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Journal of Movement Disorders 2012;5:28-32
pISSN 2005-940X / eISSN 2093-4939

CASE REPORT

Levodopa-Induced Facial Dystonia in a Case of Progressive Supranuclear Palsy

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Progressive supranuclear palsy (PSP) is frequently misdiagnosed as other Parkinsonism because of clinical heterogeneity of PSP. We present here a case of a 67-year-old male patient with frontotemporal dementia-like cognitive impairment including language difficulties and abnormal behaviors. He showed severe facial dystonia after the levodopa treatment. Herein, we describe an unusual case of a patient presenting with PSP which, we believe could contribute to our knowledge about atypical leveodopa-induced facial dystonia in PSP.

Journal of Movement Disorders 2012;5:28-32

Key Words: Progressive supranuclear palsy, Dystonia, Frontotemporal dementia.

Probable progressive supranuclear palsy (PSP) is defined as gradually progressed clinical features that occur after 40 years of age, including vertical supranuclear palsy and prominent postural instability that appear in the first year of onset.[1] The progressive non-fluent aphasia (PNFA) clinical criteria by Neary noted two core clinical features.[2] The first core feature is insidious onset with slow progression[2] and the second feature is that patients should reveal the nonfluent spontaneous speech with at least one of the followings: agrammatism, phonemic paraphasias, and anomia.[2] Recently, the cases of combined PNFA and PSP have been reported.[3-7] Approximately 10% of those with PSP had been clinically diagnosed with an apraxia of speech and PNFA.[8] Another study showed that over 30% of individuals with tau pathology had presented with progressive aphasia.[9] Of those individuals with tau pathology, 55% had corticobasal degeneration or PSP.[10]

Dystonia, especially retrocollis, is a common manifestation of PSP.[11] In addition, a wide variety of dystonias can be associated with PSP. For example, blepharospasm, limb dystonia, oromandibular dystonia or treatment-induced dystonia have been established.[11,12] In a study by Barclay and Lang,[11] of 83 patients with clinically diagnosed PSP, dystonia could be clearly induced by treatment in only three patients (one with oromandibular dystonia and blepharospasm and two with limb dystonia). Levodopa-induced facial dystonia (LIFD) is rare. We present here an unusual case of LIFD in the clinically diagnosed PSP patient who was initially suspected as having frontotemporal dementia (FTD) because the patient presented symptoms of behavior changes and language problems.

Case

Clinical course

A 67-year-old man was admitted to our hospital presenting gait disturbance and facial dystonia. His wife noted that he showed nonfluent speech having difficulty in naming objects and abnormal behavior such as hyperphagia for the first time 6 years previously. Thereafter, tremor in the lower limbs, more dominantly in the left leg, gait disturbance and postural instability insidiously progressed for 4 years. Since the age of 65, he has shown personality change and memory impairment. He had been known to be a very gentle and quiet person, but now often showed temperament. His memory worsened and cognitive function contin-

Received March 13, 2012
Revised April 23, 2012
Accepted April 23, 2012

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· The authors have no financial conflicts of interest.

ued to decline. One year previously, he began to develop stooped posture and left shuffled gait which gradually worsened. By then, his movements slowed considerably, his gait became unsteady, and he fell frequently. A trial of levodopa (200 mg/day) was prescribed dose subsequently increased to 600 mg per day over one year. However, no objective signs of improvement showed despite increased dose of levodopa, and involuntary facial dystonia began to develop.

Neurological examination taken after the levodopa medication revealed severe facial dystonia. Involuntary facial grimacing usually sustained around both eyes accompanied with hypertonicity in facial muscles and deep facial folds. His speech was more difficult because of simultaneous contraction of facial muscles. Body bradykinesia, axial rigidity and rest tremor in both limbs, and rest tremor in both arms and legs, which was more severe on the left limbs, were shown. The motor score of the Unified Parkinson's Disease Rating Scale (UPDRS) scored 59. Despite no definite supranuclear palsy, optokinetic nystagmus was not found. Motor power was intact and sensory examination was normal. There was no pathologic reflex on both feet despite increased overall deep tendon reflexes. The patient could not stand without assistance and fell down frequently.

