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【 CASE REPORT 】

Progressive Parkinsonism Three Years after Shunt Surgery in a Patient with Idiopathic Normal Pressure Hydrocephalus

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Abstract:
An 86-year-old man, who had undergone a lumboperitoneal shunt for idiopathic normal pressure hydrocephalus (iNPH) implanted 4 years earlier showed progressive parkinsonism for the past year. His clinical symptoms, including resting tremor and rapid eye movement sleep behavior disorder, responsiveness to levodopa, and abnormal findings on ^{123}I-meta-iodobenzylguanidine myocardial scintigraphy and dopamine transporter imaging, indicated that his pathological background of parkinsonism included concomitant synucleinopathy, such as Parkinson's disease or dementia with Lewy bodies, in addition to iNPH. Clinicians should consider the possibility of concomitant proteinopathies and their treatments when clinical symptoms become evident after shunt operations in patients with iNPH.

Key words: idiopathic normal pressure hydrocephalus, All Clinical Neurology, Parkinson's disease/Parkinsonism, ^{123}I-MIBG myocardial scintigraphy, dopamine transporter imaging

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Introduction

Diverse proteinopathies, including Alzheimer's disease (AD), non-AD tauopathies, and synucleinopathies [e.g. progressive supranuclear palsy (PSP), Parkinson's disease (PD) and multiple system atrophy (MSA)] are common concomitant pathologies of idiopathic normal pressure hydrocephalus (iNPH) (1). Although such concomitant pathologies may influence the clinical course (2), little is known about the clinical features of iNPH patients with concomitant proteinopathies.

We herein report a patient with iNPH who showed progressive parkinsonism several years after implantation of a lumboperitoneal (LP) shunt that was suspected to be due to concomitant synucleinopathy.

Case Report

An 86-year-old, right-handed man visited our hospital due to progressive gait disturbance and bilateral finger tremor. Four years earlier, he had begun to experience difficulty walking and developed urinary urge incontinence with no evident cognitive decline.

Computed tomography (CT) revealed dilatation of the lateral ventricles (Evans' index >0.3) and disproportionately enlarged subarachnoid space hydrocephalus (DESH). A lumbar puncture showed a normal cerebrospinal fluid (CSF) pressure as well as no abnormal cells, protein, or glucose. His gait disturbance was transiently improved according to a spinal tap test. Based on his onset age (>60 years old), clinical symptoms, radiological findings, tap test, and lack of any apparent past and/or present illness causing NPH, he was diagnosed with probable iNPH by his previous doctor (3).

He underwent LP shunt surgery, and his gait disturbance and urinary urge incontinence improved within one month. He remained complaint-free, but he later became aware of gradual worsening of his gait, and he presented to our hospital about one year ago, with no exposure to any drugs

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with antidopaminergic activity. At the same time, his wife had begun to notice his finger tremor, first on the right side and subsequently contralaterally. His wife also noticed night terrors; however, he neither showed evident abnormal behavior nor seemed to act out his dreams during his sleep.

Table. Severity of Parkinsonism before and after Levodopa Treatment.

	pre-medication	after levodopa treatment
Total score	**51**	**38**
UPDRS part III subscale		
Resting tremor	0/2/2/0/0	0/0/1/0/0
Postural tremor	2/2	0/0
Rigidity	2/2/2/2/2	2/1/2/1/2
Hand movements	2/2	2/2
DDK	2/2	2/2
Finger tapping	2/2	2/2
Leg agility	2/3	2/3
Arising from chair	3	2
Posture	2	2
Gait	3	2
Postural stability	2	2
Facial expression	2	2
Speech	2	2
Body bradykinesia	2	1

Each subscale value indicates the severity of parkinsonism in neck/left upper extremity/right upper extremity/left lower extremity/right lower extremity (resting tremor and rigidity) or left upper or lower extremity/right upper or lower extremity (postural tremor, hand movements, DDK, finger tapping, and leg agility).
UPDRS: The Unified Parkinson's Disease Rating Scale, DDK: diadochokinesis

He showed rest and postural tremor in the bilateral fingers, cogwheel rigidity in his neck and extremities, bradykinesia in his extremities, and gait disturbance with remarkable postural instability and kinesie paradoxale. He did not show any obvious motor fluctuations, dyskinesia, cerebellar ataxia, vertical supranuclear gaze palsy, aphasia, apraxia, cortical sensory deficit, visual hallucinations, or pareidolia. The Unified Parkinson's Disease Rating Scale (UPDRS) III was 51 (Table), and a psychological battery revealed that he presented with cognitive decline chiefly characterized by verbal fluency deficit. He also showed non-motor symptoms, including clinically suspected rapid eye movement sleep behavior disorder (RBD) and constipation in addition to urinary urge incontinence. In addition, he complained of subjective hyposmia; however, an objective evaluation of his olfactory function was not performed.

