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A case of Perry Syndrome responding to intestinal infusion of carbidopa/levodopa

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Perry Syndrome is an autosomal dominant disorder characterized by parkinsonism, neuropsychiatric symptoms, central hypoventilation, sleep difficulties, and weight changes [1]. It has been shown to be due to a mutation in *DCTN1*, located at 2p13.1, and is a *TDP-34* proteinopathy. Pathologically, it is characterized by gliosis in the substantia nigra and globus pallidus, with sparing of the neocortex and motor neurons [2]. Levodopa-responsiveness of the parkinsonian features can be seen in some individuals, and quality of life has been shown to improve to functional levels. However, dyskinesias occur frequently in this setting [1].

Carbidopa/levodopa intestinal gel (LCIG) is used to treat advanced Parkinson's disease patients with significant motor fluctuations and dyskinesias who may not be suitable candidates for surgical treatments such as deep brain stimulation due to cognitive or age restrictions [3]. A continuous infusion of levodopa/carbidopa intestinal gel preparation (1 ml equals 20 mg of levodopa) is given during waking hours through a percutaneous transgastric jejunostomy (PEG-J) following a morning bolus. This allows for steady levodopa serum levels within the narrow therapeutic window associated with advanced Parkinson's disease, and decreases motor fluctuations. Literature on LCIG therapy for other Parkinsonian syndromes, including Perry Syndrome, is lacking.

We report a 55-year-old Caucasian female with Perry Syndrome caused by p.G71R mutation in *DCTN1*. Symptoms – weight loss, apathy, cognitive decline, bradykinesia, and freezing of activity and gait – first manifested in 2008. She was diagnosed in 2011 and started on carbidopa/levodopa with good benefit. In 2016, on carbidopa/levodopa 25/100 mg every 2 hours, she gradually developed increasingly disabling dyskinesias. Amantadine 100 mg titrated to three times daily provided limited benefit. She also exhibited dopamine dysregulation syndrome (DDS) and excessive shopping habits, and thus no other dopaminergic agents were tried. Other medications included mirtazapine and quetiapine for depression and insomnia. She had a non-mechanical ground-level fall every month. In 2017, she was on a levodopa equivalent daily dose (LEDD) of 1900 mg (1600 mg of carbidopa/levodopa plus 300 mg of amantadine). Clinically, she demonstrated respiratory rate less than 15 breaths per minute, bilateral symmetric rigidity, bradykinesia, and flat affect. Unified Parkinson's Disease Rating Scale Motor Score (UPDRS-III) on medication was 22. Schwab and England ADL Scale (S&E) score was 50%. Moderate-to-severe dyskinesias occurred 75% of the time, with OFF times occurring 25% of the time. Montreal Cognitive Assessment score was 19/30. DDS remained a problem. LCIG therapy was recommended because of disabling motor fluctuations and dyskinesias. Following successful percutaneous endoscopic transgastric jejunostomy tube placement, LCIG was titrated to a morning dose of 11.0 ml (440 mg of levodopa) and a continuous rate of 2.8 ml/h (56 mg/h of levodopa) over 2 days. UPDRS-III score on LCIG therapy in the ON-medication state was 23, with mild dyskinesias occurring only 25% of the time. Due to persistent nocturnal bradykinesia and medication OFF times occurring 40% of the day, the LCIG dosing regimen was changed to a 24-h infusion at 3.4 ml/h (68 mg/h of levodopa, without a morning dose), an LEDD of 1088 mg. Amantadine was reduced to twice daily. Since then, she noted continued improvement of activities of daily living with an S&E score of 70%, medication OFF times at 20% of the day, and mild dyskinesias occurring 25% of the time. UPDRS-III score at 6 months was 14. She has not had any falls since starting LCIG. She continued to have some compulsive shopping behaviors but with significant improvement.

Perry Syndrome is a rare cause of hereditary Parkinsonism, with at least 50 individuals reported worldwide [1]. Large doses of carbidopa/levodopa above 2 g daily have led to dramatic reductions in parkinsonian symptoms in some families carrying a *DCTN1* mutation [4]. However, dyskinesias, as demonstrated here, may be disabling. LCIG has the benefit of reducing disabling dyskinesias and motor fluctuations in idiopathic Parkinson's Disease [3], and we have shown that it may provide similar benefit in Perry Syndrome.

Little data exists for 24-h LCIG infusion outcomes. One study in 2015 involved a small open-label trial that demonstrated 100% reduction of fall frequency and 54% improvement in 360° turn time following 24-h LCIG infusion at 6 months [5]. Our patient also had no falls in this setting, suggesting that the benefit of 24-h LCIG infusion may extend to Perry Syndrome.

We have demonstrated that improved parkinsonian symptom control with significant reduction in dyskinesias and improvement in S&E in Perry Syndrome is achievable with 24-h LCIG infusion therapy. This highlights its potential use in the treatment of these patients. Further reports should elucidate long-term efficacy of LCIG in the treatment of Perry Syndrome.

Conflicts of interest

None.

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Authors' roles

All authors were involved in the care of the patient. Dr. Moath Hamed, MD, was responsible for writing the manuscript. Dr. Aakash Shetty, MD, was responsible for critique of the manuscript. Genise Tremain was responsible for critique of the manuscript. Dr. Adriana Lazarescu, MD, was responsible for implantation of the PEG-J device and critique of the manuscript. Dr. Oksana Suchowersky, MD, FRCPC, FCCMG was the responsible physician for the patient, prescribed her LCIG therapy, and critiqued the manuscript.

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Ethical compliance statement

The authors confirm that approval of an institutional review board was not required for this work. Informed consent was obtained from the patient and her husband for sharing data in the case report. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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