weighted images and elemental concentration in brain. Neuroradiology 1997;39:546–550.
12. Nagatomo S, Umehara F, Hanada K, Nobuhara Y, Takenaga S, Arimura K, Osame M. Manganese intoxication during total parenteral nutrition: report of two cases and review of the literature. J Neurol Sci 1999;162:102–105.
13. Mena I. Manganese poisoning. In: Vinken PJ, editor. Intoxications of the Nervous System: Part 1. Amsterdam: Elsevier Science; 1979. p 217–237.
14. Feldman RG. Manganese. In: Wolff FA, editor. Intoxications of the Nervous System: Part 1. Amsterdam: Elsevier Science; 1994. p 303–322.
15. Butterworth RF. Pathogenesis of hepatic encephalopathy: update on molecular mechanisms. Ind J Gastroenterol 2003;22(Suppl. 2):11–16.
16. Neumann MA. Iron and calcium dysmetabolism in the brain with special predilection for globus pallidus and cerebellum. J Neuropathol Exp Neurol 1963;22:148–163.
17. Shulman LM, Minagar A, Weiner WJ. Reversal of parkinsonism following liver transplantation. Neurology 2003;60:519.

Cardiac [^{123}I]Metaiodobenzylguanidine Scintigraphy for Vascular Parkinsonism

Joong-Seok Kim, MD,[1] Phil-Hyu Lee, MD,[2] Kwang-Soo Lee, MD,[1] Jeong-Wook Park, MD,[1] Yeong-In Kim, MD,[1] Yong-An Chung, MD,[3] Sung-Hoon Kim, MD,[3] Seung-Hyun Kim, MD,[4] Juhan Kim, MD,[4] Yun-Young Choi, MD,[5] and Hee-Tae Kim, MD[4]*

[1]Department of Neurology, The Catholic University of Korea, Seoul, Korea; [2]Department of Neurology, Ajou University Medical College, Suwon, Korea; [3]Department of Nuclear Medicine, The Catholic University of Korea, Seoul, Korea; [4]Department of Neurology, Hanyang University Medical College, Seoul, Korea; [5]Department of Nuclear Medicine, Hanyang University Medical College, Seoul, Korea

Abstract: **The purpose of our study was to prospectively evaluate cardiac [^{123}I]metaiodobenzylguanidine (MIBG) uptake in patients with cerebrovascular disease (CVD) who develop clinical symptoms of vascular Parkinsonism (VP). A total of 19 consecutive patients who developed Parkinsonism during the course of their CVD were enrolled in the study; 15 age-matched subjects, and 29 patients with Parkinson's disease (PD) were also evaluated with cardiac MIBG uptake. MIBG uptake was assessed using the ratio of the heart to the upper mediastinum (H/M) according to planar scintigraphic data. The mean H/M ratio was significantly higher in patients with VP than in those with PD (2.28 ± 0.41 vs. 1.27 ± 0.13; $P < 0.001$). MIBG uptake did not differ between VP and controls (2.46 ± 0.33; $P > 0.05$). Our findings suggest that myocardial postganglionic sympathetic dysfunction found in PD is absent in most patients with VP. MIBG single photon emission computed tomography imaging may be useful to help distinguish between PD and VP patients in clinical practice.**

Key words: Parkinson's disease; vascular Parkinsonism; MIBG scintigraphy

Vascular Parkinsonism (VP) is defined neuropathologically as Parkinsonism occurring in patients with cerebrovascular disease, after exclusion of Lewy body disease and other neurodegenerative conditions associated with Parkinsonism.[1,2] However, VP remains difficult to distinguish clinically from Parkinson's disease (PD), because basal ganglia infarcts can occur without Parkinsonism,[3,4] and vascular pathology is commonly associated with Lewy body PD.[5] There is evidence, from magnetic resonance imaging (MRI) studies, that suggests two different types of vascular lesions may cause VP: widespread, bilateral ischemic lesions have been linked to gradual-onset Parkinsonism, whereas basal ganglia infarcts have been reported to be associated with acute-onset contralateral Parkinsonism.[6,7] The presence of these two different vascular lesions have been confirmed by a recent clinicopathological correlation study.[2]