Brain CT revealed DESH with periventricular lucency (PVL) and dilatation of the third and lateral ventricles (Figure a). He complained of transient dizziness, and an imaging abnormality related to hydrocephalus was now slightly more obvious than on CT acquired one year earlier. Dopamine transporter (DAT) single-photon emission computed tomography (DAT-SPECT) with ^{123}I-ioflupane demonstrated the profound reduction in DAT binding predominantly in the dorsal striatum, with specific binding ratios (SBRs) of 0.88 (right) and 0.95 (left) (Figure b). Furthermore, ^{123}I-meta-iodobenzylguanidine (MIBG) myocardial scintigraphy

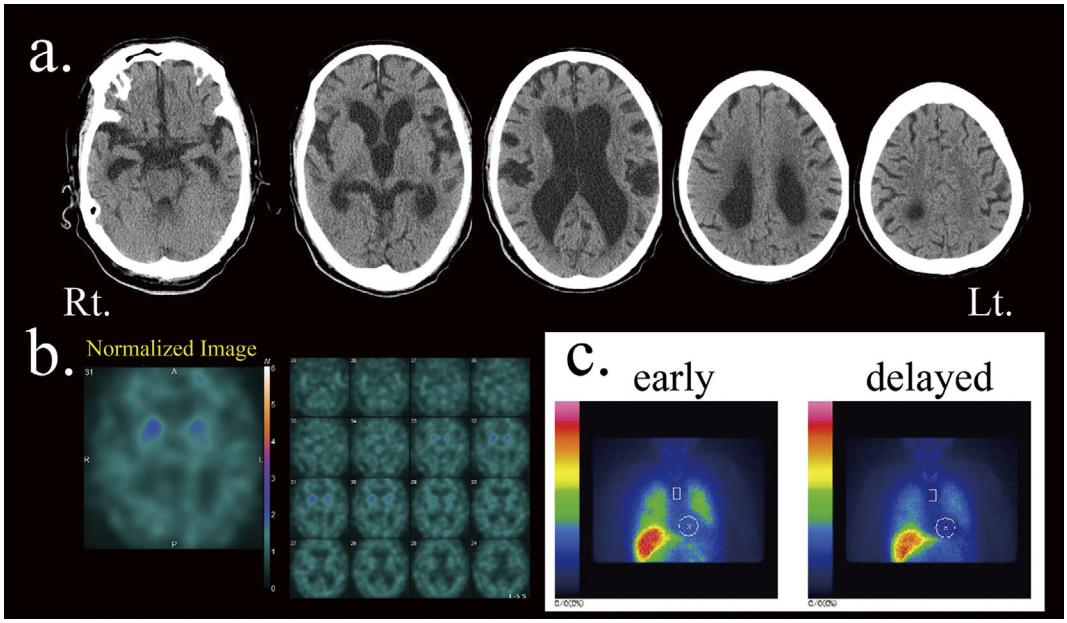

Figure. (a) Brain computed tomography showed disproportionately enlarged subarachnoid space hydrocephalus (DESH), dilatation of the third and lateral ventricles with rounding, and periventricular lucency (PVL). (b) The dopamine transporter uptake was markedly decreased, especially around the ventral striatum. The specific binding ratios (SBRs) were 0.88 (right) and 0.95 (left). (c) ^{123}I-meta-iodobenzylguanidine myocardial scintigraphy showed decreased heart-to-mediastinum (H/M) ratios. Standardized H/M ratios of early and late scans were 1.35 and 1.23, respectively.

showed decreased early and delayed heart-to-mediastinum (H/M) ratios (1.35 and 1.23) despite his lack of diabetes mellitus or severe heart failure (Figure c).

As levodopa, carbidopa hydrate was administered at gradually increasing doses up to 300 mg, and parkinsonism, including rest and postural tremor, bradykinesia, and gait disturbance were partially improved (UPDRS III became 38) (Table), leading to a slight improvement in his activity of daily living (ADL), including eating, transferring or ambulating, and walking. Later, his previous attending neurosurgeon confirmed that the LP shunt was still working, and his LP shunt pressure was adjusted; however, his motor disability and ADL did not improve.

Given these findings, his condition satisfied two supportive criteria ("rest tremor of a limb" and "presence of either olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy"), and he presented no absolute exclusion criteria or red flags for PD. Therefore, he was diagnosed with clinically established PD based on the Movement Disorder Society (MDS) Clinical Diagnostic Criteria for PD (4). In addition, he was also diagnosed with mild cognitive impairment in PD [PD-mild cognitive impairment (MCI)]; however, NPH may have been another primary explanation for his cognitive impairment (5).

