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Ropinirole monotherapy induced severe reversible dyskinesias in Parkinson's disease

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Severe troublesome dyskinesias from dopamine agonist (DA) monotherapy are very rare in humans. Of course, dyskinesias have been described, but generally these are not severe.[1] However, in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) primate models of Parkinson's disease (PD), severe dyskinesias from DA monotherapy may occur if the animals are primed with levodopa.[2] We describe here an unusual case of a patient with early PD who developed severe dyskinesia on ropinirole monotherapy that resolved completely on reducing the dose. She had received levodopa previously, which was stopped much earlier. We demonstrate, on serial videos, the reversibility of the dyskinesias with dose reduction.

A 46-year old woman of Asian-Indian origin presented with a 3-month history of left leg resting tremor. She had left hemiparkinsonism and bilaterally reduced striatonigral uptake on dopamine transporter imaging, worse on the right. There was no family history of PD, and she was negative for Parkin, LRRK2, G2019S, and synuclein multiplication. Routine blood tests and magnetic resonance imaging of brain and cervical spine were normal. She

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was diagnosed with PD (Hoehn & Yahr II) and started on levodopa (150 mg/day). She developed dyskinesias of the left foot within a month after starting treatment, suggesting that this patient was prone to develop early dyskinesias under dopaminergic treatment. Levodopa was therefore gradually stopped, and ropinirole was started and increased slowly initially to 9 mg/day and then over 6 months to 15 mg/day. Within a month of reaching this dose, she developed severe choreiform dyskinesias of the trunk, pelvis, fingers, hands, and feet (8 of 14 on Unified Parkinson's disease Rating Scale-IV [UPDRS-IV]). In fact, the choreiform movements were so pronounced that a possibility of Huntington's disease (HD) or similar disorders was considered. Genetic tests for HD and dentato-rubro-pallido-luysian atrophy were negative.

Ropinirole was reduced to 12 mg/day and dyskinesias improved (UPDRS-IV = 5; Video Segment 1) and then reduced to 6 mg/day and dyskinesias completely disappeared. However, signs of parkinsonism reemerged (Video Segment 2), and she was again treated with ropinirole, reaching a dose of 9 mg/day, which benefited her but again resulted in some mild dyskinesias (Video Segment 3).

Levodopa-induced dyskinesias are common and seen in around 50% of PD patients at 5 years.[3] These are usually at higher doses, as evidenced in the Elldopa study.[4] Dyskinesias developed in equal numbers of patients at 9 months (3.3%) in the 150 mg/day and placebo groups; however, they were significantly higher (16.5%) in 600 mg/day group. In contrast, dyskinesias with DA monotherapy are uncommon (5%–7%), are milder in severity,[5] and appear much later (mean, 8.6 years of treatment with or without levodopa) than levodopa-induced-dyskinesias.[6] Initial priming with levodopa may have contributed to the marked dyskinesias in this patient, similar to that seen in animal models of PD.[7] Reversibility has been described with dopamine agonist-induced axial dystonia,[8] but this has not been reported yet with dyskinesia.

Indeed, MPTP-treated marmosets, briefly primed with levodopa several months prior to DA introduction, developed dose-dependent dyskinesias with ropinirole. These were similar in type and severity to those induced by levodopa.[2] In contrast, in nonprimed animals, dyskinesias were seen in only 50%, were mild, and occurred at higher doses.[2] Upregulated opiate transmission has been seen in 6-hydroxydopamine-lesioned rat models of levodopa-induced-dyskinesia and may be one of the possible pathways for dyskinesia accentuated with levodopa priming.[9]

Although marked dyskinesias are recognized in animal models, our case is unique as these have not been described in human patients on DA monotherapy. This case highlights that similar to animal models, some PD patients may develop marked dyskinesias with DA monotherapy when primed earlier with levodopa, even with a small dose for a short duration. It is possible that this particular patient may have developed dyskinesias on DA monotherapy even without levodopa priming, but this is speculative. Which PD patients are vulnerable to such DA-induced, levodopa-primed dyskinesias remains unanswered and may be established by larger cohort studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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