It is well established that cardiac [^{123}I]metaiodobenzylguanidine (MIBG) uptake is significantly reduced in patients with PD.[8] This feature corresponds to the presence of myocardial postganglionic sympathetic dysfunction as part of the neurodegenerative process in PD. This impairment occurs early in the course of the disease, and its severity depends on disease progression and treatment.[9,10]

Cardiac MIBG scintigraphy has been investigated in other neurodegenerative conditions associated with Parkinsonism. Impairment has been found in patients who had dementia with Lewy bodies, mild impairment in multiple system atrophy, and progressive supranuclear palsy; normal findings have been reported in patients with parkin-positive Parkinsonism.[10–12]

The role of cardiac MIBG scintigraphy in the diagnosis of VP has not been evaluated to date. In the present study, we performed cardiac MIBG scintigraphy to prospectively evaluate postganglionic sympathetic dysfunction in patients with cerebrovascular disease who develop clinical symptoms of VP.

*Correspondence to: Dr. Hee-Tae Kim, Department of Neurology, Hanyang University Hospital, 17, Haengdang-dong, Sungdong-gu, Seoul, 133-792, Korea. E-mail. kimht@hanyang.ac.kr

Received 13 February 2006; Revised 9 May 2006; Accepted 3 June 2006

Published online 21 September 2006 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21112

PATIENTS AND METHODS

Only eligible patients who fulfilled published clinical diagnostic criteria for VP,[7] were recruited for the study. The patients were classified as VP with acute-onset and with insidious-onset by assessing the temporal relationship between stroke and the onset of Parkinsonism, and the association of the localization of MRI lesions to clinical findings. Additionally, the vascular rating scale proposed by Winikates and Jankovic was assessed to aid the diagnosis of VP. Initial and long-term levodopa response was determined, based on subjective patient assessment and case notes, but was not used as an exclusion criterion for VP.

Consecutive patients attending the movement disorders clinic at the Kangnam St. Mary's Hospital, Seoul, and at the Hanyang Medical Center, Seoul, who fulfilled the outlined criteria were asked to participate. Patients with VP were matched for age and smoking status with normal controls, and with patients with PD from the same clinic population. PD was diagnosed according to the United Kingdom Parkinson's disease Society Brain Bank Clinical Diagnosis Criteria.[13] For the PD patients, vascular lesions on MRI precluded participation, the only exception being minimal evidence of small vessel disease in areas other than the basal ganglia; these were interpreted as normal for age by an independent radiologist.

We excluded patients with (1) a history of neuropathy or previous relevant cardiac disease, or any abnormalities on routine chest radiography and electrocardiography, and (2) those taking medications reported to influence cardiac MIBG uptake.

MIBG scintigraphy was obtained after informed consent from each patient. Data were collected for 240 minutes after injection of 111 MBq of [^{123}I]MIBG using a dual-head camera (Siemens, Germany), and a static image was obtained with a 128 $\times$ 128 matrix. Regions of interest were manually drawn around the heart, mediastinum, and lung, and tracer uptake was measured within each region of interest to calculate the heart to mediastinum (H/M) ratio.

An unpaired *t* test was used for examining the intentional difference between two groups using a commercially available software package (SPSS, Version 13.0). All *P* values less than 0.05 were considered statistically significant.

RESULTS

A total of 19 patients with VP, 30 patients with PD, and 16 healthy controls were prospectively included in this study. Table 1 shows the demographic and clinical details, imaging results, and vascular risk factors for the 19 patients with VP. The mean age was 70.6 $\pm$ 9.1 years in the VP group, 64.3 $\pm$ 9.3 years in PD group, and 66.9 $\pm$ 7.0 in the controls. Mean disease duration was 2.3 $\pm$ 2.9 years for the VP group and 2.4 $\pm$ 2.1 years for the PD group. There were significant differences between the two groups of patients in the age at onset, presence and distribution of vascular risk factors, clinical symptoms, vascular rating scale, and response to L-dopa (Table 2).

