsons Dis*. 2021;11(1):3-8. doi:10.3233/JPD-212573

9. Victorino DB, Guimarães-Marques M, Nejm M, Scorza FA, Scorza CA. COVID-19 and Parkinson's disease: are we dealing with short-term impacts or something worse? *J Parkinsons Dis.* 2020;10(3):899-902. doi:10.3233/JPD-202073

10. Wadman M. Public needs to prep for vaccine side effects. Science. 2020;370(6520):1022. doi:10.1126/science.370.6520.1022

11. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2021;384(5):403-416. doi:10.1056/NEJMoa2035389

12. News in context for the Parkinson's community: what we're learning about COVID-19 vaccines. The Michael J. Fox Foundation COVID-10 Resource Hub. January 6, 2021. Accessed June 16, 2021. https://www.michaeljfox.org/news/news-context-parkinsons-community-what-were-learning-about-covid-19-vaccines

13. Magennis B, Corry M. Parkinson's disease: top 10 causes of sudden deterioration. *Br J Neurosci Nurs.* 2013;9(5):234-239. doi:10.12968/bjnn.2013.9.5.234

14. The immune system and immunization. The Immunisation Advisory Centre. Updated January 2020. Accessed January 12, 2022. https://www.immune.org.nz/immunisation/immune-system-vaccination

15. Toom S, Wolf B, Avula A, Peeke S, Becker K. Familial thrombocytopenia flare-up following the first dose of mRNA-1273 COVID-19 vaccine. *Am J Hematol.* 2021;96(5):E134-E135. doi:10.1002/ajh.26128

16. Connolly CM, Ruddy JA, Boyarsky BJ, et al. Disease flare and reactogenicity in patients with rheumatic and musculoskeletal diseases following two-dose SARS-CoV-2 messenger RNA vaccination. *Arthritis Rheumatol*. 2022;74(1):28-32. doi:10.1002/art.41924

17. Jeon YH, Lim DH, Choi SW, Choi SJ. A flare of Still's disease following COVID-19 vaccination in a 34-year-old patient. *Rheumatol Int.* 2022;42(4):743-748. doi:10.1007/s00296-021-05052-6

18. Livingston EH. Necessity of 2 doses of the Pfizer and Moderna COVID-19 vaccines. *JAMA*. 2021;325(9):898. doi:10.1001/jama.2021.1375

19. Possible side effects after getting a COVID-19 vaccine. Centers for Disease Control and Prevention. Accessed June 16, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/expect/after.html

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.