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^{123}I-metaiodobenzylguanidine myocardial scintigraphy-normal Parkinsonism with radiological features of Alzheimer's disease - Parkinsonism variant of Alzheimer's disease or Alzheimer's disease with brainstem involvement?-

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ABSTRACT

The pathological findings of brainstem nuclei in Alzheimer's disease are reported, however, the clinical manifestation based on these affected brainstem nuclei has been uncertain. We describe some clinical manifestation possibly associated with brainstem

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pathological changes in Alzheimer's disease. Most Parkinson's disease patients show decreased ^{123}I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy uptake. A decreased heart/mediastinum (H/M) ratio in MIBG scintigraphy has been attributed to Lewy body pathology in cardiac sympathetic nerves. Certain diseases such as Alzheimer's disease, the Lewy body variant of Alzheimer's disease, progressive supranuclear palsy (PSP), corticobasal degeneration, multiple system atrophy, and some cases of Parkinson's disease can present with MIBG normal Parkinsonism. We aimed to elucidate the clinical and radiological features of MIBG-normal Parkinsonism or its subgroup. Sixty-one patients with Parkinsonism underwent MIBG myocardial scintigraphy, of which 22 showed normal MIBG. Of these patients, 5 demonstrated both magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT) findings consistent with Alzheimer's disease. Here, we describe the clinical characteristics of these patients. Characteristics of these patients can be summarized as follows: >80 years of ages, predominantly male, and exhibiting Parkinsonism with rigidity and gait disturbance. Three patients exhibited tremor. Two patients demonstrated supranuclear ophthalmoparesis of vertical gaze. Two patients showed dementia. Neuropatholgical examination of an autopsied patient demonstrated pure Alzheimer's disease pathology without PSP pathology or Lewy body pathology. Alzheimer's disease can present initially and predominantly with Parkinsonism. Alzheimer's disease should be considered as a differential diagnosis of Parkinsonism.

Keywords: 123I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy, Parkinsonism, Alzheimer's disease, single photon emission computed tomography (SPECT), supranuclear ophthalmoparesis

Abbreviations: MIBG-metaiodobenzylguanidine

1. INTRODUCTION

Several studies report the selective pathological changes of brainstem nuclei in Alzheimer's disease (Ishino et al., 1975; Parvizi et al., 2000; Parvizi et al., 2001; Kasahata et al., 2012; Lee at al., 2015), however, the clinical manifestation based on these affected brainstem nuclei has been uncertain. We describe some clinical manifestation possibly associated with brainstem pathological changes in Alzheimer's disease.

Certain diseases present with ^{123}I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy normal Parkinsonism. Alzheimer's disease can present with extrapyramidal symptoms (Mitchell et al, 1999; Burns et al., 2005; Attems et al., 2007; Toru et al., 2010; King et al., 2011). The Lewy body variant of Alzheimer's disease can present with Parkinsonism, although clinical characteristics are not sufficiently established and MIBG myocardial scintigraphy may be abnormal (Hansen, 1997; Heyman et al., 1999; Serby et al., 2003; Yokota et al., 2007). Progressive supranuclear palsy (PSP) can present with MIBG myocardial scintigraphy normal Parkinsonism (Yoshita et al., 1997; Yoshita, 1998; Orimo et al., 2004; Rascol and Schelosky, 2009; King et al., 2011), as can corticobasal degeneration (CBD) (Orimo et al., 2004; Shin et al. 2006). Parkinsonism-predominant multiple system atrophy (MSA-P; previously known as SND or striatonigral degeneration) can present with normal (or mildly abnormal) MIBG myocardial scintigraphy (Yoshita et al., 1997; Yoshita, 1998; Orimo et al., 1999; Druschky et al., 2000; Orimo et al., 2001; Orimo et al., 2004; Lee et al., 2006; Chung et al., 2009; Nagayama et al., 2010). Some cases of Parkinson's disease can also present with MIBG myocardial scintigraphy normal Parkinsonism (Orimo et al, 1999).

MIBG myocardial scintigraphy normal Parkinsonism:

Decreased MIBG myocardial scintigraphy uptake is well correlated with denervation of cardiac sympathetic nerve. Therefore, Decreased MIBG myocardial scintigraphy uptake represents Lewy body pathology in cardiac sympathetic nerve and used as a diagnostic examination of Parkinson's disease. Normal MIBG myocardial scintigraphy uptake represents that the possibility Lewy body pathology or Parkinson's disease is low. MIBG myocardial scintigraphy normal Parkinsonism means that Parkinsonism of the patient is not associated with Lewy body pathology or Parkinsonism of the patient is probably other than Parkinson's disease. If MIBG myocardial scintigraphies show normal in Parkinsonism patients, other diagnosis should be considered.