After the discontinuation of levodopa, motor score of UPDRS dropped to 38 points and facial dystonia completely disappeared. There was bilateral symmetric parkinsonism on the proximal parts. When answering questions or having conversation, he showed groping speeches, intermittent palilalia and severe anomia. However, single word comprehension was preserved. A month later, levodopa administration

Table 1. Neuropsychological performances

	Jan. 23, 2008	Mar. 02, 2011
MMSE	29 (57.53 percentile)	26 (0.99 percentile)
Attention		
Digit		
Forward span	8 (87.7 percentile)	7 (66.64 percentile)
Backward span	3 (14.46 percentile)	3 (14.46 percentile)
Letter cancellation	Normal	Normal
Neglect	N/A	N/A
Speech and Language		
Fluency	Fluent	Fluent
Comprehension	Normal	Normal
Repetition	15 (≥ 16 percentile)	15 (≥ 16 percentile)
Naming	43 (12.1 percentile)	40 (4.85 percentile)
Reading	Normal	Normal
Writing	Normal	Normal
Visuospatial function	31 (28.77 percentile)	29 (10.03 percentile)
Memory (delayed recall)		
Verbal	5 (29.46 percentile)	3 (5.82 percentile)
Visual	18.5 (57.14 percentile)	16.5 (37.07 percentile)
Frontal and executive function		
Motor impersistence	Normal	Normal
Contrasting program	19 (< 16 percentile)	20 (≥ 16 percentile)
Go-no-go test	18 (< 16 percentile)	4 (< 16 percentile)
Fist-edge-palm	Normal	Abnormal
Alternating hand movement	Normal	Normal
Alternating square & triangle	Normal	Deformed, perseveration
Luria loop	Normal	Perseveration
Stroop color test	51 (2.68 percentile)	13 (0.02 percentile)
COWAT		
Semantic knowledge		
Animal	9 (3.07 percentile)	5 (0.22 percentile)
Supermarket	7 (3.75 percentile)	3 (0.48 percentile)
Phonemic knowledge	12 (3.36 percentile)	2 (0.13 percentile)

Descriptions of the specific measures used can be found in Seoul Neuropsychological Screening Battery (2003). N/A: not applicable, COWAT: Controlled Oral Word Association Test, MMSE: Mini Mental Status Examination.

restarted and doses were gradually increased to 150 mg per day. This increased medication caused reemergence of his facial dystonia. Motor score of UPDRS worsened to 45 points.

Results of routine laboratory investigations for dementia with Parkinsonism and gene (*MAPT* and *progranulin*) study for FTD were normal. Fourteen months later, at the age of 68 years, he became completely unable to walk even with assistance. His upward and downward gazes were absent and he finally showed supranuclear palsy.

Neuropsychologic evaluation

Results of neuropsychologic assessment performed 3 years previously showed naming difficulty (12.1 percentile) and severely impaired frontal executive function (2.68 percentile). Verbal and visual memory, attention, and visuospatial function were still preserved. Follow-up neuropsychologic assessment in our laboratory also showed a more significant decline in Boston naming test result (4.85 percentile) and frontal executive function (0.02 percentile) than the past examination. In addition, the performance of visuospatial function evaluated with the Rey Complex Copy test and memory ability evaluated with auditory verbal learning test marked several standard deviations below those of normal control subjects. Because of facial dystonia, he seldom spoke during hospitalization. He underwent the Korean version of the Western Aphasia Battery (KWAB) after the discontinuation of levodopa. Language was severely impaired, based on KWAB test results. Speech was non-fluent and marked by anomia. Comprehension was normal but repetition was impaired. Mini-Mental State Examination scored decreased to 26 from 29 in 2 years. His neuropsychologic results were summarized in Table 1.