The mean H/M ratio was significantly higher in patients with VP than in those with PD (2.28 $\pm$ 0.41 vs 1.27 $\pm$ 0.13; $P < 0.001$). However, the mean H/M ratio for the VP group was slightly lower, but not statistically different from that of the control group (2.46 $\pm$ 0.33). Note Figure 1 that shows a scatter plot of the individual cardiac MIBG uptake in 19 patients with VP, compared with the PD patients and the controls. Of 19 patients with VP, 16 had an H/M ratio that was within 2 SDs of the normal mean. However, 3 had findings that were more than 2 SDs of the mean for the PD patients, even though there was no definite perfusion abnormality in these 3 patients using myocardial methoxyisobutyl isonitrile (MIBI) scintigraphy.

DISCUSSION

For many years, it has been believed that VP is a lower body Parkinsonism associated with multiple small bilateral infarcts in the basal ganglia and/or white matter with no, or poor, response to L-dopa.[14] Differentiation of VP from PD is important because of the different pathogenesis, prognosis, and response to treatment. However, a recent clinicopathological study found that 9 of 17 patients with VP had been diagnosed as having PD,[2] reflecting the difficulties in diagnosis in clinical practice. To the best of our knowledge, there is no single, useful, and convenient tool to differentiate these two diseases.

Recently, reliable and clear evidence for the usefulness of MIBG scintigraphy, for the diagnosis of PD, has accumulated, and it has become a diagnostic tool for PD used widely in Korea. The disease is characterized pathologically by distinctive neuronal inclusions called Lewy bodies in many surviving cells of dopaminergic neurons of the substantia nigra pars compacta and other specific brain regions.[15] Furthermore, Lewy body type degeneration, in the cardiac plexus, has also been observed in PD.[16] In patients with PD, cardiac MIBG uptake is reduced markedly even in the early stages of disease; therefore, MIBG imaging can be used as an indicator of the presence of PD rather than disease severity.

In our study, cardiac MIBG uptake in patients with a clinical diagnosis of VP is substantially higher than in patients with probable PD in whom relevant vascular lesions have been excluded. The uptake ratio in patients with VP was slightly lower than that in age-matched

