Official Journal of Erciyes University Faculty of Medicine

DOI: 10.14744/cpr.2024.94596
J Clin Pract Res 2024;46(3):305–308

The Effect of Apomorphine Therapy in the Coexistence of Parkinson's Disease and Myasthenia Gravis: A Case Report and Review of the Literature

Fidel Demir,[1] Abdullah Acar,[2] Sema Akkus[3]

[1]Department of Neurology, Selahaddin Eyyubi State Hospital, Diyarbakir, Türkiye
[2]Department of Neurology, Dicle University Faculty of Medicine, Diyarbakir, Türkiye
[3]Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

ABSTRACT

Background: The simultaneous occurrence of Parkinson's disease (PD)—a progressive neurodegenerative disorder marked by the loss of monoaminergic neurons in the substantia nigra—and Myasthenia gravis (MG)—a neuromuscular junction disease—is exceptionally rare. Although these conditions have different pathophysiological foundations, literature reports at least 29 cases of individuals diagnosed with both disorders.

Case Report: We present the case of a 66-year-old patient treated for Parkinson's disease for four years before being diagnosed with MG, following the onset of dysphagia and bilateral ptosis. Apomorphine infusion, an advanced treatment option, was safely initiated.

Conclusion: This case highlights the coexistence of PD and MG and illustrates the potential benefits of apomorphine infusion therapy. Apomorphine was effective in reducing symptoms, improving motor function, and enhancing the patient's quality of life.

Keywords: Parkinson's disease, myasthenia gravis, bradykinesia, ptosis, apomorphine infusion therapy.

Cite this article as:
Demir F, Acar A, Akkus S. The Effect of Apomorphine Therapy in the Coexistence of Parkinson's Disease and Myasthenia Gravis: A Case Report and Review of the Literature. J Clin Pract Res 2024;46(3):305–308.

Address for correspondence:
Fidel Demir.
Department of Neurology, Selahaddin Eyyubi State Hospital, Diyarbakir, Türkiye
Phone: +90 531 583 93 71
E-mail:
fideldemir2605@gmail.com

Submitted: 18.09.2023
Revised: 06.02.2024
Accepted: 14.05.2024
Available Online: 22.05.2024

Erciyes University Faculty of Medicine Publications - Available online at www.jcpres.com

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder marked by the loss of monoaminergic neurons in the substantia nigra. This loss leads to motor symptoms such as bradykinesia, rigidity, and tremor, as well as various non-motor symptoms. The annual incidence of PD is estimated to range from 8 to 18.6 cases per 100,000 individuals.[1] Conversely, myasthenia gravis (MG) is a rare autoimmune disease that impairs the neuromuscular junction, with an estimated annual incidence of 3 to 30 new cases per 1 million individuals.[2]

The first documented association between PD and MG was made in 1987. Despite their distinct pathophysiological mechanisms, there have been at least 29 reported cases of individuals diagnosed with both PD and MG in the literature.[3] This case report introduces a unique instance of a 66-year-old male patient who developed MG four years after being diagnosed with PD.