Neuroimaging studies

Magnetic resonance images of the brain showed markedly bilateral fronto-temporal lobe, midbrain and cereballar atrophy (Figure 1). ^{18}F-fluorodeoxyglucose positron emission tomography showed hypometabolism definitely in the bilateral fronto-temporal area (Figure 2). Lesser hypometabolic deficits were observed in the left parietal lobe. ^{123}I-metaiodobenzylguanidine scintigraphy revealed normal early and delayed H/M ratios (early H/M ratio: 1.91, delayed H/M ratio: 2.38).

Discussion

Language problem of the patient insidiously and slowly progressed once started. In addition, anomia and impaired repetition, which were documented by KWAB, were supportive of the diagnostic features of PNFA.[2] Therefore, this initially

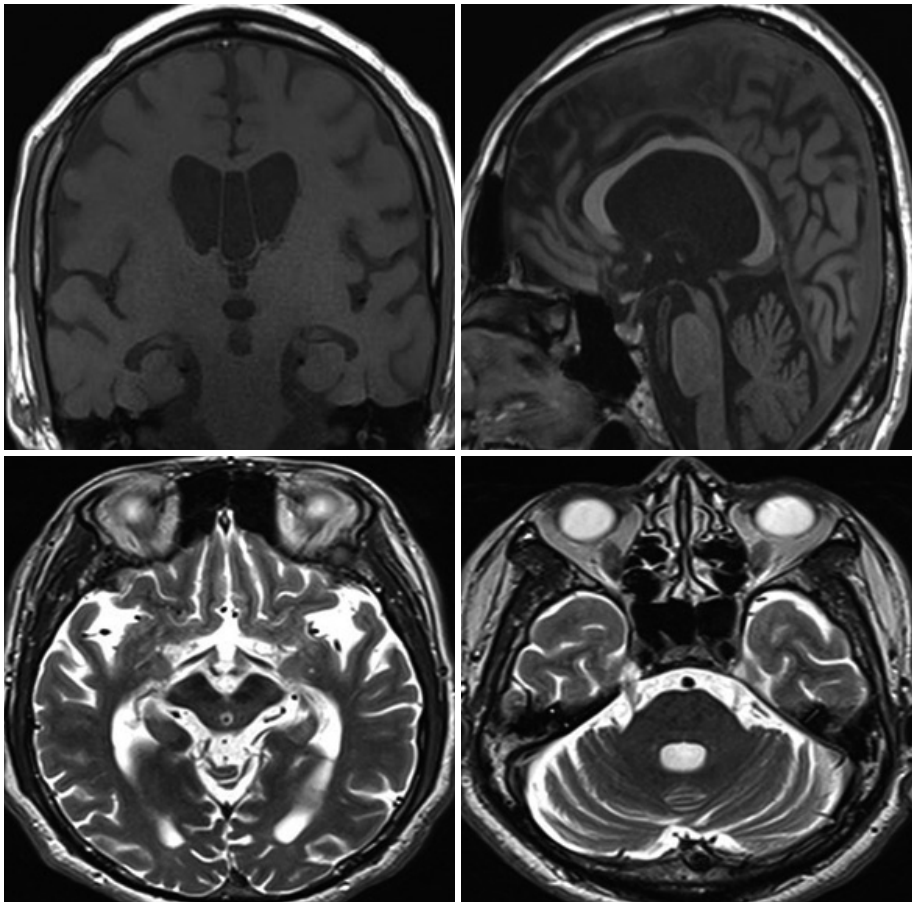

Figure 1. Brain MRI. MRI shows diffuse cerebral cortex (especially bilateral fronto-temporal lobe), brain stem and cerebellar atrophy. In particular, midbrain atrophy is shown.

