LETTER TO THE EDITOR

To the Editor

A Man With Persistent Dopamine Agonist Withdrawal Syndrome After 7 Years Being Off Dopamine Agonists

Keywords: Parkinson's disease, dopamine agonists, dopamine agonist withdrawal syndrome

Dopamine agonist withdrawal syndrome (DAWS) is a recently described condition that occurs upon discontinuation of dopamine agonists for the treatment of Parkinson's disease (PD).[1] DAWS may occur in as many as 19% of PD patients when dopamine agonists are tapered, and its occurrence has also been reported when dopamine agonists are discontinued in non-PD patients (e.g. restless leg syndrome).[2] The clinical spectrum of DAWS encompasses dysphoria, depression, generalized pain, and fatigue, to name a few.[3] Because DAWS has been described relatively recently, the natural evolution and duration of the condition are unknown; for instance, important information missing is whether DAWS would eventually abate or would persist for as long as patients remain off dopamine agonists. It has been reported that, in a subset of patients, DAWS does not abate and that some patients have to be kept on low-dose dopamine agonists to prevent DAWS reemergence[2,4]; as such, the evolution of DAWS when patients are kept off dopamine agonists for several years has not been documented.

This article relates the case of a 64-year-old man who experienced impulse-control disorder (ICD) while being treated with dopamine agonists, developed DAWS upon discontinuation of dopamine agonists, and remained off dopamine agonists for 7 years, despite presenting symptoms that significantly impaired his quality of life.

A 64-year-old right-handed man with a 10-year history of PD was seen at the movement disorder clinic. The patient had no history of depression or psychiatric condition. Nine years before the current visit, he had been treated with pramipexole and had experienced features of an ICD[5] (e.g. excessive spending), which led to discontinuation of pramipexole. However, he did not tolerate pramipexole discontinuation and developed pain that affected his right leg, in addition to marked apathy, anxiety, depression, dizziness, and generalized fatigue; he would spend most of his waking time watching television and would not engage in any social or recreational activities. Because of this symptomatology, which significantly affected his quality of life, pramipexole was reintroduced 1 year after and resulted in an improvement of mood and the painful sensation disappeared, although the excessive spending reemerged and pramipexole was discontinued once again, leading to the reappearance of pain, apathy, anxiety, and depression. A few months later, a trial of ropinirole was undertaken and resulted in an improvement of DAWS symptoms, but this benefit was, once again, accompanied by excessive spending and the drug was also ceased, after which DAWS symptoms reemerged. Trials of venlafaxine and pregabalin did not provide relief to his symptoms.

The patient was seen at the movement disorder clinic 7 years after being off dopamine agonists. During this period, he was followed by his family physician and a general neurologist. He did not see a psychiatrist and no medication besides venlafaxine and pregabalin were tried to alleviate his symptoms. According to the patient and his spouse, the symptoms had been constant and unremitting since discontinuation of the dopamine agonists. He was then taking rasagiline 1 mg once a day and a total daily dose of 900 mg of L-3,4-dihydroxyphenylalanine with carbidopa (L-DOPA). Unified Parkinson's Disease Rating Scale (UPDRS) part III score was 45, assessed 2.5 hours after the last L-DOPA dose. Upon questioning, it appeared that the symptoms of pain, apathy, anxiety, and depression had remained essentially unchanged since pramipexole and ropinirole were discontinued, despite therapy with rasagiline and incremental doses of L-DOPA.

A trial of rotigotine was undertaken. Three months later, under rotigotine 3 mg/24 hours, UPDRS part III score was 25, assessed 3 hours after the last dose of L-DOPA, the DAWS symptoms had disappeared and the patient had developed interest in social activities. However, excessive spending had resumed and he gained 20 pounds. Rotigotine had to be reduced to 1 mg/24 hours, at which an acceptable balance between DAWS and ICDs was achieved.

Whereas we believe that this patient had DAWS, it is noteworthy that an improvement of 20 points on the UPDRS part III is impressive after addition of rotigotine 3 mg/24 hours; we cannot completely exclude that a psychiatric condition contributed to the symptoms presented by the patient. However, as mentioned in the introduction, a significant part of DAWS phenomenology is akin to depression; that all of the symptomatology began after dopamine agonists were withdrawn, failed to respond to 900 mg L-DOPA daily and improved upon reintroduction of dopamine agonists are, in our opinion, strongly suggestive of DAWS.

DAWS is usually a self-limited condition, although an inability to discontinue dopamine agonists has been reported in as many as 15% of PD patients,[4] and patients alternating between ICDs and DAWS are usually kept on a dose of dopamine agonists that is low enough to minimize the occurrence of ICDs, yet high enough so that they do not experience DAWS, although the longitudinal follow-up does not extend beyond 3 years in the PD literature.[1,3,4] To our knowledge, this case is the first to report a patient with DAWS who has been kept off dopamine agonists for as long as 7 years despite presenting DAWS symptoms that were significantly hindering his quality of life. Based on the patient's history, there was no improvement of DAWS symptoms over the 7-year period in which he was not exposed to dopamine agonists. Whether the patient's symptomatology would eventually have abated had he been kept off dopamine agonist for a longer period remains unknown. Because DAWS is still a poorly understood condition, it is difficult to speculate upon the reasons and mechanisms as to why it may be persistent in cases such as this one.

In combination with the DAWS literature in PD,[1,3,4] this case suggests DAWS may be an unremitting condition in a subset of patients, whether therapy with dopamine agonists is maintained or not, even after several years. Further cases like this one, possibly with longer longitudinal follow-up, are necessary to learn more about the natural history of "untreated" DAWS.

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NTH, LS-O and MP reviewed and critiqued the manuscript. PH conceived, organized, and executed the research project and wrote, reviewed, and critiqued the manuscript.

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