Restless Legs Syndrome Responsive to Rasagiline Treatment: A Case Report

Gulsen Babacan-Yildiz, MD, Esra Gursoy, MD, Mehmet Kolukisa, MD, and Arif Celebi, MD

Abstract: We describe a patient with idiopathic restless legs syndrome (iRLS) who was responsive to rasagiline treatment. A 70-year-old woman presented with an 8-year history of iRLS symptoms and a 1-year history of resting tremor. The patient met the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria (UK Parkinson Disease [PD] Brain Bank criteria) for the diagnosis of idiopathic PD and the criteria of the International Restless Legs Syndrome Study Group for the diagnosis of iRLS. One milligram of rasagiline once daily was started with the diagnosis of early PD as monotherapy. At week 8, the patient was almost iRLS symptoms free. Rasagiline has also been shown to mildly improve PD symptoms. Rasagiline was well tolerated during the follow-up.

We suggest that rasagiline could represent a useful therapeutic option in the treatment of iRLS.

Key Words: restless legs syndrome, Parkinson disease, rasagiline

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Idiopathic restless legs syndrome (iRLS) is a neurological disorder characterized by an irresistible urge to move the legs, accompanied by uncomfortable sensations, paraesthesias, and motor restlessness. Symptoms begin or worsen during rest, mainly at night, and seem to be at least temporarily relieved by movement.[1]

Although the cause of iRLS still remains unclear and the etiological relationship between idiopathic Parkinson disease (iPD) and iRLS is not fully understood, many studies have proposed that iRLS may share an underlying pathophysiology with iPD.[2] Furthermore, some studies reported the higher prevalence rate of iRLS in patients with iPD than in the general population.[3,4] Dopamine is likely to be the most important mechanism involved in the pathophysiology of iPD and iRLS disease,[1,5] and dopaminergic agents can be dramatically effective in the symptomatic relief for both diseases.[6,7]

Rasagiline is a second-generation propargylamine that is an irreversible inhibitor of monoamine oxidase type B (MAO-B). It blocks the MAO-B oxidation of dopamine in the brain, thus increasing dopamine levels in the synapse. It has a modest antiparkinsonian effect and is used either as monotherapy in the early stages of the disease or as adjuncts to levodopa.[8]

We describe a patient with iRLS who was responsive to rasagiline treatment.

CASE REPORT

A 70-year-old woman with tremor and insomnia was referred to our department. She had an 8-year history of iRLS symptoms, including creeping or crawling sensations in the lower legs during periods of rest or inactivity, and a 1-year history of resting tremor—approximately 4 to 5 cycles per second (Hz)—developing gradually. Daytime fatigue and depression were also reported. Although she was aware of having iRLS symptoms and insomnia, she never sought any treatment. Before referring to us, she had experienced iRLS symptoms on at least 20 nights during the month.

Neurological examination disclosed mild cogwheel rigidity, bradykinesia, and resting tremor predominantly on the right side. She had no postural instability and no urinary incontinence. The patient had a masked face and monotonous speech. We observed the reduction of right-arm swing during gait. The diagnosis of iPD was made by a specialist in movement disorders using the UK PD Brain Bank criteria.[9] Her score in the United Parkinson's Disease Rating Scale in the first visit was 23, and the modified Hoehn and Yahr stage of PD was 1.5. She had a family history of PD. Her history included no smoking and excessive caffeine intake. She noticed for approximately 8 years the development of anosmia initially described as a decreased capacity to detect the smell of foods. She has chronic constipation and excessive sweating, which were usually considered to occur before the motor symptoms of iPD.[10] The patient's RLS symptoms fulfilled all the cardinal diagnostic criteria for iRLS published by the International Restless Legs Syndrome Study Group. The severity of the patient's RLS symptoms was scored as 29 points on the RLS rating scale.[1] Secondary RLS was excluded by biochemical tests. After making the diagnosis of early PD, we decided to start rasagiline as monotherapy.

DISCUSSION

The current report concerns a patient who had both severe iRLS and early iPD and whose iRLS symptoms were responsive to rasagiline.

The exact pathogenetic mechanisms leading to iRLS are not fully understood; however, several lines of evidence support a role for dopamine in the pathogenesis of iRLS.[11] For this reason, studies were conducted to confirm the effectiveness, safety, and tolerability of dopaminergic agents in reducing iRLS symptoms.[12] The dopamine agonists ropinirole and pramipexole became the first approved drugs for the treatment of moderate to severe iRLS,[13,14] but prolonged use of these drugs may cause increased severity associated with a worsening of RLS symptoms, also known as augmentation. This adverse effect may limit the use of these drugs and require the discontinuation of dopaminergic agents.[15]

From baseline to week 12, the iRLS rating scale scores decreased from 29 to 6. At week 12, the mean change in total score in the United Parkinson's Disease Rating Scale was 2 points, indicating that, in our patient, rasagiline improved her iRLS symptoms almost completely and iPD symptoms mildly.

For the dopaminergic effect, rasagiline is clearly inferior to dopamine agonists and levodopa; however, it may be a good candidate for initial treatment of iRLS because iRLS is a neurological chronic disorder with substantial negative impact on

Department of Neurology, Faculty of Medicine, Bezmi Alem Vakif University, Istanbul, Turkey.

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Address correspondence and reprint requests to: Gulsen Babacan-Yildiz, MD, Department of Neurology, Faculty of Medicine, Bezmialem Vakif University, Vatan Cad. 34093 Fatih, Istanbul, Turkey; E-mail: gbabacan@hotmail.com

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quality of life. This choice of treatment may be advantageous from a strategic perspective, facilitating the sparing of stronger dopaminergic drugs for later stages of iRLS.

To the best of our knowledge, this is the first patient reported in the literature whose iRLS has been treated by rasagiline. Furthermore, no study in the literature reports the effect of any inhibitor of MAO-B treatment in patients with RLS. We do not know whether other inhibitors of MAO-B might have been similarly effective for our patient because we did not try these drugs. Our patient reported an almost immediate improvement in iRLS symptoms, including reduced sleep latency, increased sleep efficiency, and reduced daytime sleepiness. The complete remission of iRLS symptoms indicate that rasagiline could represent a useful therapeutic option in the treatment of iRLS.

To sum up, it is not known whether rasagiline would provide a beneficial effect on motor symptoms in each patient with iRLS; however, rasagiline could represent a useful therapeutic option for the initial treatment of iRLS. We hope that our impression will be endorsed by prospective, randomized, placebo-controlled, and double-blind studies.

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