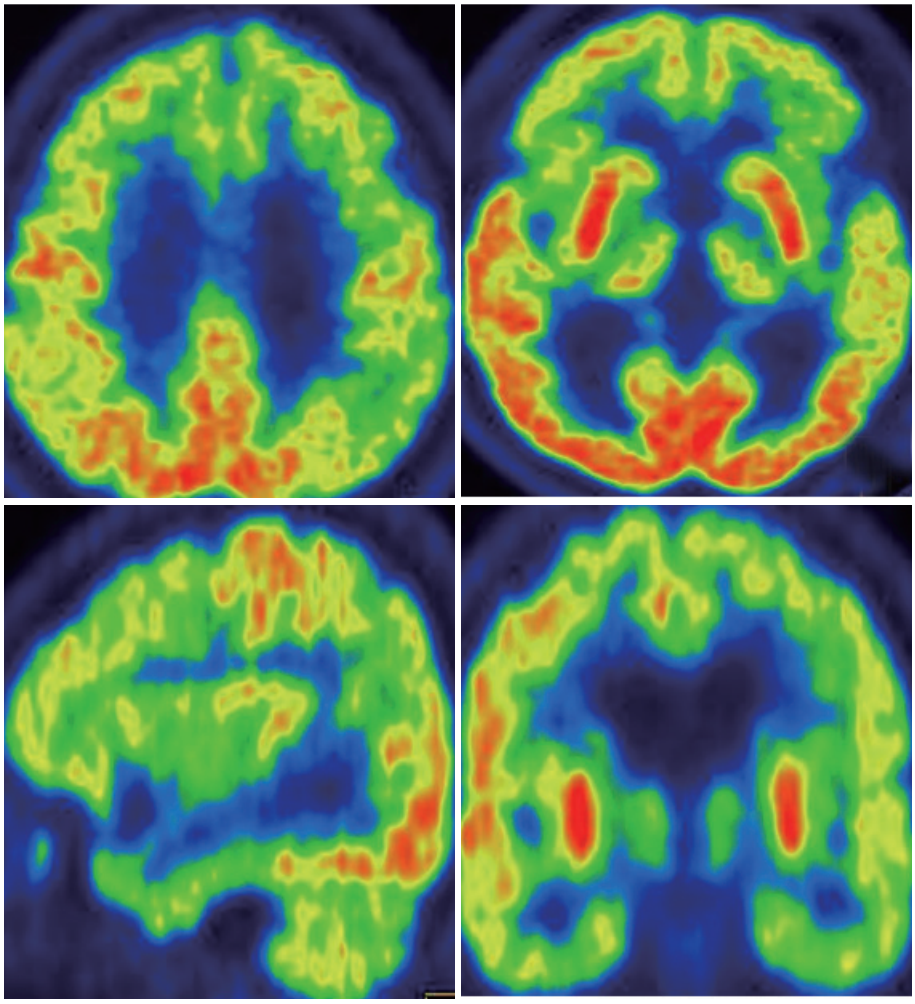

Figure 2. F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) image. The FDG-PET showed decreased metabolism in caudate nucleus, bilateral frontal, temporal and parietal cortex, especially lower FDG uptake in the left hemisphere.

led us to clinically suspect his condition as FTD. On the other hand, the *MAPT* and *progranulin*, the most popular genes in the FTD,[13] were not found.

Despite the lack of typical clinical symptoms of PSP in the early stage, this patient showed some positive features that conform to the criteria,[1] which are symmetric proximal parkinsonism, retrocolic posture, poor response of levodopa, and early onset cognitive impairment including frontal dysfunction. Over the six years from the symptom onset, gait disturbance and falling gradually became more severe and extraocular movement impairment began to show (from initial negative optokinetic nystagmus to supranuclear palsy eventually). These findings led to the diagnosis of clinically probable PSP.

