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Levodopa-Responsive Benign Tremulous Parkinsonism

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Key Words
Benign tremulous parkinsonism · Essential tremor · Levodopa · Parkinson's disease · Rest tremor

Abstract
Background: Benign tremulous parkinsonism (BTP) is a tremor dominant syndrome characterized by mild, levodopa-resistant parkinsonism with limited disability or progression. ***Case Presentation:*** A 56-year-old woman presented with a 2-year history of tremor. Neurological examination revealed right-hand rest tremor and slow finger tapping with decreased amplitude; however, we did not observe posture tremor, rigidity, bradykinesia, or posture disability. She was diagnosed with Parkinson's disease (PD) and received levodopa/carbidopa, effectively treating her rest tremor. At the age of 61 years, reoccurrence of the rest tremor was successfully treated again with levodopa/carbidopa and selegiline. Approximately 11 years have passed since symptom onset and the patient shows no further disease progression. ***Conclusion:*** This case broadens the characterization of BTP to include levodopa-responsive PD.

Background

Parkinson's disease (PD) is a neurodegenerative disorder that results in progressive extrapyramidal motor dysfunction primarily related to the loss of dopaminergic nigrostriatal function. The loss of dopamine leads to difficulty with movement, including slowness or lack of movement, rest tremor, and rigidity. Benign tremulous parkinsonism (BTP) is a unique clinical course of PD, and patients with BTP fulfill the criteria for PD with prominent rest tremor; however, nontremor components of parkinsonism remain mild and there is an absence of gait disorders apart from reduced arm swing or mild stooping. Additionally, with

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the exception of tremor, patients with BTP show no more than a mild progression of symptoms despite at least 8 years of parkinsonism, and are generally free of disability [1]. A previous report noted that the rest tremor is typically unresponsive to medications, including maximally tolerated levodopa [2]. In addition, more than half of BTP patients have a family history of PD and/or tremor [1, 2].

We report a case of BTP that was successfully treated with levodopa twice for rest tremor.

Case Report

A right-handed 56-year-old woman presented at our hospital with a 2-year history of right-hand tremor and complaints of fumbling with buttons. The patient had neither tremor nor family members with PD in her family history, and her past medical history was unremarkable. Physical examination showed blood pressure of 138/90 mm Hg and her cognitive function was normal. The neurological examination revealed pill rolling typical rest tremor (4–6 Hz) and slow finger tapping with decreased amplitude on her right hand; however, we did not observe posture tremor, rigidity, bradykinesia, or posture disability. Laboratory tests were all within normal limits, including thyroid function. T2-weighted magnetic resonance imaging did not show high-intensity spots in deep white matter, allowing us to rule out vascular parkinsonism (fig. 1). Decreased cardiac uptake of ^{123}I-metaiodobenzylguanidine (MIBG) during myocardial scintigraphy was observed [H/M ratio (early: 1.88, delayed: 1.78)]. Her Unified Parkinson's Disease Rating Scale III motor score was 4/108 points. She was diagnosed as having PD (Hoehn and Yahr stage 1) and received levodopa/carbidopa 200 mg/day, which effectively treated the rest tremor. When she was 61 years old, the right-hand rest tremor reoccurred and she was treated with levodopa/carbidopa (a total of 300 mg/day) and selegiline (2.5 mg/day). Slow finger tapping with decreased amplitude continued; however, her rest tremor improved. Approximately 11 years have passed since the patient's onset of symptoms and her parkinsonism is slowly progressive; however, she does not show disability apart from continuing to fumble with buttons.

Discussion

According to the Sydney multicenter study of PD, 10 years after the onset of symptoms of idiopathic PD, 41% of patients were Hoehn and Yahr stage 3–5, and 43% had died [3]. Therefore, BTP has a better prognosis than idiopathic PD. Several papers have alluded to cases such as this patient as having 'benign tremulous PD/parkinsonism' or 'tremor-predominant PD/parkinsonism' or 'monosymptomatic rest tremor' [4–8]. Of note, a family history of PD and/or tremor has previously been reported in more than 60% of BTP patients. *LRRK2* and *parkin* gene mutations have been reported in patients with BTP, suggesting a relatively strong genetic linkage for this form of PD [2, 9, 10]. Selikhova et al. [2] reported the neuropathological findings of BTP, and they identified 16 cases of pathologically confirmed benign tremulous PD; another 5 cases conformed to the definition of BTP but did not have the pathology of PD. In 4 out of 16 patients with pathologically confirmed benign tremulous PD, the initial diagnoses were essential tremor (ET), drug-induced tremor, dystonic tremor, and ET with rest tremor. On the other hand, in 4 of the 5 patients with BTP without pathologically confirmed PD, the initial diagnosis was PD. In addition, dyskinesia

and/or motor fluctuation and/or features of advanced disease (falls, hallucinations and dementia) occurred in all of the pathologically confirmed BTP patients later in their disease course. These results indicate that BTP is a subtype of PD only when the patient shows an eventual progression of the disease to include symptoms of dyskinesia and/or motor fluctuation and/or advanced disease features, and that response to levodopa treatment is not a reliable factor in diagnosing BTP.

Pathologically confirmed BTP had less severe neuronal loss in the substantia nigra post mortem than in PD controls, correlating with the slower clinical progression of BTP. The most important and common differential diagnosis is ET; therefore, DatSCAN SPECT might be a good way to distinguish PD from ET [11].

Whether BTP represents a subtype of PD is controversial. Rest tremor in BTP is typically resistant to medications and only a few BTP patients, including those who are pathologically confirmed to have PD, have been reported to respond to even maximally tolerated levodopa [1, 9, 10]. Thus, our case presents a relatively rare patient with BTP whose rest tremor was improved twice after initiating levodopa therapy during her 11-year history of PD. Consequently, this case report further broadens the characteristics of BTP to include not only levodopa-resistant PD, but also levodopa-responsive PD and suggests that further studies are needed to define the full spectrum of BTP.

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Disclosure Statement

The authors declare that they have no competing interest. There are no financial conflicts of interest.

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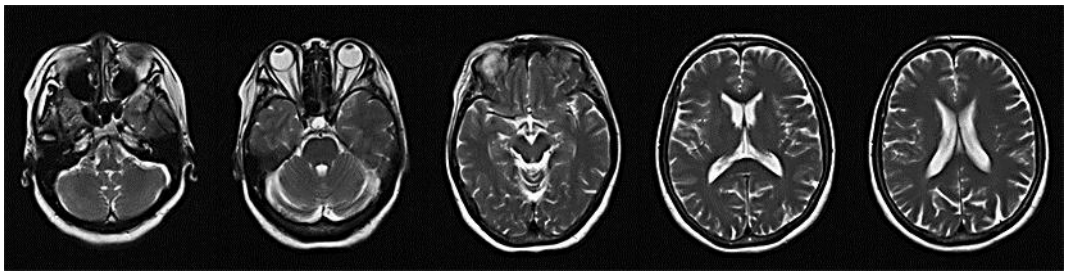

Fig. 1. T2-weighted magnetic resonance images. The patient presented with unremarkable magnetic resonance images.