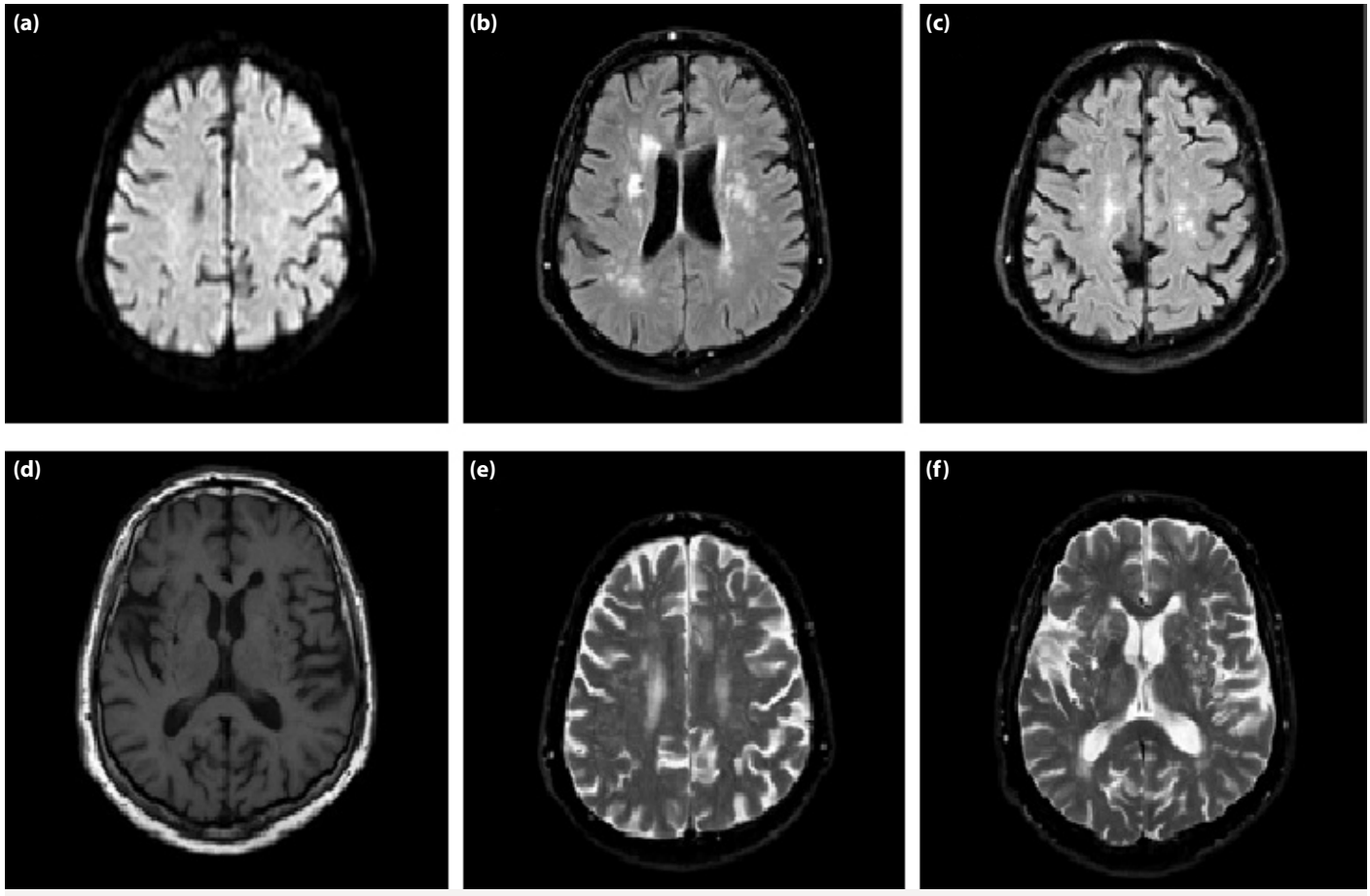

Figure 1. DWI MRI **(a)**; FLAIR MRI **(b, c)**; T1-weighted axial image **(d)**; T2-weighted axial image **(e, f)**.

DWI: Diffusion-weighted imaging; FLAIR: Fluid-attenuated inversion recovery; MRI: Magnetic resonance imaging.

CASE REPORT

This report discusses a 66-year-old male who has been managing PD for four years. He initially presented with slowed gait and reduced dexterity in his right hand. His treatment regimen includes levodopa + benserazide 125 mg four times daily, a slow-release formulation of levodopa + benserazide using a Hydrodynamically Balanced System (HBS) once daily, and pramipexole 1.5 mg once daily. Recently, he has experienced difficulty swallowing for the past two months and has noted bilateral eyelid drooping—predominantly in the right eye—over the last 15 days. Additionally, he has reported poor sleep quality and significant challenges with initiating movement and turning.