Parkinsonism variant of Alzheimer's disease:

Some patients of Alzheimer's disease present with Parkinsonism as initial and predominant manifestation. Neuropathological examinations of some Parkinsonism patients, whom are sometimes diagnosed as Parkinson's disease, reveal pure Alzheimer's disease pathology. We defined such patients as Parkinsonism variant of Alzheimer's disease in this article.

MIBG myocardial scintigraphy is used to differentiate Parkinson's disease from MSA or PSP (Yoshita et al., 1997; Yoshita, 1998; Orimo et al., 1999; Druschky et al., 2000; Orimo et al., 2001; Orimo et al., 2004; Lee et al., 2006; Rascol and Schelosky, 2009; Chung et al., 2009; Nagayama et al., 2010; King et al., 2011). A decreased heart/mediastinum (H/M) ratio in MIBG has been attributed to Lewy body pathology in cardiac sympathetic nerve. Lewy body pathology, such as that observed in Parkinson's disease or dementia with Lewy bodies (DLB), displays a decreased H/M ratio in MIBG myocardial scintigraphy (Yoshita et al., 1997; Yoshita, 1998)(MSA-P exhibits a decreased H/M ratio, but the decreases are mild)(Yoshita

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Alzheimer's disease with brainstem involvement:
The pathological findings of brainstem nuclei in Alzheimer's disease are reported. We described some clinical manifestation associated with brainstem pathological changes in Alzheimer's disease. Supranuclear ophthalmoparesis and neck dorsiflexion were probably associated with brainstem involvement. Parkinsonism was possibly associated with brainstem involvement. Midbrain atrophy was probably associated with brainstem involvement.

Radiological features of Alzheimer's disease (MRI):
Alzheimer's disease patients usually show atrophy of the medial temporal lobe and/or the parietal lobe or sometimes show whole brain atrophy.

et al., 1997; Yoshita, 1998; Orimo et al., 1999; Druschky et al., 2000; Orimo et al., 2001; Orimo et al., 2004; Lee et al., 2006; Chung et al., 2009; Nagayama et al., 2010). PSP exhibits a normal H/M ratio (Yoshita et al, 1997; Yoshita, 1998; Orimo et al., 2004; Rascol and Schelosky, 2009). Therefore, only Parkinson's disease presents Parkinsonism with a decreased H/M ratio in MIBG (Yoshita et al., 1997; Yoshita, 1998; Orimo et al., 1999; Druschky et al 2000; Orimo et al., 2001; Orimo et al., 2004; Lee et al., 2006; Shin et al, 2006; Rascol and Schelosky, 2009; Chung et al., 2009; Nagayama et al., 2010).

We investigated 61 patients with parkisonism using MIBG myocardial scintigraphy. Twenty-two of the 61 Parkinsonism patients revealed normal MIBG. Of these patients, 5 demonstrated both magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT) findings consistent with Alzheimer's disease. Neuropathological examination of 1 patient revealed Alzheimer's disease (Kasahata et al., 2014). Here, we report the clinical characteristics and radiological features of these patients.

2. MATERIALS AND METHODS

This study has been approved by the Ethical Standard Committee of Tokyo Metropolitan Ohtsuka Hospital and has therefore been performed in accordance with the standards laid down in the 1964 Declaration of Helsinki. We assessed 61 patients with Parkinsonism who underwent MIBG myocardial scintigraphy between October 2008 and July 2011. Twenty-two of 61 patients with Parkinsonism had normal MIBG (Table 1). Of these, 5 patients had both MRI and SPECT findings consistent with Alzheimer's disease. Here, we describe clinical characteristics of these patients.

PATIENT 5 (Kasahata et al., 2014)

An 85-year-old man presented to our hospital with gait disturbance. He was well until 8 years prior to admission when he developed rigidity, pill-rolling tremor at rest, and walking difficulty in going up the stairs. L-dihydroxyphenylalanine (l-dopa) and dopamine agonist improved his symptoms. Thereafter, his dementia developed. One year earlier, he became completely bedridden. Neurological examination showed dementia, supranuclear ophthalmoparesis of vertical gaze, neck dorsiflexion, neck and upper extremities dominant cog-wheel rigidity, and tremor and myoclonus induced on action of both upper extremities. MIBG myocardial scintigraphy revealed a normal early H/M ratio of 2.40. MRI revealed atrophy in the midbrain tegmentum and the medial temporal lobe dominant cerebral atrophy. SPECT revealed decreased blood flow in the frontotemporal and temporoparietal lobes and the posterior cingulate gyri.