Facial dystonia in this patient was thought to be a motor complication from levodopa therapy and could be considered as a form of levodopa-induced dyskinesia (LID). The development of LID in Parkinson's disease usually depends on neuroplastic changes in the basal ganglia circuitry caused by degeneration of nigrostriatal dopaminergic neurons after the prolonged levodopa treatment.[14] In contrast, the rarity of dyskinesias in PSP is associated with multilevel damage in the nigrostriatal and striatopallidal systems.[15] Abnormal movements of this patient included facial dystonia, which occurred when the patient was on levodopa medication.

In conclusion, we presented a PSP patient with FTD-like behavioral problems. Although LIFD was rarely reported in PSP, our case suggested that LIFD could be considered as an atypical feature of PSP.

REFERENCES

1. Litvan I, Agid Y, Calne D, Campbell G, Dubois B, Duvoisin RC, et al. Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): report of the NINDS-SPSP international workshop. Neurology 1996;47:1-9.
2. Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. Neurology 1998;51:1546-1554.
3. Mochizuki A, Ueda Y, Komatsuzaki Y, Tsuchiya K, Arai T, Shoji S. Progressive supranuclear palsy presenting with primary progressive aphasia--clinicopathological report of an autopsy case. Acta Neuropathol 2003;105:610-614.
4. Rohrer JD, Paviour D, Bronstein AM, O'Sullivan SS, Lees A, Warren JD. Progressive supranuclear palsy syndrome presenting as progressive nonfluent aphasia: a neuropsychological and neuroimaging anal-

ysis. Mov Disord 2010;25:179-188.
5. Boeve B, Dickson D, Duffy J, Bartleson J, Trenerry M, Petersen R. Progressive nonfluent aphasia and subsequent aphasic dementia associated with atypical progressive supranuclear palsy pathology. Eur Neurol 2003;49:72-78.
6. Josephs KA, Boeve BF, Duffy JR, Smith GE, Knopman DS, Parisi JE, et al. Atypical progressive supranuclear palsy underlying progressive apraxia of speech and nonfluent aphasia. Neurocase 2005;11:283-296.
7. Josephs KA, Duffy JR, Strand EA, Whitwell JL, Layton KF, Parisi JE, et al. Clinicopathological and imaging correlates of progressive aphasia and apraxia of speech. Brain 2006;129(Pt 6):1385-1398.
8. Josephs KA, Petersen RC, Knopman DS, Boeve BF, Whitwell JL, Duffy JR. Clinicopathologic analysis of frontotemporal and corticobasal degenerations and PSP. Neurology 2006;66:41-48.
9. Forman MS, Farmer J, Johnson JK, Clark CM, Arnold SE, Coslett HB, et al. Frontotemporal dementia: clinicopathological correlations. Ann Neurol 2006;59:952-962.
10. Josephs KA, Duffy JR. Apraxia of speech and nonfluent aphasia: a new clinical marker for corticobasal degeneration and progressive supranuclear palsy. Curr Opin Neurol 2008;21:688-692.
11. Barclay CL, Lang AE. Dystonia in progressive supranuclear palsy. J Neurol Neurosurg Psychiatry 1997;62:352-356.
12. Tan EK, Chan LL, Wong MC. Levodopa-induced oromandibular dystonia in progressive supranuclear palsy. Clin Neurol Neurosurg 2003;105:132-134.
13. Rabinovici GD, Miller BL. Frontotemporal lobar degeneration: epidemiology, pathophysiology, diagnosis and management. CNS Drugs 2010;24:375-398.
14. Olanow CW, Agid Y, Mizuno Y, Albanese A, Bonuccelli U, Damier P, et al. Levodopa in the treatment of Parkinson's disease: current controversies. Mov Disord 2004;19:997-1005.
15. Kim JM, Lee KH, Choi YL, Choe GY, Jeon BS. Levodopa-induced dyskinesia in an autopsy-proven case of progressive supranuclear palsy. Mov Disord 2002;17:1089-1090.