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Clinical and pathologic characteristics of a patient with LRRK2 (G2019S) mutation

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Background: Parkinson's disease is the second most common neurodegenerative disease and although it is usually sporadic, various hereditary forms presenting clinical phenotypes similar to those of sporadic PD have been recognized. Among these, cases of parkinsonism with an autosomal dominant pattern of transmission and variable penetrance have been shown to be caused by mutations in the gene for leucine-rich repeat kinase (LRRK2), also known as PARK8.To date, reported cases of LRRK2 parkinsonism have shown variable clinical and pathological characteristics, ranging from typical LB pathology to nigral degeneration without LB or even tau pathology consistent with AD.

Materials and methods: We report the clinical and pathologic characteristics of a patient with the G2019S mutation, which is the most common LRRK2 mutation and is responsible for about 3% of sporadic and about 8% of familial cases of PD. To our knowledge 20 cases of patients with this mutation have been described from a pathological point of view. The patient had clinical features consistent with idiopathic Parkinson's disease, consisting of slowly progressive resting tremor with lateralized onset and bradikinesia, with cognitive impairment appearing only in the final stages of the disease. Interestingly, he never showed a significant response to levodopa and never developed symptoms of LTS.

Results: Pathologic examination revealed gliosis and severe neuronal loss with depigmentation in the substantia nigra; Lewy Bodies were absent.

Conclusion: These findings support the concept that the neurodegeneration associated with LRRK2 mutations might be clinically indistinguishable from typical PD.

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Speech and voice disorders in early untreated Parkinson's disease

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Background: Hypokinetic dysarthria (HD) in Parkinson's disease (PD) includes the symptoms of hypomimia, orofacial hypokinesia, and dysdiadochokinesia, deficits in respiration, phonation, and phonetics. As yet, it is unclear whether HD has been present since early stages of PD.

Aim: To identify symptoms of HD in patients with early untreated PD.

Methods: We studied 17 male patients with early PD [mean age 62.5 (±SD 11.7); duration of PD 2.3 (±1.4), Hoehn and Yahr stage 1-2, UPDRS III score 18.4 (±7.2)], before starting symptomatic pharmacotherapy and 16 healthy male controls (HC) of comparable age. All subjects were examined with modified version of Dysarthric Profile 3F (DP3F). The examinations were digitally recorded for subsequent acoustic analysis.

Results: DP3F revealed signs of HD in 12 out of 17 PD patients and in none of HC. The most frequent symptoms of HD were hoarse voice in phonation of vowels (16 cases), hypomimia (15), and a reduced voice pitch range (14). Acoustic analysis demonstrated higher proportion of jitter (0.74% vs. 0.18%) and shimmer (5.53% vs. 1.29%) in PD patients than in HC. Melody of speech was measured in short question (PD 7.6 semitones, ±1.8, HC 10.58, ±2.96, $p<0.01$), in reading (PD 1.4 semitones, ±0.54, HC 2.12, ±0.51, $p<0.001$), and in monologue (PD 1.2, ±0.25, HC 2.25, ±0.8, $p<0.001$).

Conclusions: Both clinical examination with DP3F and acoustic analysis of speech demonstrate signs of incipient HD in patients with early untreated PD.

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