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Case Report

Long-Standing Parkinson's Disease with Severe Dyskinesia and Response to Clozapine

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Background

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms, often complicated by long-term dopaminergic therapy (Rafieipour et al., 2020; Gopalakrishna & Alexander, 2015). We reported a case of early-onset PD with a strong family history, marked disease progression over three decades, and severe levodopa-induced dyskinesias showing partial response to clozapine.

Case Presentation

A 61-year-old retired teacher was evaluated at Lady Reading Hospital (LRH) with a long history of Parkinson's disease. He was initially diagnosed in 1998 at the age of 35 after developing progressive hand and foot tremors, right lower limb weakness, frequent falls, and excessive sweating. Initial treatment with propranolol did not result in symptomatic improvement. On neurological examination at the time of diagnosis, the patient exhibited cogwheel rigidity at the wrists, mild bradykinesia predominantly affecting the left upper limb, and resting tremors. His gait was abnormal, characterized by dragging both legs. There was a significant family history of Parkinson's disease, involving his grandfather and a maternal cousin. Notably, his son later developed PD and subsequently died due to disease-related complications. Given his relatively preserved functional status, pharmacological treatment was initially deferred. However, approximately 1.5 years later, his condition worsened with increasing sluggishness and recurrent backward falls. He then started on levodopa-benserazide (200/50 mg, half tablet per dose), which resulted in marked clinical improvement by 2006. Despite motor improvement, the patient continued to experience progressive lower limb weakness and bilateral knee swelling. He was later diagnosed with osteoarthritis of the knees, which significantly impaired mobility. A brain MRI performed in 2016 demonstrated mild cerebral and cerebellar atrophy; however, imaging records were subsequently lost. By 2024, the patient was admitted to severe generalized dyskinesias and had developed significant hand contractures. His mobility was profoundly limited, largely due to advanced knee osteoarthritis, rendering him wheelchair bound. At that time, his medication regimen included levodopa-benserazide (200/50 mg up to eight times daily), pramipexole (1.5 mg three times daily), amantadine (100 mg three times daily), and clonazepam (0.5 mg at night). He also reported moderate aural hallucinations that had begun approximately one year earlier.

Therapeutic Intervention and Outcome

Given the severity of levodopa-induced dyskinesias, clozapine was initiated at a low dose of 6.25 mg nightly. Gradual dose escalation led to noticeable clinical benefit. At a dose of 50 mg daily, dyskinesias improved by approximately 30%. Further titration to 75–100 mg resulted in an estimated 50% reduction in dyskinesias; however, this was accompanied by increased drooling. Reducing the dose to 3.75 mg was ineffective. Improvement in dyskinesias was consistently confirmed during regular follow-up visits.

Discussion

This case highlights several important aspects of Parkinson's disease, including early onset, strong familial aggregation, long disease duration, and the development of severe levodopa-induced dyskinesias (Kwon et al., 2022). The partial but clinically meaningful response to clozapine underscores its utility in refractory dyskinesias, even at low doses, while emphasizing the need to balance efficacy with adverse effects.

Conclusion

Patients with long-standing Parkinson's disease and severe motor complications present significant therapeutic challenges (Lang et al., 2018). Low-dose clozapine may offer meaningful improvement in levodopa-induced dyskinesias when conventional therapies fail, though careful monitoring for side effects remains essential (Durif et al., 1997).

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