Parkinson's disease showing progressive conduction aphasia

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Abstract

Patients with Parkinson's disease (PD) may develop progressive dementia late in their clinical course. Dementia in PD is mostly related to neuropathological findings of extensive Lewy bodies (LBs), with or without the coexistence of Alzheimer's disease (AD) pathology. Aphasia has been reported in patients with LB diseases with AD pathology; however, there have been no reports of typical PD patients developing progressive aphasia during their clinical course. We describe a female PD patient who later developed progressive conduction aphasia characterized by phonemic paraphasia and disturbance in repetition of short sentences without disturbance in writing or auditory comprehension. No episodes of fluctuations of attention, memory complaints, or planning errors were observed. She experienced episodes of visual hallucination. Her low scores on the Mini-Mental State Examination suggested impairment of orientation and attention, and her scores on Raven's Coloured Progressive Matrices test indicated impaired visuospatial functions. However, her cognitive deficits were not sufficiently severe to impair her daily life. Brain magnetic resonance images revealed atrophy of the left superior temporal gyrus and widening of the left Sylvian fissure.

[^{18}F]-fluorodeoxyglucose positron emission tomography revealed glucose hypometabolism in the left cerebral hemisphere. These findings may be related to conduction aphasia. During the progression of PD lesions, the brainstem LB is assumed to take an upward course, extend to the limbic system, and then extend to the neocortex. Conduction aphasia observed in our patient may be associated with an unusual progression of the LB pathology from the brainstem to the left temporoparietal lobe.

(247 words)

Key words: Parkinson’s disease; conduction aphasia; paraphasia; Lewy body

Introduction

Patients with Parkinson's disease (PD) may develop progressive dementia late in their clinical course [1-3]. Dementia in PD is mostly related to neuropathological findings of extensive Lewy bodies (LBs), with or without the coexistence of Alzheimer's disease (AD) pathology involving various subcorticocortical neural systems [1, 4]. PD with dementia (PDD) shares neuropathological features with dementia with LB (DLB). The general term LB diseases (LBD) represents the disease spectrum that includes PDD and DLB [4]. In addition, a rare case of PD accompanied by Pick's disease has been described [5]. Aphasia has been reported in patients with LBD with AD pathology [6]; however, there have been no reports of typical PD patients developing progressive aphasia during their clinical course. In this paper, we describe a female PD patient without apparent dementia who showed progressive conduction aphasia characterized by phonemic paraphasia and disturbance in repeating short sentences. These symptoms suggested an unusual progression of the cortical LB pathology.

Case report

A 75-year-old right-handed Japanese woman complaining of progressive aphasia was admitted to our hospital. She had no family history of dementia or other neurological disorders. Her history was not contributory. She had been experiencing gait disturbance, bradykinesia, and mild bilateral hand rigidity since the age of 67. No other symptoms or signs, including rest tremor, supranuclear gaze palsy, cerebellar signs, autonomic signs, or dementia with disturbance of memory, language, or praxis, were observed. All her initial symptoms had responded well to levodopa therapy. At the age of 68, mild diffuse brain atrophy with lateral ventriclular dilatation was observed on brain magnetic resonance images (MRI) (Fig. 1a) and her myocardial accumulation of 123I-metaiodobenzylguanidine (^{123}I-MIBG) decreased, leading to diagnosis of PD without dementia. Although she had received treatment with a combination of levodopa, pramipexole, and amantadine, her gait disturbance and bradykinesia progressed gradually and postural instability appeared. At the age of 74, she experienced three times episodes of transient visual hallucinations showing formed visions of a man that was vivid in coloration. Around this age, progressive speech disturbance characterized by phonemic paraphasia appeared. However, her social behavior was appropriate according to an

interview of her caregiver. No episodes of fluctuations of attention, memory complaints, or planning errors were observed at the time of admission to our hospital. In addition, episodes of rapid eye movement sleep behavior disorders, apathy, changes in personality and mood, delusions or excessive daytime sleepiness have not yet been observed. At the age of 75, an examination showed rigidity in her neck and left upper extremity. Her motion was bradykinetic. She had bilateral hyperreflexia with positive plantar reflexes that may have resulted from cervical spondylotic myelopathy. She showed postural instability but orthostatic hypotension was not observed. Although no anarthria was observed in her spontaneous speech, phonemic paraphasia and disturbances in repetition of short sentences were apparent. She recognized her errors and tried to rectify them. Her writing and auditory comprehension were normal. She had no signs of the following apraxias or agnosias on the bedside testing: limb kinetic apraxia, ideomotor apraxia, ideational apraxia, dressing apraxia, constructional apraxia, visual agnosia, hemiasomatognosia, right–left disorientation, or hemispatial agnosia. Her Mini-Mental State Examination (MMSE) score was 24 out of 30 because of the subject missing 2 points on place orientation, 3 points on serial 7’s and 1 point on sentence repetition. The

