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Case Report
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Frequency of Levodopa-Related Dyskinesias in Advanced Stage Parkinson's Disease

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Introduction

Parkinson's Disease (PD) is a common neurological disorder in older adults, estimated to affect nearly 2% of those over 65 years of age. According to the World Health Organization, the number of disabilities and deaths caused by PD is higher than any other neurological disorder. That nearly one million Americans are living with PD. Most evidence suggests that the disease affects nigrostriatal dopaminergic neurons in the basal ganglia and produces less dopamine, which causes movement problems associated with PD. The classic PD motor features cardinal symptoms of bradykinesia, cogwheel-like rigidity, tremor at rest, and postural instability. Treatment is symptomatic and there is no treatment to prevent progression of the disease [1,2].

Case Presentation

The patient is a 64-year-old female who presents to the emergency department with seizure and consciousness disturbance. She was diagnosed with PD at the age of 51, received regular medication (Madopar, Switane, Bromocriptine, Lexapro, Lexotan), and got well-controlled. This was accompanied by decreased tendon reflexes and rigidity of four limbs, resting tremor, bradykinesia, and progressive change with wheelchair bound since 2019/02. The Hoehn and Yahr Scale was from stage IV to V. According to her family, she has frequent tremors, sweating and trismus episodes about twice a day after COVID-19 pneumonia in May 2022. On outpatient Examination Electroencephalography (EEG) on September 2022, showed diffuse background slowing, predominantly at 7 Hz to 8 Hz, and frequent sharp waves in the right temporal. In October 2022, she has discharged from our hospital for bloodstream infection and urinary tract infection. During admission, intermittent seizure episode without consciousness change was noted, and Valproic acid was prescribed. The EEG was followed and showed excessive beta activity (14 Hz to 18 Hz) in the frontal area, but no epileptiform discharge. However, a seizure was noted again and consciousness disturbance (E2 V2 M4) and the patient came to our ER. Desaturation and bilateral pneumonia were noted, intubation was performed, and she was transferred to the intensive care unit for further management.

At admission, intermittent generalized tonic-clonic seizures developed and fluctuated consciousness level, which subside after Lorazepam injection. The lumbar puncture was performed, CSF routine and panel of meningitis pathogens showed no evidence of CNS infection. Bloodstream with *Corynebacterium* species infection and sputum FilmArray concern of MDR K. pneumonia ESBL, Carbapenem was prescribed as ID physician recommendation. Bronchoscopy was performed, and the final sputum report Burkholderia cepacia complex (Meropenem MIC 1 mg/L). We kept catheter free due to urinary tract infection with Escherichia coli (only Amikacin MIC 16 mg/L). The cEEG was performed showed no epileptiform discharge. Because of the generalized dyskinesia in the cluster and intermittent agitation, we already gave her Lorazepam, charged the AEDs to Briviact with Lacosamide, tapered Madopar, and added Biperiden regularly, but to no avail. Under the impression of time-locked to Levodopa administration, we discontinued Levodopa and titrated Biperiden, but no response was noted. We then titrated a low dose Midazolam infusion, and her consciousness returned to clearness. Yo-yoing or biphasic dyskinesia was suspected, and Amantadine, Neupro patch and low dose Clozapine were administrated. The patient showed no more motor complications in the recent 72 h and we discontinued Briviact. However, an episode of involuntary movement with alert consciousness was detected, it was resolved 10 mins after the infusion of Lorazepam. HLA-B typing revealed that the patient was not a carrier of the warning gene, and we switched Lacosamide to Trileptal. The patient passed the weaning test and was extubated with smooth respiratory pattern.

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Discussion

Uncontrollable movement disorders associated with the use of certain medications, especially the side effects of anti-psychiatric drugs, include dyskinesia and akathisia. Parkinson's disease is the best-known movement disorder, causing recurrent involuntary movements without disturbance of consciousness. Dyskinesia is characterized by short, twisting movements of the face, mouth, fingers, or extremities. Akathisia as a type of internal agitation, excessive and purposeless movement, probably rocking back and forth, striding, or making a fist repeatedly [3,4]. Our patient's clinical manifestations include unusual movements, mouth twisting, writhing movements of the four limbs, tightly closed eyes, and sweating. The movements may resemble tics corresponding to dyskinesia.

Ahlskog and Muenter [5] reported in a meta-analysis that patients who received levodopa treatment for 4 to 6 years had about 40% motor fluctuations and up to 90% median dyskinesia when treated for 9 years. In advanced disease stages of the disease, the therapeutic window of levodopa becomes narrower and the major of patients develop motor complications, which are especially more common in young onset PD. We need to reduce the levodopa to preserve the levels and avoid treatment complications such as motor and nonmotor fluctuations and Levodopa-Induced Dyskinesia (LID). Long-term motor complications of levodopa therapy were response fluctuations (hypokinetic phenomena) and involuntary movements (hyperkinetic phenomena), such as yo-yoing or diphasic dyskinesia [6-8]. In Hoehn and Yahr stage 4 or 5 patients, motor fluctuations were present in 71% and dyskinesias in 60% [9].

Fluctuations in motor symptoms of different states PD patients alternate between ON with peak-dose dyskinesia to being OFF. "ON" the satisfactory effect of treatment for the good motor function is described. In contrast, "OFF" is the reduced effect of treatment due to marked parkinsonian symptoms. However, as the disease progresses and gastric empty slowly, it can be observed to switch rapidly and unpredictably change between the "ON- and OFF-status" of the motor status in PD patients. Sometimes referred to as “yo-yoing”, possible explanations include altered pharmacodynamics as well as pharmacokinetics [6,7,9,10].

In addition to fluctuations, abnormal involuntary movements were also a common complication, called dyskinesia or dystonia. Our patient’s clinical symptoms appeared in the form of twisting movements involving the limbs, face, and trunk, which was closer to the diagnosis of the athetoid. Initially, the dyskinesia improved after a reduction in levodopa dosage. However, as the progress diseases, dyskinesia can occur at peak levels as well as when the effect of an individual dose is waning, causing repeat dyskinesia-improvement-dyskinesia, also called diphasic dyskinesia [11,12].

Medication management of motor complications includes non-ergoline dopamine receptor agonists and N-Methyl-D-Aspartate (NMDA) receptor antagonist is an adjunct in fluctuating disease. They caused a significant reduction in daily OFF times and increased ON time without troublesome dyskinesia. The Serotonin 5HT-2A and dopamine receptor antagonist is an atypical neuroleptic, responsible for less dyskinesia or tremor, and low propensity to cause or exacerbate parkinsonism [13,14]. Our patient’s previous hospitalization was treated as an epileptic seizure, and the family was also unable to provide complete information COVID-19 period, resulting in repeated hospitalization of the patient due to ineffective treatment [15,16]. Only by detailed clinical manifestations and history taking will the physician be able to clarify the situation and find a targeted approach for the treatment of advanced PD complicated by motor fluctuations and dyskinesias.

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