Neurological examination revealed prominent asymmetric bradykinesia and rigidity, predominantly in the right extremity. The cogwheel sign was positive, with the patient exhibiting hypophonic speech and a dull facial expression. Meyerson's sign was positive. He also displayed postural instability, necessitating the use of a cane, and was classified as Hoehn & Yahr stage III. Notably, he reported that the drooping of his eyelids worsened with fatigue. An ice pack test was performed, resulting in significant improvement of bilateral ptosis. The neostigmine test also yielded positive results.

Laboratory investigations, including a complete blood count, comprehensive metabolic panel (biochemistry), erythrocyte sedimentation rate, glycated hemoglobin (HbA1c), and thyroid function tests, demonstrated results within normal ranges. Repetitive electromyography (EMG) showed a decremental response of 20%, indicating impaired neuromuscular transmission. Cranial magnetic resonance imaging (MRI) using a fluid-attenuated inversion recovery (FLAIR) sequence revealed chronic ischemic foci, classified as Fazekas stage 2, which indicates moderate white matter changes and suggests the presence of small vessel disease or white matter lesions (Fig. 1).

The patient's serum anti-acetylcholine receptor antibody (anti-AChR Ab) level was significantly elevated at 76.7 nmol/L (normal range <0.25 nmol/L), indicating the presence of MG. Tests for anti-muscle-specific kinase (anti-MuSK) antibodies were negative. There was also no evidence of thymoma associated with the MG diagnosis.

Intravenous immunoglobulin was administered at a dosage of 35 g daily for five days, totaling 175 g. Treatment with Mestinon (pyridostigmine) was initiated at a dosage of 60 mg three times daily. Importantly, there were no signs of symptom aggravation or deterioration following the initiation of these treatments, suggesting that the patient tolerated the therapies well without any adverse effects or decline in his overall clinical condition. Considering the patient's condition, treatment with Prednol (prednisolone) was planned. A Dual-Energy X-ray Absorptiometry (DEXA) scan showed a lumbar vertebra T-score of -2.6, confirming osteoporosis. To address this, treatment with alendronate and calcium supplementation was initiated. Furthermore, prednisolone and azathioprine were planned as part of the treatment regimen. After revising the patient's oral treatments, the PD treatment regimen was modified. Levodopa + benserazide dosage was adjusted to 125 mg four times daily, and levodopa + benserazide HBS (slow-release formulation) was prescribed twice daily. Pramipexole was adjusted to 1 mg once daily in the morning and 0.5 mg once in the noon and evening. Despite these adjustments, the patient continued to experience frequent freezing and severe nocturnal symptoms. Therefore, a decision was made to proceed with a continuous subcutaneous apomorphine infusion (CSAI), one of the advanced surgical treatment options. The patient underwent an apomorphine test, which was well-tolerated and showed no side effects. Subsequently, an apomorphine pump was implanted through a minor surgical procedure to facilitate continuous infusion. Therapy commenced with a continuous infusion of apomorphine at a dose of 2 mg per hour for approximately 12-14 hours per day. This therapeutic approach significantly reduced the frequency of freezing episodes and improved nocturnal symptoms, leading to enhanced sleep quality and overall patient comfort and quality of life.

DISCUSSION

The number of patients with PD and MG together is very few and the data on this subject are mostly at the case level. A literature review revealed approximately 29 reported cases of individuals diagnosed with both PD and MG, exhibiting a male-to-female ratio of about 3:1. The primary pathological finding in PD is the degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to a reduction in dopamine levels and the development of bradykinesia and rigidity.[4] Although the precise mechanism of this degeneration is unclear, there is evidence suggesting that α-synuclein is a target of autoimmune attacks. In addition to autoantibodies directed against α-synuclein, antibodies against GM1 ganglioside, a muscle protein, have also been identified in PD patients.[5]