The patient died of brest cancer. Neuropathological examination demonstrated pure Alzheimer's disease without apparent PSP pathology or Lewy body pathology.

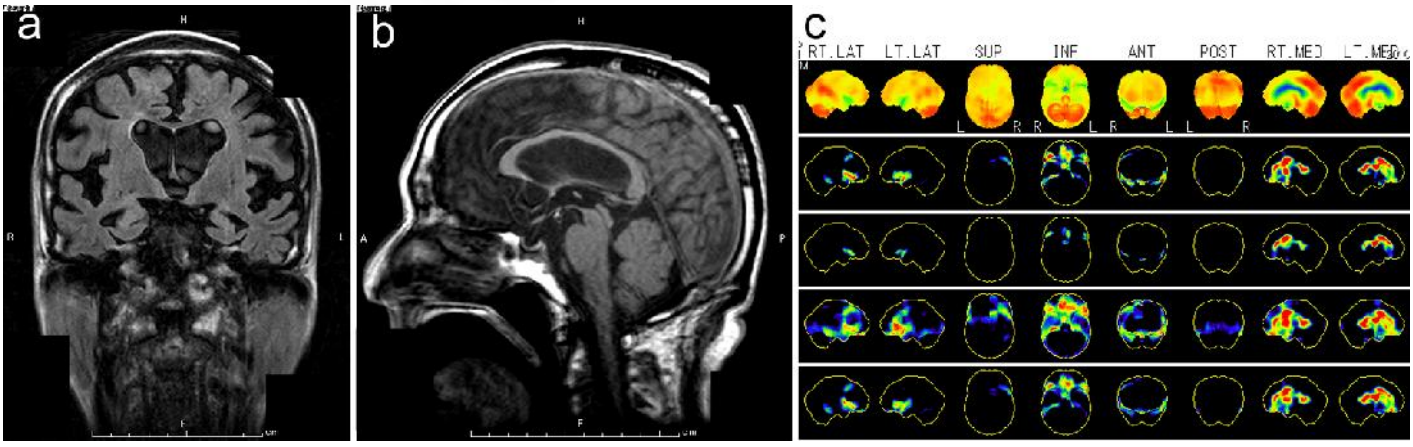

Figure 1 Magnetic Resonance Images (MRI) and three dimensional stereotactic surface projection (3D-SSP) iodoamphetamine (IMP)-single photon emission computed tomography (SPECT) findings in Patient 9.
(a) MRI revealing atrophy in the bilateral medial temporal lobes.
(b) MRI revealing atrophy in the midbrain tegmentum.
(c) 3D-SSP IMP-SPECT revealing decreased blood flow in the bilateral posterior cingulate gyri and the bilateral temporal lobes.

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PATIENT 9

An 80-year-old man presented to our hospital with gait disturbance. He was well until 2 months earlier when he developed walking difficulty. He was unable to raise his knees sufficiently and he stumbled, sometimes backward. He presented with démarche à petit pas. He had become difficulty to awaken. His movement had slowed, and he became rigid. He had occasional tremor in both hands. He did not complain of laterality. He did complain forgetfulness. Neurological examination showed neck-dominant rigidity and rigidity of the lower extremities without laterality, démarche à petit pas without arm swing and with freezing gait, as well as pulsion. MIBG myocardial scintigraphy revealed a normal early H/M ratio of 2.272. MRI revealed atrophy in the bilateral medial temporal lobes and the midbrain tegmentum (Figure 1a and b). 3D-SSP of IMP-SPECT revealed decreased blood flow in the bilateral temporal lobes and the posterior cingulate gyri (Figure 1c).

PATIENT 13

An 87-year-old man presented to our hospital with tremor of his left hand. He was well until approximately 6 months earlier when he developed tremor of the left hand, primarily when he held a saucer of a certain weight. He did not complain stiffness. He walked slowly, but his gait did not present with démarche à petit pas. Neurological examination showed left hand tremor at rest, rigidity of the neck, and his left arm showed little arm swing or dystonic posture when he walked. MIBG myocardial scintigraphy revealed a normal early H/M ratio of 2.056. MRI revealed atrophy in the bilateral medial temporal and the parietal lobes (Figure 2a and b). 3D-SSP IMP-SPECT revealed decreased blood flow in the posterior cingulate gyri (Figure 2c).

