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【 CASE REPORT 】

Spastic Paraplegia Accompanied by Extrapyramidal Sign and Frontal Cognitive Dysfunction

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Abstract:
A complicated form of spastic paraplegia is a neurodegenerative disorder presenting as progressive spasticity in the bilateral lower limbs accompanied by some clinical features. The present case showed spastic paralysis and hyperreflexia in all extremities as well as lead pipe rigidity in the neck and bilateral upper extremities (R < L), decreased scores on frontal cognitive tests, a decreased accumulation of the right dorsal putamen on a DAT scan, and hypoperfusion of the bilateral frontal lobes on ^{99m}Tc-ECD single photon emission computed tomography (SPECT). The present case provides a new spectrum of spastic paraplegia based on the evidence of clinical scores and the findings of brain functional imaging.

Key words: spastic paraplegia, extrapyramidal sign, frontal cognitive dysfunction

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Introduction

Spastic paraplegia is a heterogeneous group of inherited neurological disorders in which the main clinical feature is progressive lower limb spasticity. A complicated form of spastic paraplegia is accompanied by additional neurological features such as mental retardation, cognitive impairment, ataxia, neuropathy or other symptoms (1), but a few cases have shown extrapyramidal signs (2, 3) without any general cognitive impairment (4) or frontal lobe dysfunction (5). We herein report the known first case of spastic paraplegia accompanied by both an extrapyramidal sign and frontal cognitive dysfunction which was evaluated by cognitive tests and the findings of brain functional imaging.

Case Report

A 6-year-old boy was not good at running fast, but he had no problem with walking. However, symptoms associated with spasticity gradually developed and he could not play any sports well in his schooldays or even in adulthood. He developed a gait disturbance at 60 years of age, difficulty in climbing stairs at 63 years of age, and a tendency to fall easily while walking at 65 years of age. He was subsequently admitted to our hospital at 67 years of age. He had been diagnosed to have bilateral otitis media at 9 years of age, but had no particular history of neurological disease, mental abnormalities, behavioral disorder nor any family history of intermarriage, although his father's family and mother's family were from Osaka and Hikone, which are both in the Kansai area of Japan.

He was 164.0 cm tall and weighed 51.8 kg. A neurological examination showed the presence of mild bradykinesia, a mild lower gaze limitation, severe hearing loss in his bilateral ears (right > left), and mild lingual dysarthria. He also presented with mild muscle weakness in his neck and bilateral lower extremities (Manual muscle testing; neck and bilateral L/E 4/5), severe spasticity in all extremities (A/E), spastic gait, bilateral pes cavus, mild lead pipe rigidity in his

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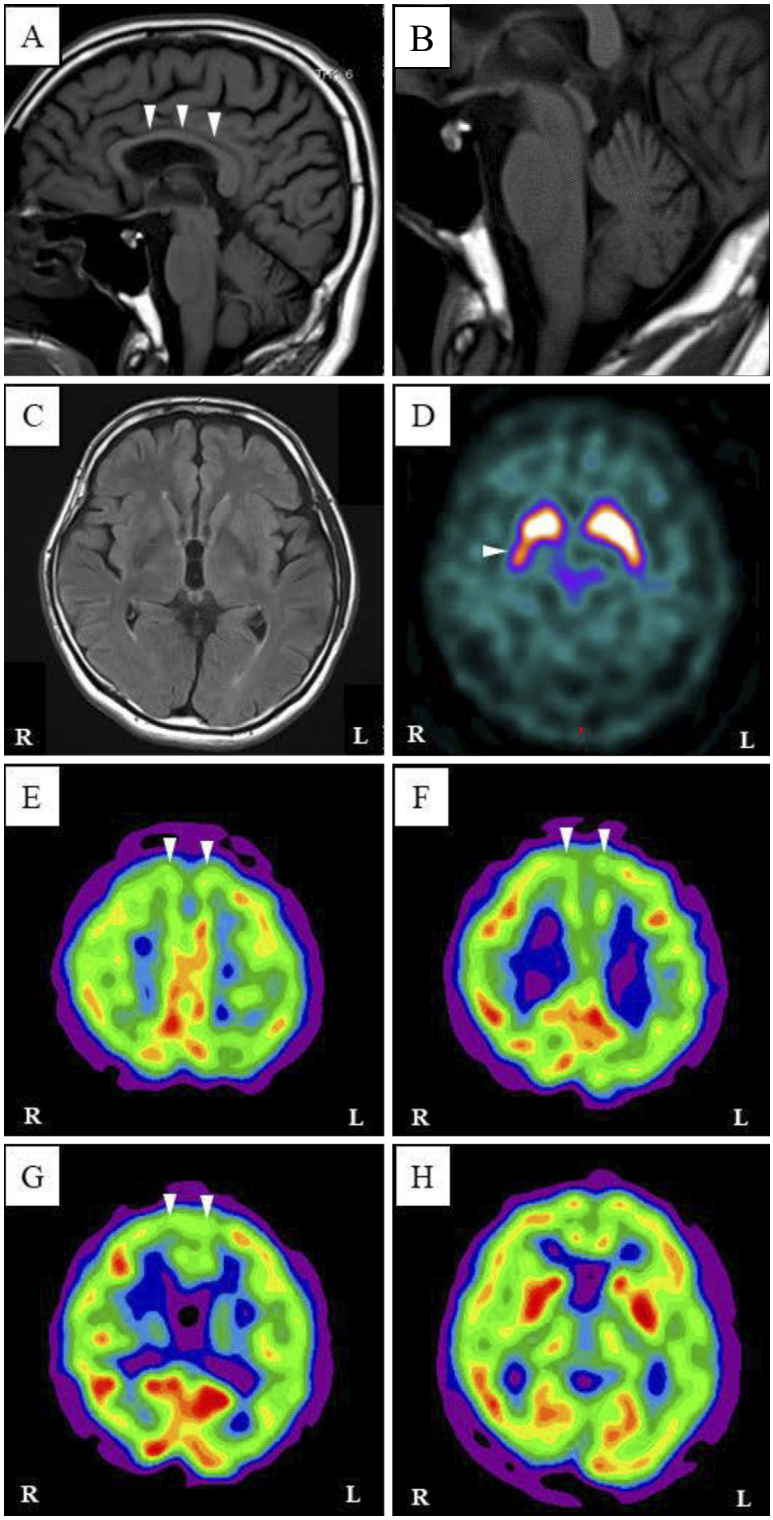