Raven's Coloured Progressive Matrices test (RCPM) score was 9 out of 36, while the mean RCPM score (SD) in the Japanese normal population aged between 70 and 79 years old is 27.9 (5.396). The Clock Drawing Test was appropriate. Blood chemistry analysis showed nothing unusual. Brain MRI disclosed diffuse cortical atrophy, which was marked in the left superior temporal gyrus, and widening of the left Sylvian fissure (Fig. 1b). [^{18}F]-fluorodeoxyglucose positron emission tomography (PET) revealed glucose hypometabolism in the left cerebral hemisphere, which was more apparent in the frontal and temporal lobes, and the bilateral parietal and occipital lobes (Fig. 1c). Three-dimensional stereotactic surface projection (3D-SSP) [7] disclosed these findings (Fig. 1d, e). No significant findings were observed by ^{11}C-labeled Pittsburgh Compound-B (PIB) PET study.

Discussion

In this paper, we describe a PD patient who later developed progressive aphasia without apparent dementia. Her initial clinical features and good response to levodopa therapy satisfied the Queen Square Brain Bank clinical diagnostic criteria for PD [8]. In addition,

according to the decreased myocardial accumulation of ^{123}I-MIBG [1, 9], we diagnosed her with PD before the appearance of speech disturbance. Although she experienced episodes of visual hallucinations and language disturbances and showed a low score on MMSE suggesting impairment of orientation and attention as well as on a RCPM test indicating impaired visuospatial functions, her features did not meet the criteria for PDD diagnosis because her cognitive deficits were not sufficiently severe to impair her daily life [1-3].

Her speech disturbance was characterized by phonemic paraphasia, disturbances in repeating short sentences, and no anarthria in her spontaneous speech, which has been classified as conduction aphasia [10, 11]. Generally, conduction aphasia is found to be caused by infarcts in the left temporoparietal lobe, especially in the superior temporal gyrus, supramarginal gyrus, and inferior parietal lobe [10]. Patients with neurodegenerative diseases rarely show conduction aphasia, and this has been previously reported in only one patient who had pathologically proven corticobasal degeneration (CBD) with severe atrophy and tau-positive lesions in the left superior temporal gyrus [11]. Our patient showed atrophy of the left superior temporal gyrus, dilatation of the left

Sylvian fissure (Fig. 1b), and obvious glucose hypometabolism in the left frontal and temporal lobes on 3D-SSP (Figs. 1d, e). These findings may be related to conduction aphasia.

There have been no reports of PD patients with progressive conduction aphasia. Preserved core language functions are characteristic for PDD patients [1, 3]. Our patient had no infarcts or PIB-positive amyloid accumulation, indicating no evidence of additional AD pathology in the brain. A significant proportion of elderly people with dementia have combined degenerative disorders [12], and thus, the possibility of coexistence of other neurodegenerative conditions, including CBD [11], could not be excluded. However, the episodes of transient visual hallucinations in our patient suggested the presence of cortical LB pathology [1, 13]. A voxel-based morphometric study concluded in LBD with dementia patients showed cerebral cortical atrophy in the occipital, frontal, and parietal lobes [1, 14]. During the progression of PD lesions, the brainstem LB pathology may take an upward course, extend to the limbic system, and then extend to the neocortex [15]. The superior temporal gyrus, which observed atrophy in our patient, is usually involved in the late stage [15]. The unique cortical manifestation

and conduction aphasia observed in our PD patient may be associated with an unusual progression of the LB pathology from the brainstem to the left temporoparietal lobe.