L-dopa treatment improved his Parkinsonism. Approximately 1 year after the onset, he did complain forgetfulness and apathy.

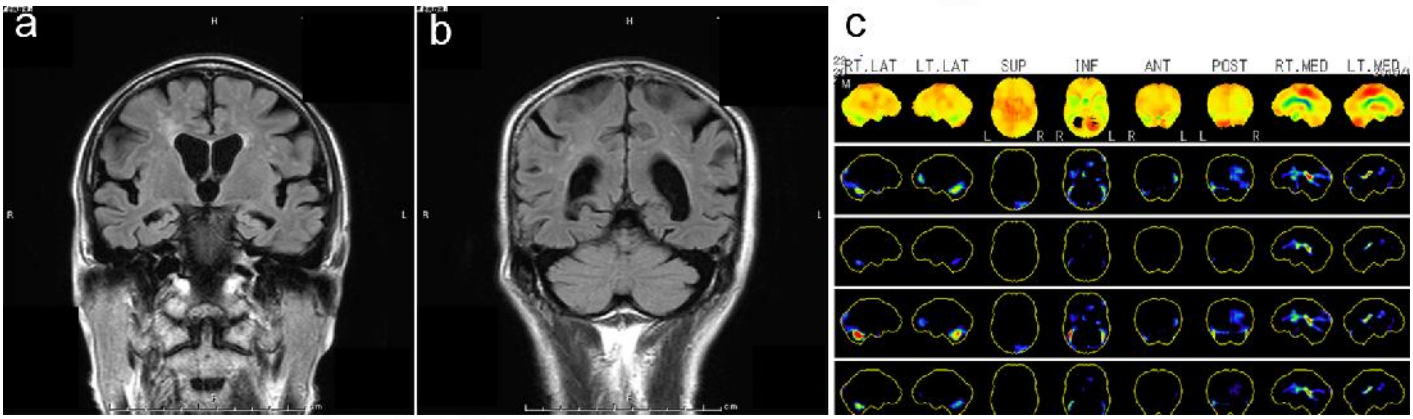

Figure 2 MRI and 3D-SSP IMP-SPECT findings in Patient 13.
(a) MRI revealing atrophy in the bilateral medial temporal lobes.
(b) MRI revealing atrophy in the bilateral parietal lobes.
(c) 3D-SSP IMP-SPECT revealing decreased blood flow in the posterior cingulate gyri.

PATIENT 14

An 82-year-old woman presented to our hospital with forgetfulness. She was well until approximately 10 years earlier when she first presented with forgetfulness. She lost economic sense and repeated the same words. She travelled by bicycle and forgot her way back home. She experienced hallucination of small, black bugs. Seven years earlier, she hallucinated the presence of her brother and sisters. She presented with urinary incontinence. She wandered, and sometimes police officers returned her to her home. Recently, 1 year earlier, she had leaned and slid down from her chair, and she presented with gait disturbance. Her vocabulary became decreased. She was able to understand only very easy words, and was unable to say long sentences. Neurological examination showed disorientation, amnesia, fluent aphasia with difficulty in understanding basic commands and in repeating sentences (Wernicke-like aphasia), and neck and left upper extremity-dominant cog-wheel rigidity. She presented with démarche à petit pas. MIBG myocardial scintigraphy revealed a normal early H/M ratio of 2.335. MRI revealed atrophy in the bilateral temporal lobes, particularly in the medial temporal lobes, and mild atrophy in the frontal and parietal lobes (Figure 3a and b). 3D-SSP IMP-SPECT revealed decreased blood flow in the bilateral frontotemporal, and parietotemporal lobes, and the posterior cingulate gyri (Figure 3c).