TABLE 1. *Clinical and imaging findings in patients with vascular parkinsonism*

Age (yr)	Sex	Duration (yr)	Onset	Clinical features	MRI findings	Vascular risk factors for stroke	Vascular rating score[a]	Levodopa response	H/M ratio
72	F	0.1	Acute	Hemiparkinsonism following stroke, later shuffling gait	Lesion contralateral GP	None	3	Poor	2.35
69	F	2	Insidious	Asymmetric tremor predominant parkinsonism	Lesion both GP, midbrain, PVWML	Hypertension	3	Poor	2.55
67	M	0.2	acute	Lower body parkinsonism < 2 months after stroke	PVWML, DWML	Hypertension, smoking	4	Poor	1.98
70	M	3	Insidious	Shuffling gait, lower body parkinsonism	Lesion right LN, PVWML, DWML	Hypertension, smoking	3	Poor	2.68
65	M	2	Insidious	Shuffling gait, lower body parkinsonism	Lesions both LN, PVWML, DWML	Smoking	4	Poor	2.42
73	F	0.5	Acute	Tremor predominant parkinsonism following stroke, later shuffling gait	Lesion contralateral LN, PVWML	Hypertension, hyperlipidemia	2	Poor	1.81
86	M	0.1	Acute	Shuffling gait later bradykinesia including right upper limb	Lesion contralateral LN, PVWML	Hypertension, smoking, hyperlipidemia	3	Equivocal	2.46
79	M	4	Insidious	Hemiparkinsonism following stroke, later shuffling gait	PVWML, DWML	Smoking	3	Equivocal	2.31
73	F	0.5	Insidious	Lower body parkinsonism	PVWML, DWML	Hypertension	3	Initially good, but insufficient long-term response	1.87
66	F	0.5	Insidious	Hemiparkinsonism following stroke, later shuffling gait	PVWML, DWML	Hypertension	3	Initially good, but insufficient long-term response	2.40
85	M	9	Insidious	Hemiparkinsonism with action tremor, shuffling gait 1 year after stroke	Lesion contralateral GP, PVWML, DWML	Hypertension	3	Equivocal	1.93
66	F	0.7	Acute	Tremor predominant asymmetric parkinsonism < 1 month after stroke, later shuffling gait	Lesion contralateral GP, PVWML, DWML	Hypertension, diabetes mellitus	2	Poor	1.71
77	M	2	Insidious	Tremor predominant asymmetric parkinsonism following stoke,	Lesions both LN, PVWML	None	2	Poor	2.79
68	F	7	Insidious	Hemiparkinsonism 1 year after stroke	PVWML, DWML	Hypertension, smoking	3	Poor	2.52
80	M	3	Insidious	Shuffling gait, lower body parkinsonism	PVWML, DWML	Hypertension, diabetes mellitus	4	Poor	1.74
67	F	2	Insidious	Tremor, shuffling gait, later upper limb bradykinesia	PVWML, DWML	Hypertension, diabetes mellitus	2	Initially good, but insufficient long-term response	1.66
45	F	0.3	Acute	Tremor predominant parkinsonism after stroke	PVWML, DWML	None	3	Initially good, but insufficient long-term response	2.35
71	F	0.2	Acute	Tremor predominant parkinsonism after stroke	Lesions both LN	Hypertension	2	Initially good, but insufficient long-term response	2.81
63	M	9	Insidious	Lower body parkinsonism	PVWML	Hypertension	3	Poor	2.99

[a]Winikates and Jankovic vascular rating scale for vascular parkinsonism. GP, globus pallidus; WML, white matter lesion; PVWML, periventricular WML; DWML, deep WML; LN, lentiform nucleus.

normal controls, but this was not significant. In our study, three patients with VP showed reduced H/M ratio below 1.75, although there was no myocardial perfusion defect in MIBI scintigraphy. The possible explanation of these cases would be associated with diabetes mellitus.[17] Therefore, our findings suggest that cardiac MIBG scintigraphy may be a useful adjuvant for differentiating between PD and suspected VP.

TABLE 2. *Clinical features of PD and VP patients*

	PD patients	VP patients	*P* value
Gender (male/female)	11/19	8/11	0.70
Mean age (yr)	64.3 ± 9.3	70.6 ± 9.1	0.04
Disease duration (yr)	2.38 ± 2.07	2.42 ± 2.90	0.96
Presence of vascular risk factors[a]	8 (26.7)	19 (100)	<0.001
Acute onset	0	7 (38.6)	<0.001
Insidious onset	30 (100)	12 (63.2)	<0.001
Tremor (rest or postural)	20 (66.7)	8 (42.1)	0.09
Hypokinesia	26 (86.7)	16 (84.2)	0.81
Asymmetric onset	25 (83.3)	11 (57.9)	0.05
Gait disorder	11 (36.7)	14 (73.7)	0.01
Pyramidal signs	2 (6.7)	6 (31.6)	0.02
Falling	1 (3.3)	6 (31.6)	<0.01
Freezing	1 (3.3)	7 (36.8)	<0.01
Lower body predominance	4 (13.3)	14 (73.7)	<0.001
Presence of long-term response to levodopa treatment	30 (100)	0	<0.001
Vascular rating scale	0.50 ± 0.57	2.90 ± 0.65	<0.001

Values represent number of patients with percentages in parentheses. The two groups were compared by two-sample *t*-test for continuous variables and χ^2 test for nominal variables.

[a]Hypertension, hyperlipidemia, diabetes mellitus, heart disease, presence of cerebrovascular disease.

PD, Parkinson's disease; VP, vascular Parkinsonism.