(1,120 words)

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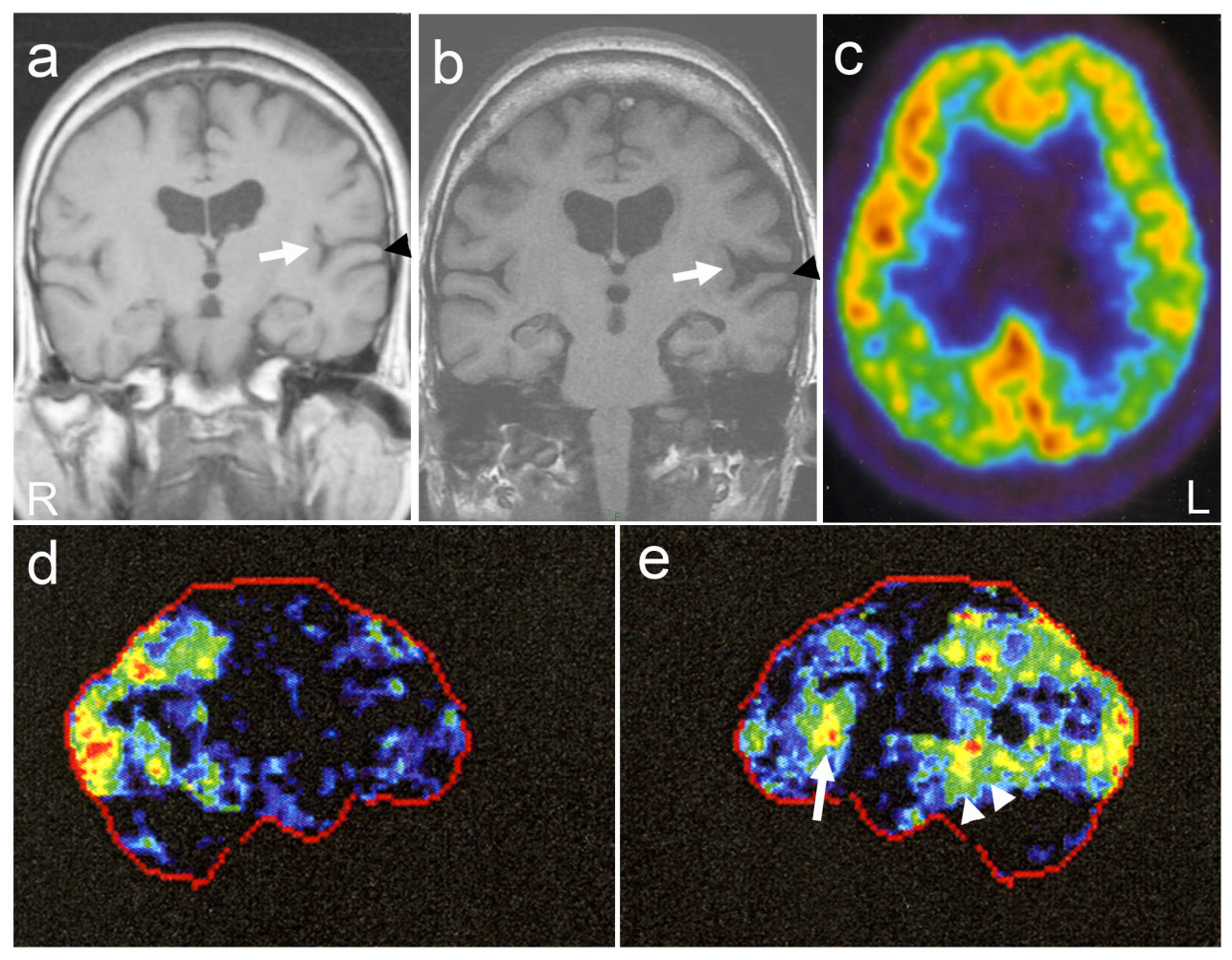
Figure legend

Figure 1: T1-weighted magnetic resonance images of coronal sections of the patient at the age of 68 (a) and 75 (b) show the progression of dilatation of the left Sylvian fissure (white arrows) and atrophy of the left superior temporal gyrus (black arrowheads). [^{18}F]-fluorodeoxyglucose positron emission tomography (c) and three-dimensional stereotactic surface projection (3D-SSP) images (d, e) show glucose hypometabolism in the left frontal (arrow) and temporal (arrowheads) lobes compared with the right cerebral hemisphere. In addition, glucose hypometabolism was observed in the bilateral parietal and occipital lobes. Right-lateral (d) and left-lateral (e) views of 3D-SSP.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