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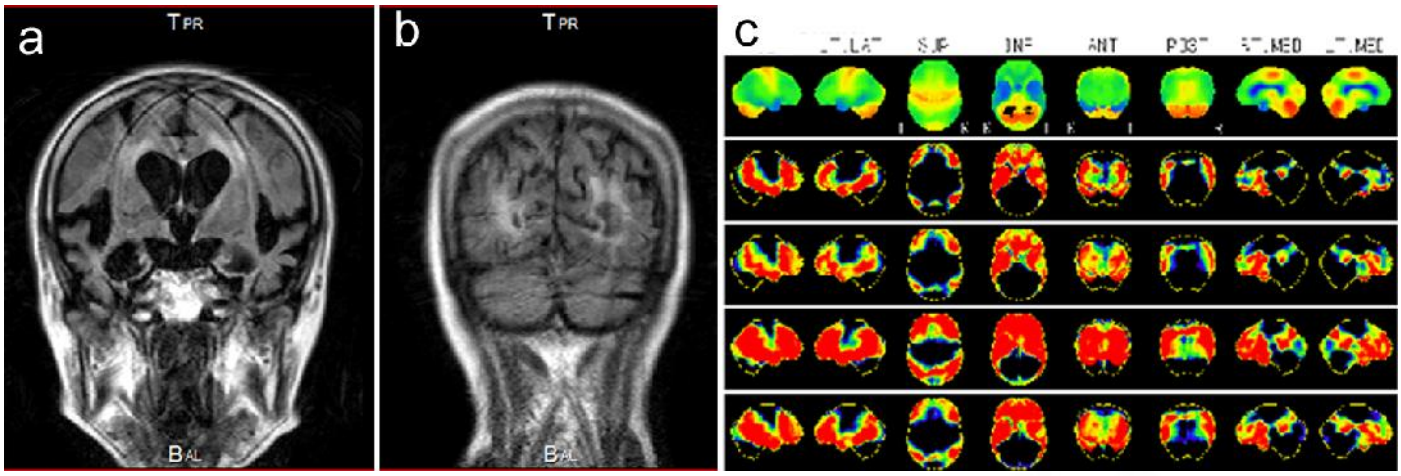

Figure 3 MRI and 3D-SSP IMP-SPECT findings in Patient 14.
(a) MRI revealing atrophy in the bilateral temporal lobes.
(b) MRI revealing atrophy in the bilateral parietal and occipital lobes.
(c) 3D-SSP IMP-SPECT revealing decreased blood flow in the frontotemporal and parietotemporal lobes, as well as the posterior cingulate gyri.

PATIENT 16

An 87-year-old man presented to our hospital with gait disturbance. He was well until approximately 5 years earlier when he began using a cane to walk. He moved slowly, and his body became rigid. Two years earlier, his left hand became clumsy. Seven months earlier, he developed difficulty going upstairs and downstairs; going downstairs was more difficult because of unsteadiness. Five months earlier, he presented with a falling tendency. Neurological examination showed supranuclear ophthalmoparesis of vertical gaze, rigidity of neck and upper extremity, occasional tremor in both hands, slightly widely based gait, and démarche à petit pas. MIBG myocardial scintigraphy revealed a normal early H/M ratio of 2.16. MRI revealed atrophy in the whole brain, especially in the parietal lobes (Figure 4a). 3D-SSP IMP-SPECT revealed decreased blood flow in the right frontal lobe and the bilateral posterior cingulate gyri (Figure 4b).

Although we did not ask, he usually talked about World War II and peace movement for long time.