A limitation of this study was the use of diagnostic criteria for VP that has not yet been validated. In addition, we did not carry out neuropathological investigations, to confirm Lewy body pathology, because the patients were still alive. However, we attempted to reduce these confounders by including patients who fulfilled two sets of diagnostic criteria, although this selection procedure might have been an obstacle to a priori clinical suspicion of VP.

As expected, our data revealed a high frequency of a low H/M ratio in patients with VP, suggesting additional factors for low MIBG uptake. Because VP is a form of a vascular accident, latent cardiac disorders might be responsible for the low uptake. In addition, it is possible that that some of the VP patients had subclinical or comorbid Lewy body changes in addition to cerebrovascular disease. Therefore, further studies using fluorodopa positron emission tomography or dopamine transporter imaging need to be done to identify whether VP patients, with reduced cardiac MIBG uptake, may be accompanied by nigral dopaminergic degeneration.

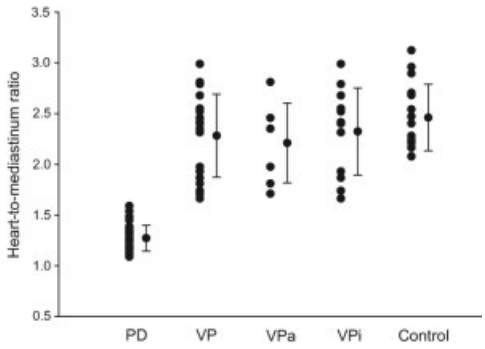

FIG. 1. Scatter diagram of individual heart to mediastinum ratio (H/M ratio) of [^{123}I]metaiodobenzylguanidine (MIBG) uptake in patients with vascular Parkinsonism (VP; VPa; VPi), compared with patients with Parkinson's disease (PD) and controls. The results are also presented as mean ± SD. VPa, VP with acute onset; VPi, VP with insidious onset.

In summary, we conclude that, in contrast to PD, a majority of patients with VP show a normal range of cardiac MIBG uptake, suggesting that these patients may have a clinical diagnosis unrelated to PD. As this procedure is more widely available, requires less-sophisticated equipment and analytic procedures, and has a lower cost, testing MIBG scintigraphy may help in the differential diagnosis between two important causes of Parkinsonism in the elderly.

Acknowledgments: This work was supported in part by the research fund of Hanyang University (HY-2005-000-0000-1734) to H.T.K.

REFERENCES

1. Critchley M. Arteriosclerotic parkinsonism. Brain 1929;52:23–83.
2. Zijlmans JC, Daniel SE, Hughes AJ, Revesz T, Lees AJ. Clinicopathological investigation of vascular parkinsonism, including clinical criteria for diagnosis. Mov Disord 2004;19:630–640.
3. Weiller C, Ringelstein EB, Reiche W, Thron A, Buell U. The large striatocapsular infarct. A clinical and pathophysiological entity. Arch Neurol 1990;47:1085–1091.
4. Peralta C, Werner P, Holl B, et al. Parkinsonism following striatal infarcts: incidence in a prospective stroke unit cohort. J Neural Transm 2004;111:1473–1483.
5. Hughes AJ, Daniel SE, Blankson S, Lees AJ. A clinicopathologic study of 100 cases of Parkinson's disease. Arch Neurol 1993;50:140–148.

