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CASE REPORT

Prolonged Drug-induced Parkinsonism in a Case of First Episode Mania: A Case Report

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Abstract

Drug-induced parkinsonism (DIP) is a familiar phenomenon seen with the use of antipsychotic drugs. In the majority of patients, this side effect is reversible. However, about one-third of the patient's DIP can persist for months even after the offending agent is removed. We have described one such case of first-episode mania with psychotic symptoms where DIP developed with both olanzapine and sodium valproate and persisted for more than 3 months in the absence of any risk factors inducing the same.

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Introduction

Parkinsonism is a known adverse effect of antipsychotic medications as well as many mood stabilizers like sodium valproate. The symptoms are known to be caused due to the inhibition of postsynaptic dopamine D2 receptors in the nigrostriatal dopaminergic pathway.[1] The prolonged extrapyramidal symptoms (EPS) are commonly associated with old age, female gender, pre-existing extrapyramidal disorder, accompanying brain damage and atrophy, human immunodeficiency virus (HIV) infection and dementia.[2] We herein are describing a case of a 20-year-old female with first-episode mania who developed extrapyramidal symptoms with antipsychotics as well as mood stabilizers, and which persisted after remission of the manic episode.

Case History

A 20-year-old unmarried female with a well-adjusted premorbid personality and no family history or personal history of psychiatric illness or any movement disorders presented to our center with an illness of seven months, which was acute in onset and continuous in the course. Birth and developmental history was normal and there were no clinical indicators suggestive of borderline intelligence or intellectual disability. After a detailed evaluation by a psychiatrist, she was diagnosed with mania with psychotic symptoms (delusion of grandiosity) as per the International Classification of Diseases (ICD-10) criteria. She had a body mass index (BMI) of 19.1 kg/m.[2] She was started on Olanzapine after in-patient admission which was gradually built up to 20 mg/day over a period of two weeks

and was observed further for another two weeks. There was less than 20% improvement in symptoms on the above treatment. She also developed EPS in the form of rigidity and slowing of movements and gait with olanzapine. Lithium was added to her treatment regimen and gradually increased to 900 mg/day. In view of the severity of manic symptoms, lithium was added with a plan to cross-taper the antipsychotic later after symptomatic improvement. After three weeks of treatment with the above drug combination, there was an inadequate improvement in manic symptoms, along with the persistence of EPS. The score on the Simpson Angus scale was 15 and trihexyphenidyl had to be given till 6 mg/ day dosages for the management of EPS. The young mania rating scale (YMRS) score was 28 suggesting a non-significant response to medications. In view of the same, olanzapine was cross tapered with haloperidol, gradually increasing to 15 mg/day over two weeks. Following two weeks of treatment with haloperidol, sodium valproate was also added and built up to 750 mg/day. There was a significant improvement noted in manic symptoms, with YMRS score reduced to 11 over a period of two weeks of treatment with the above drug combination. However, the patient developed increased rigidity, bradykinesia, slurring speech, coarse tremors, ataxia and hypersalivation, fever, and abdominal pain. A full blood workup, liver and kidney function tests, serum creatine phosphokinase (CPK), lithium and valproate levels were obtained along with malaria, dengue and typhoid serology. All psychotropic medications were stopped considering the possibility of neuroleptic malignant syndrome, and supportive treatment was administered to the patient. The serum valproate and lithium level were 78.9 mg/mL and 0.64 mEq/L, respectively (reference level: valproate 50–100 mg/mL; lithium 0.6–1.20 mEq/mL). Also, the remaining investigations were within normal limits and did not reveal any significant abnormality. When the psychotropic medications were stopped, the manic symptoms persisted to a lesser severity in the form of decreased sleep, over talkativeness and increased goal directed activity, which was managed with clonazepam up to 1.5 mg/day. After symptomatic improvement, sodium valproate was restarted and gradually built up to 750 mg/ day, primarily because of prior improvement in manic symptoms after the addition of valproate. However, the EPS persisted even when she was only on sodium valproate 750 mg/day, prompting an evaluation for any other organic cause for the same. This included magnetic resonance imaging (MRI) of brain, electroencephalogram (EEG), serum copper and ceruloplasmin levels to rule out Wilson's disease, serum anti-nuclear antibodies (ANA), anti-nuclear cytoplasmic antibodies (ANCA) and anti-N-methyl-D-aspartate (NMDA) receptor antibodies to rule out autoimmune etiology. TRODAT scan was normal, which ruled out any presynaptic dopaminergic receptor abnormalities. The EEG, MRI and remaining investigations also did not reveal any abnormality. She was finally discharged on sodium valproate 1 g/day with YMRS score of eight, but EPS persisted in the form of tremors and rigidity at the bilateral elbow and wrist joints. The improvement in maniac symptoms also persisted during follow-up visits, but the extrapyramidal symptoms as during discharge persisted even after three months. The score on Simpson Angus scale was nine.

Discussion and Conclusion

Drug-induced Parkinsonism is reversible on stopping the offending agent in most cases. However, In about thirty percent of cases, DIP may persist or have worsened beyond six months following drug withdrawal or dose reduction.[2] Also, in about 10% cases the condition is not reversible and is associated with the likelihood of increased morbidity and mortality, especially in the elderly.[3.] The incidence of DIP with classical antipsychotics has been reported to vary between 4 and 40%.[4,5.] People after 50 years of age have declining dopamine D2 receptor density and might exhibit DIP with approximate D2 receptor occupancy levels less than 80% in the basal ganglia. With centrally acting dopaminergic antagonists, the majority of the cases emerge inside three-months. However, drug exposure up to 12 months may sometimes be required. Prolonged extrapyramidal symptoms could be seen in the geriatric age group, females, those with some antecedent brain damage, and neurological illnesses like dementia, familial Parkinson's disease and HIV infection. Lithium-

associated adverse motor effects could be possibly due to varied mechanisms, including glycogen synthase kinase-3 enzyme inhibition shared with neuroleptics.[6] The drug-induced parkinsonism have also been reported in long-term sodium valproate users with an estimated prevalence of about six percent, constituting a ten-fold rise in EPS vis-a-vis the general population.[7]

Our patient developed EPS with both classes of antipsychotics and possibly with two different class of mood stabilizers (valproate and lithium). She did not have any other organic brain disease or any systemic abnormalities that might explain the persistence of EPS for a prolonged duration. Further research to look into the neurobiological mechanisms behind production of extrapyramidal symptoms is necessary, so that at-risk individuals could be identified and treated promptly.

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