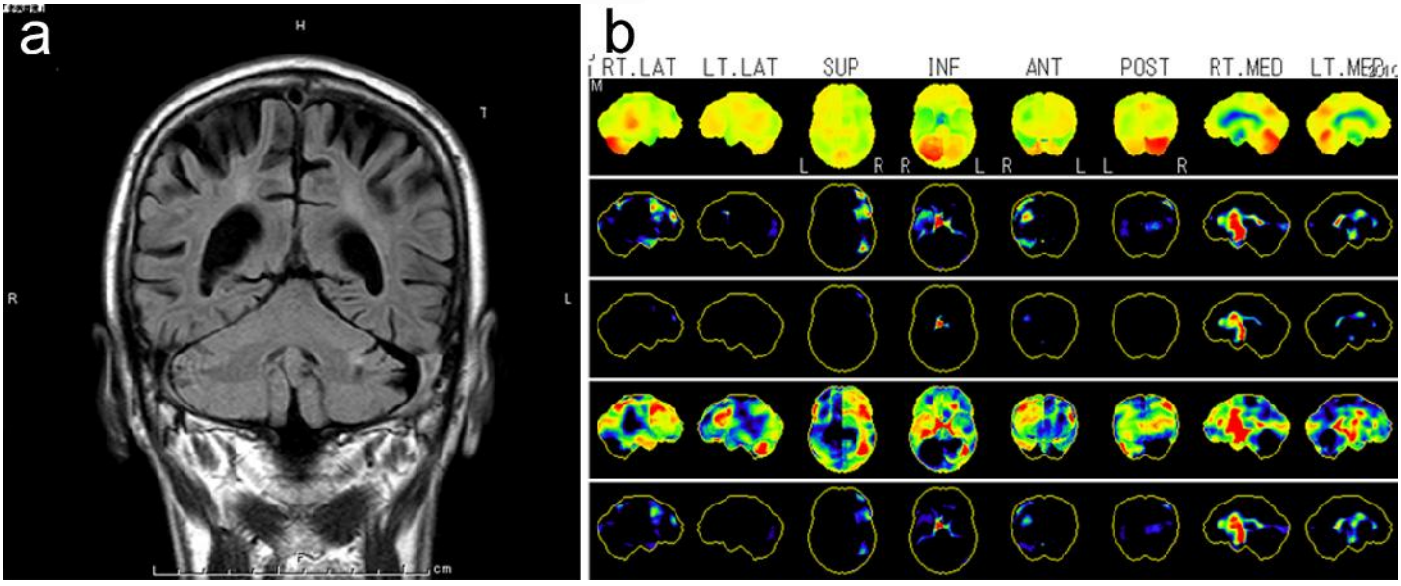

Figure 4 MRI and 3D-SSP IMP-SPECT findings in Patient 16.
(a) MRI revealing cerebral atrophy, particularly in the parietal lobes.
(b) 3D-SSP IMP-SPECT revealing decreased blood flow in the right frontal lobe and the posterior cingulate gyri.

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We investigated clinical characteristics, MRI findings, and 3D-SSP IMP-SPECT findings of these patients.

3. RESULTS

Clinical Characteristics

All patients were over 80 years of age. Four patients were male and 1 was female. All patients exhibited Parkinsonism (Table 1 and 2). Two of 4 patients were improved by treatment with l-dopa. Two patients exhibited supranuclear ophthalmoparesis of vertical gaze. All patients demonstrated rigidity; of these, 3 patients showed bilateral rigidity, 1 patient showed unilateral rigidity, and 1 patient exhibited only neck rigidity. Two patients had cog-wheel rigidity. Three patients showed tremors. Patient 5 showed bilateral tremors at rest and patient 13 showed unilateral tremors at rest. Although patient 9 had had history of occasional tremor in both hands, he has never shown tremor on neurological examination. All patients had a gait disturbance. Three patients (patient 9, 14, and 16) showed démarche à petit pas. One patient (patient 9) showed démarche à petit pas and freezing gait. One patient (patient 16) showed démarche à petit pas and a wide base gait. One patient (patient 13) exhibited slowed walking. Two patients (patient 5 and 14) exhibited apparent dementia. Dementia of 1 patient (patient 5) had already progressed and was difficult to examine using Mini-Mental State Examination (MMSE). Initially, this patient had developed predominantly Parkinsonism, and, according to his history, dementia developed thereafter. The MMSE score of the other dementia patient (patient 14) was 3. Furthermore, other 2 patients (patient 9 and 13) complained forgetfulness. Patient 13 complained apathy. Remaining one patient (patient 16) presented with disinhibition-like behaviour. One patient exhibited pulsion. One patient exhibited fluent sensory aphasia, similar to Wernicke aphasia.

Table 1

Clinical characteristics of Parkinsonism patients with normal ^{123}I-metaiodovenzylguanidine (MIBG) myocardial scintigraphy

Patient	Age/G	C.C.	Clinical syndrome	MRI	SPECT	Diagnosis
1	81/F	Fall	Parkinsonism	Bil. central		PSP or CBD
2	74/F	Dysarth.	Parkinsonism	Bil. central		CBD S/O
3	54/M	Gait d.	Parkinsonism	Bil. striate atrophy		SND (MSA-P)
4	80/M	Dysph.	Parkinsonism	Temporopalietal	Bil.BG	Familial parkin.
5	85/M	Gait d.	Parkinsonism, dementia, supranuclear ophthalmo.	MT, temporal	FT, TP, PC	AD (pathological)
6	87/F	Gait d.	l-dopa responsive Parkinsonism	Etát cribré	Bil. Frontal	Parkinsonism
7	83/F	Akinesia	Parkinsonism, dementia	MT (m), F, P	Frontal	PSP or AD, multiple infarction
8	78/M	Gait d.	Demarche à petit pas	Multiple inf.		Multiple infarction
9	80/M	Gait d.	Parkinsonism	MT, hippo., F, P	PC, T	AD
10	68/M	Tremor	Demarche à petit pas	IWL, c4-5, 5-6		c. myelopathy
11	69/M	Gait d.	Dystonia of right U/E	Postcentral a., multiple infarction		CBD or multiple inf.
12	79/F	Gait d.	Demarche à petit pas	Cerebral atrophy, MT (m)		AD or PSP
13	87/M	Tremor	Parkinsonism	Hippo., P	PC	AD
14	82/F	Forget	Dementia (sensory aphasia), Parkinsonism	T, F, P	F, T , P, PC	AD
15	80/F	Gait d.	Parkinsonism	Bil. central		PD or CBD
16	87/M	Gait d.	Parkinsonism	Cerebral atrophy, P	Rt F, PC	AD
17	88/M	Tremor	Parkinsonism, dementia	P, MT		AD?