In an experimental study, it was reported that rats injected with plasma antibodies from patients with PD experienced a significant loss of dopaminergic neurons.[6] MG often manifests subsequent to PD. In such instances, MG is thought to occur as a secondary consequence of the autoimmune mechanisms associated with PD. It is not yet known whether the drugs used in the treatment of PD are linked to autoimmunity. Further evidence and case studies are necessary to establish the relationship between autoimmunity and the co-occurrence of MG and PD.[7]

The coexistence of MG and PD poses diagnostic challenges due to its rarity. Diagnosis is based on clinical observations, electrophysiological studies, serum antibody levels, and cholinesterase inhibitor tests.[8] The presence of anti-AChR Ab, along with positive edrophonium and neostigmine tests, suggests autoimmune involvement and impaired neuromuscular transmission in PD patients with concurrent MG.[9]

CSAI is a device-assisted surgical treatment option that has been shown to benefit both motor and non-motor symptoms in patients with advanced Parkinson's disease. It is one of the device-assisted surgical treatment options shown to be beneficial on dysphagia, chronic pain, anxiety, depression symptoms.[10] Our patient experienced significant benefits from CSAI treatment without any worsening of muscle disease-related symptoms.

CONCLUSION

This case report highlights the coexistence of PD and MG and demonstrates the potential benefits of CSAI treatment. Given the rarity of the coexistence of PD and MG, and considering that only case reports are available in the literature, sharing treatment outcomes upon detecting such cases will guide physicians in making informed treatment decisions.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Author Contributions: Concept – FD, AA; Design – FD, AA; Supervision – FD, AA; Resource – FD, AA; Materials – FD, AA; Data Collection and/or Processing – FD; Analysis and/or Interpretation – FD, SA; Literature Search – FD, SA; Writing – FD, SA; Critical Reviews – FD, AA.

Conflict of Interest: The authors have no conflict of interest to declare.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

REFERENCES

1. de Lau LM, Breteler MM. Epidemiology of Parkinson's disease. Lancet Neurol 2006; 5(6): 525–35. [CrossRef]
2. McGrogan A, Sneddon S, de Vries CS. The incidence of myasthenia gravis: a systematic literature review. Neuroepidemiology 2010; 34(3): 171–83. [CrossRef]
3. Ueno S, Takahashi M, Kajiyama K, Okahisa N, Hazama T, Yorifuji S, et al. Parkinson's disease and myasthenia gravis: adverse effect of trihexyphenidyl on neuromuscular transmission. Neurology 1987; 37(5): 832–3. [CrossRef]
4. Odajiu I, Davidescu EI, Mitu C, Popescu BO. Patients with Parkinson's disease and Myasthenia Gravis-A report of three new cases and review of the literature. Medicina (Kaunas) 2019; 56(1): 5. [CrossRef]
5. De Virgilio A, Greco A, Fabbrini G, Inghilleri M, Rizzo MI, Gallo A, et al. Parkinson's disease: Autoimmunity and neuroinflammation. Autoimmun Rev 2016; 15(10): 1005–11.
6. Chen S, Le WD, Xie WJ, Alexianu ME, Engelhardt JI, Siklós L, et al. Experimental destruction of substantia nigra initiated by Parkinson disease immunoglobulins. Arch Neurol 1998; 55(8): 1075–80. [CrossRef]
7. Zhang Q, Xu E, Li HF, Chan P, Zhao Z, Ma J. Parkinson's disease and comorbid myasthenia gravis: a case report and literature review. Front Neurol 2024; 14: 1303434.
8. Alshaikh JT, Mills K. Coincident parkinsonism and myasthenia gravis: A case series. Parkinsonism Relat Disord 2021; 89: 4–5. [CrossRef]
9. Uludag IF, Korucuk M, Sener U, Zorlu Y. Myasthenia gravis as a cause of head drop in Parkinson disease. Neurologist 2011; 17(3): 144–6. [CrossRef]
10. Metta V, Dhamija RK, Batzu L, Mrudula R, Kumar NSS, S A, et al. Safety and tolerability of long-term apomorphine infusion in advanced Parkinson's disease: an Indian multi-center (APO-IND) experience. Sci Rep 2023; 13(1): 18681.