Figure. **(A-C) Brain MRI showing a thin corpus callosum (A, arrowheads), but no significant lesions in the brainstem or bilateral basal ganglia (B and C). (D) A DAT scan showing a decreased accumulation in the right dorsal putamen (arrowhead). (E-H) ^{99m}Tc-ECD SPECT showing hypoperfusion in the bilateral frontal lobes (arrowheads).**

neck and bilateral elbows and wrists and retropulsion. General cognitive tests were otherwise normal with a mini mental state examination (MMSE) score of 28/30, and a Hasegawa dementia rating scale-revised (HDS-R) score of 29/30. However, his frontal cognitive function had decreased with a frontal assessment battery (FAB) score of 11/18, and a Montreal cognitive assessment (MoCA) score of 20/30.

Serum analyses showed a normal creatine phosphokinase (CPK) level (210 U/L, normal 59-248 U/L) and negative antibodies to human T-lymphotropic virus 1 (HTLV-1) and human immunodeficiency virus (HIV) as well as normal findings for a spinal fluid analysis. A nerve conduction study showed no abnormalities in his tibial nerves.

Brain magnetic resonance imaging (MRI) showed a

slightly thin corpus callosum (Figure A, arrowheads), but no significant lesions in the mesencephalic tegmentum (Figure B), bilateral basal ganglia, white matter, or the pyramidal tract (Figure C). ^{123}I-Ioflupane single-photon emission computed tomography (^{123}I-Ioflupane SPECT: DAT scan) showed a slightly decreased accumulation in the right dorsal putamen (SBR; right 6.15, left 7.02, average of the same age data 7.45, Z-score; right -0.96, left -0.32) (Figure D, arrowhead). ^{99m}Tc-ethyl cysteinate dimer (^{99m}Tc-ECD) SPECT showed hypoperfusion in the bilateral frontal lobes (Figure E-H, arrowheads). We carried out the whole exome sequencing of genomic DNA (Tokyo University, Japan), but no pathological variants in the coding exons were observed.

He was therefore diagnosed to have a complicated form of spastic paraplegia accompanied by an extrapyramidal sign and frontal cognitive dysfunction. He was treated by baclofen (15 mg/day, orally) and L-dopa (increased to 600 mg/day), but his symptoms did not improve significantly. He has been followed by a neurologist at a nearby clinic.

Discussion

Spastic paraplegia is a heterogeneous neurodegenerative disorder presenting with progressive spasticity and muscle weakness in bilateral L/E. Spastic paraplegia is clinically divided into two subtypes based on the absence or presence of combined clinical features such as mental retardation, cognitive impairment, ataxia, neuropathy, extrapyramidal sign, or other symptoms (1). Although a few cases of SPG11 presented as early-onset parkinsonism (6, 7) and other cases of spastic paraplegia were accompanied by a thin corpus callosum plus parkinsonism (2), parkinsonism is rarely found in complicated spastic paraplegia. Similar to the present case (Figure D, arrowhead), a previous case of spastic paraplegia case showed a decreased accumulation of DAT with parkinsonism (8). The present case showed severe spasticity in all extremities (A/E) plus mild bradykinesia, mild lead pipe rigidity in his neck and bilateral elbows and wrists, retropulsion, and a decreased accumulation of DAT (Figure D, arrowhead), thus suggesting the presence of spastic paraplegia accompanied by parkinsonism.

In contrast to well preserved general cognitive functions, the frontal lobe function had evidently decreased in the present case to 11/18 of FAB and 20/30 of MoCA, concomitant with hypoperfusion of bilateral frontal lobes (Figure E-H). There are some types of hereditary spastic paraplegia with a thin corpus callosum such as SPG 11, 15, and 21 (9, 10), accompanied by parkinsonism, cognitive dysfunction, or frontal lobe dysfunction. However, no previously reported SPG case has ever been reported to show all of these symptoms. In addition, the whole-exon sequence method is associated with some limitations due to the fact that the intron has not yet been comprehensively analyzed, and it also remains unclear as to whether or not some new variants are pathogenic. In the future, further genetic analyses are needed to clarify the present case as a possible subtype of complicated spastic paraplegia.

This is the first case report of spastic paraplegia accompanied by both an extrapyramidal sign and frontal cognitive dysfunction, and which was diagnosed based on the findings of cognitive tests and brain functional imaging. The present case provides a new spectrum of spastic paraplegia based on the findings of clinical scores, a DAT scan and ECD-SPECT.

The authors state that they have no Conflict of Interest (COI).

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