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18	66/M	Fall	Parkinsonism	MI, hippo., P, MT		MI or AD
19	71/F	O. D.	Parkinsonism	Cerebral, hippo.		AD?
20	73/M	Tremor	Parkinsonism	MT		AD
21	72/F	Gait d.	Parkinsonism, dementia	MT	F, C	PSP
22	74/F	Bradyk.	Parkinsonism	P		AD?

Abbreviations: a.: atrophy; AD: Alzheimer's disease; BG: basal ganglia; bil.: bilateral; bradyk.: bradykinesia; C: cingulate; c.: cervical; CBD: corticobasal degeneration; C.C.: chief complaint; d.: disturbance; dysarth.: dysarthria; dysph.: dysphagia; F: frontal; forget.: forgetfulness; FT: frontotemporal; G.: Gender; hippo.: hippocampus; inf.: infarction; IWL: ischemic white matter lesions; m: mild; MI: multiple infarction; MRI: magnetic resonance imaging; MSA-P: Parkinsonism-predominant multiple system atrophy; MT: midbrain tegmentum; O.D.: oral dyskinesia; ophthalmo.: ophthalmoparesis; P: parietal; parkin.: Parkinsonism; PC: posterior cingulate; PD: Parkinson's disease; PSP: progressive supranuclear palsy; Rt: right; SND: striate-nigral degeneration; SPECT: single photon emission computed tomography; T: temporal; TP: temporoparietal; U/E: upper extremity

Table 2

Clinical characteristics of ^{123}I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy normal patients exhibiting radiological features of Alzheimer's disease

Patient	5	9	13	14	16
Age/Gender	85/M	80/M	87/M	82/F	87/M
l-dopa response	+	-	+	-	N.E.
Supranuclear ophthalmoparesis	+	-	-	-	+
Rigidity	b. co.	b.	Neck	u. co.	b.
Tremor	b.r.	-	u. r.	-	+
Gait disturbance	+	f., d.	Slow	d.	w., d.
MMSE score	N.E.	30/30	28/30	3/30	25/30
Dementia	+	Forgetfulness	Forgetfulness, Apathy	+	Disinhibition -like behaviour
Yahr stage	5	3	2	3	4
Others	a.	Pulsion		s.a.	
MRI atrophy	m.t., t.	m. t., t.	m. t., p.	m. t., p.	wh. p.
3D-SSP IMP SPECT hypoperfusion	ft, tp, c.	b. temporal, c.	c.	ft, tp, c.	fr, c.

Abbreviations: a.: autopsy confirmed; b.: bilateral; c: posterior cingulate; co.: cogwheel; d.: démarche à petit pas; f.: freezing; fr: frontal lobe; ft: frontotemporal; l.: lead pipe; l-dopa: l-dihydroxyphenylalanine; MMSE: Mini-Mental State Examination; MRI: magnetic resonance imaging; m.t.: medial temporal; N.E.: not evaluated; p.: parietal lobe; r.: resting; s.a.: sensory aphasia; t. midbrain tegmentum; 3D-SSP IMP-SPECT: three-dimensional stereotactic surface projection iodoamphetamine single photon emission computed tomography; tp: temporoparietal; u.: unilateral; w.: widely base gait; wh: whole brain

Magnetic Resonance Imaging Findings

All patients showed atrophy in the medial temporal lobes (Table 1, 2 and Figure 1b, Figure 2b, Figure 3b, Figure 4a). Three patients showed atrophy in the parietal lobes (Figure 2b, Figure 3b, Figure 4a), while 2 showed atrophy in the midbrain tegmentum (Figure 1b).

Single Photon Emission Computed Tomography Findings

All patients demonstrated hypoperfusions in the posterior cingulate gyri (Table 1, 2 and Figure 1c, Figure 2c, Figure 3c, Figure 4b). Three patients showed hypoperfusion in the frontal lobes (Figure 3c, Figure 4b), 3 showed hypoperfusion in the temporal or the medial temporal lobes (Figure 1c, Figure 3c), and 2 showed hypoperfusion in the temporoparietal lobes (Figure 3c).