Discussion

Our patient presented with gradually worsening parkinsonism, including rest tremor with moderate responsiveness to levodopa. Rest tremor is a supportive criterion of PD (3). He also showed cardiac sympathetic denervation on ^{123}I-MIBG scintigraphy, another criterion of PD (4). In contrast, he did not meet the absolute exclusion criteria for PD (4). He also complained of constipation, subjective hyposmia, and clinically suspected RBD, which are all frequently observed as premotor symptoms of PD (6). RBD is also one of the core clinical features of dementia with Lewy bodies (DLB) (7). Furthermore, a reduced cardiac ^{123}I-MIBG uptake and low striatal dopamine transporter uptake are also indicative biomarkers of DLB (7). Taken together, his clinical features and imaging results indicated that his pathological background of parkinsonism included a concomitant synucleinopathy, such as PD/PD-MCI or prodromal DLB, in addition to iNPH.

Odagiri et al. reported that iNPH patients with cardiac sympathetic dysfunction, suggesting concomitant Lewy body pathology, had clinical characteristics including a younger onset (74.1±4.6 years old), less severe urinary dysfunction (urinary scale of iNPH grading scale = 1.0±0.6) than NPH patients without cardiac sympathetic dysfunction (77.9±2.8 years old, urinary scale of iNPH grading scale = 2.0±1.2, respectively), as well as kinesie paradoxale and cogwheel rigidity (8). Although the age of our patient at the onset was over 80 years old and he showed moderate urinary dysfunction (urinary scale of iNPH grading scale = 2), he also had kinesie paradoxale and cogwheel rigidity. Responsiveness to cues, known as kinesie paradoxale, and cogwheel rigidity are more frequently observed in PD than iNPH, while urinary disturbance may be non-specific (9).

Temporal changes on brain CT suggested that the worsening of iNPH in our patient was due in part to his clinical course; however, the cardiac sympathetic denervation demonstrated by ^{123}I-MIBG cannot be explained solely by iNPH. Furthermore, clinical symptoms including unilateral and subsequent bilateral rest tremor and RBD are also uncommon in iNPH. Indeed, adjusting the LP shunt pressure did not alter his clinical symptoms, while levodopa administration clearly improved his parkinsonism and ADL. Although the reason why his hydrocephalus worsened after LP shunt surgery is not clear, one possible reason may be that the concomitant synucleinopathy had some effect on the CSF flow dynamics.

In conclusion, evaluations of disease-specific symptoms (e.g., rest tremor, RBD, cogwheel rigidity, kinesie paradoxale) and diverse biomarkers (e.g., ^{123}I-MIBG myocardial scintigraphy, DAT-SPECT) appear useful for the clinical diagnosis of concomitant proteinopathies in patients with iNPH. Since additional therapies targeting concomitant diseases may improve the clinical symptoms and ADL to some extent, clinicians should consider a careful clinical evaluation and the appropriate use of biomarkers when clinical symptoms become evident, even after shunt operations, in patients with iNPH.

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

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References

1. Allali G, Laidet M, Armand S, Assal F. Brain comorbidities in normal pressure hydrocephalus. Eur J Neurol **25**: 542-548, 2018.
2. Malm J, Graff-Radford NR, Ishikawa M, et al. Influence of comorbidities in idiopathic normal pressure hydrocephalus - research and clinical care. A report of the ISHCSF task force on comorbidities in INPH. Fluids Barriers CNS **10**: 22, 2013.
3. Mori E, Ishikawa M, Kato T, et al. Guidelines for management of idiopathic normal pressure hydrocephalus: second edition. Neurol Med Chir (Tokyo) **52**: 775-809, 2012.
4. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord **30**: 1591-1601, 2015.
5. Litvan I, Goldman JG, Tröster AI, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord **27**: 349-356, 2012.
6. Siderowf A, Lang AE. Premotor Parkinson's disease: concepts and

definitions. Mov Disord **27**: 608-616, 2012.
7. McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium. Neurology **89**: 88-100, 2017.
8. Odagiri H, Baba T, Nishio Y, et al. Clinical characteristics of idiopathic normal pressure hydrocephalus with Lewy body diseases. J Neurol Sci **359**: 309-311, 2015.
9. Cucca A, Biagioni MC, Sharma K, et al. Comorbid normal pressure hydrocephalus with parkinsonism: a clinical challenge and call for awareness. Case Rep Neurol Med **2018**: 2513474, 2018.