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4. DISCUSSION

Of 22 patients, 5 with MIBG myocardial scintigraphy normal Parkinsonism showed both MRI and SPECT findings consistent with Alzheimer's disease. Neuropathological examination of an autopsied patient revealed pure Alzheimer's disease without PSP pathology or Lewy body pathology. Clinical characteristics of the patients included the following: > 80 years of age, predominantly male, exhibiting Parkinsonism with rigidity and gait disturbance. Three patients exhibited tremor. Two patients had supranuclear ophthalmoparesis of vertical gaze. Two patients showed dementia.

New and important findings of this study were that 5 of 22 patients with MIBG myocardial scintigraphy normal Parkinsonism demonstrated both MRI and SPECT findings consistent with Alzheimer's disease. In addition, neuropatholgical examination of an autopsied patient demonstrated pure Alzheimer's disease. Alzheimer's disease should be considered as a differential diagnosis of Parkinsonism.

It has previously been reported that Alzheimer's disease may present with extrapyramidal signs (Mitchell, 1999; Mitchell and Rockwood, 2000; Attems et al., 2007; Toru et al., 2010; King et al., 2011). However, patients in these previous studies have been associated with Alzheimer's disease symptoms, as they predominantly presented with dementia. Only Daniel's patients and our patient present predominantly with l-dopa responsive Parkinsonism caused by pathological Alzheimer's disease (Daniel and Lees, 1991; Kasahata et al., 2014). In this study, 3 patients presented with predominantly Parkinsonism. One autopsy proven Alzheimer's disease patient presented initially and predominantly with Parkinsonism. Only one patient in this study presented with Parkinsonism after Alzheimer's disease symptoms appeared, those being Wernicke-type sensory aphasia and dementia. The predominant presentation of Parkinsonism in most of these patients differed from previous study.

The background pathology of these patients seemed to be Alzheimer's disease. However, PSP may complicate the Alzheimer's disease picture. Patient 5 with supranuclear ophthalmoparesis and midbrain tegmental atrophy demonstrated only Alzheimer's disease pathology. Patient 9 with atrophy of midbrain tegmentum obtained an MMSE score of 30/30, and demonstrated hypoperfusion in the posterior cingulate gyri and the medial temporal lobe, but not in the frontal lobes; therefore, PSP seemed unlikely. Patient 16 with supranuclear ophthalmoparesis and hypoperfusion in the right frontal lobe showed no midbrain tegmental atrophy. Therefore, possibility of PSP pathology complication was not so high. Another differential diagnosis is the Lewy body variant of Alzheimer's disease. However, normal MIBG myocardial scintigraphy was negative for Lewy body pathology.

The limitations of this study were as follows: only 1 patient had autopsy proven Alzheimer's disease. Exclusion of PSP pathology or Lewy body pathology was insufficient. However, we believe that the results of this study are very important. Both clinical and neuropathological evaluation will clarify the neuropatholgocial background of those patients who exhibited MIBG myocardial scintigraphy normal Parkinsonism associated with radiological Alzheimer's disease features.

5. CONCLUSION

We reported 5 MIBG myocardial scintigraphy normal Parkinsonism having both MRI and SPECT findings consistent with Alzheimer's disease. Alzheimer's disease can present initially and predominantly with Parkinsonism. Alzheimer's disease should therefore be considered as a differential diagnosis of Parkinsonism.

SUMMARY OF RESEARCH

1. The pathological findings of brainstem nuclei in Alzheimer's disease are reported, however, the clinical manifestation based on these affected brainstem nuclei has been uncertain. We describe some clinical manifestation possibly associated with brainstem pathological changes in Alzheimer's disease.
2. Sixty-one patients with Parkinsonism underwent MIBG myocardial scintigraphy, of which 22 showed normal MIBG. Of these patients, 5 demonstrated both MRI and SPECT findings consistent with Alzheimer's disease.
3. Characteristics of these patients can be summarized as follows: >80 years of ages, predominantly male, and exhibiting Parkinsonism with rigidity and gait disturbance. Three patients exhibited tremor. Two patients demonstrated supranuclear ophthalmoparesis of vertical gaze. Two patients showed dementia. Neuropatholgical examination of an autopsied patient demonstrated pure Alzheimer's disease pathology.
4. Alzheimer's disease can present initially and predominantly with Parkinsonism. Alzheimer's disease should be considered as a differential diagnosis of Parkinsonism.

FUTURE ISSUES

I believe that clinical picture and diagnosis of Parkinsonism due to Alzheimer's disease will be elucidated. I believe that clinical characteristics due to brainstem pathology in Alzheimer's disease will also be apparent.

DISCLOSURE STATEMENT

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