6. Zijlmans JC, Thijssen HO, Vogels OJ, et al. MRI in patients with suspected vascular parkinsonism. Neurology 1995;45: 2183–2188.
7. Winikates J, Jankovic J. Clinical correlates of vascular parkinsonism. Arch Neurol 1999;56:98–102.
8. Goldstein DS. Dysautonomia in Parkinson's disease: neurocardiological abnormalities. Lancet Neurol 2003;2:669–676.
9. Spiegel J, Mollers MO, Jost WH, et al. FP-CIT and MIBG scintigraphy in early Parkinson's disease. Mov Disord 2005;20:552–561.
10. Nagayama H, Hamamoto M, Ueda M, Nagashima J, Katayama Y. Reliability of MIBG myocardial scintigraphy in the diagnosis of Parkinson's disease. J Neurol Neurosurg Psychiatry 2005;76:249–251.
11. Druschky A, Hilz MJ, Platsch G, et al. Differentiation of Parkinson's disease and multiple system atrophy in early disease stages by means of I-123-MIBG-SPECT. J Neurol Sci 2000;175:3–12.
12. Suzuki M, Hattori N, Orimo S, et al. Preserved myocardial [123I]metaiodobenzylguanidine uptake in autosomal recessive juvenile parkinsonism: first case report. Mov Disord 2005;20:634–636.
13. Gibb WRG, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. J Neurol Neurosurg Psychiatry 1988;51:745–752.
14. FitzGerald PM, Jankovic J. Lower body parkinsonism: evidence for a vascular etiology. Mov Disord 1989;4:249–260.
15. Braak H, Del Tredici K, Rub U, et al. Staging of brain pathology related to sporadic Parkinson's disease. Neurobiol Aging 2003;24: 197–211.
16. Wakabayashi K, Takahashi H. Neuropathology of autonomic nervous system in Parkinson's disease. Eur Neurol 1997;38:S2–S7.
17. Scott LA, Kench PL. Cardiac autonomic neuropathy in the diabetic patient: does 123I-MIBG imaging have a role to play in early diagnosis? J Nucl Med Technol 2004;32:66–71.

^{123}I-Ioflupane SPECT in the Diagnosis of Suspected Psychogenic Parkinsonism

Carles Gaig, MD,[1] Maria José Martí, MD, PhD,[1]*
Eduardo Tolosa, MD, PhD,[1]
Francesc Valldeoriola, MD, PhD,[1] Pilar Paredes, MD,[2]
Francisco Juan Lomeña, MD, PhD,[2]
and Fernando Nakamae, MD[1]

[1]Movement Disorders Unit, Neurology Service, Institut Clínic de Neurociències, Hospital Clínic, University of Barcelona, Barcelona, Spain; [2]Nuclear Medicine Service, Hospital Clínic, University of Barcelona, Barcelona, Spain

Abstract: **Psychogenic Parkinsonism (PsyP) can be clinically difficult to differentiate from Parkinson's disease (PD). Striatal dopamine transporter (DAT) imaging could be helpful in differentiating them. We performed ^{123}I-Ioflupane single-photon emission computed tomography (SPECT) in 9 patients with suspected PsyP. In 1 patient, ^{123}I-Ioflupane SPECT disclosed bilateral decrease of striatal tracer uptake that indicated nigrostriatal degeneration. In this patient, a *parkin* gene mutation was detected. In the other 8 patients, ^{123}I-Ioflupane SPECT was normal and supported the initial suspicion of PsyP. Normal DAT imaging supports the diagnosis of PsyP, whereas reduced striatal tracer uptake suggests an underlying neurodegenerative Parkinsonism and should encourage the search for additional causes for the syndrome.** © 2006 Movement Disorder Society

Key words: psychogenic Parkinsonism; ^{123}I-Ioflupane SPECT; DAT imaging; *parkin* gene mutation

Psychogenic Parkinsonism (PsyP) represents 1.9% to 7% of all psychogenic movement disorders and can be clinically difficult to differentiate from Parkinson's disease (PD).[1,2] Difficulties in diagnosis arise from lack of specific laboratory or neuroimaging diagnostic tests and the possibility that PsyP can occur in a patient with underlying PD.[2,3] Another confounding factor is that PsyP can be difficult to classify into psychiatric disturbances classically related to psychogenic disorders like somatoform disorders, factitious disorders, or malingering, and frequently is associated with depression, which is also usually observed in patients with PD.[2] Furthermore, some neurologists are sometimes reluctant to diagnose PsyP because of the potential medicolegal consequences that can arise from misdiagnosing an organic disease. An accurate diagnosis of PsyP, however, is important to provide an adequate and potentially effective treatment and to avoid unnecessary, and potentially harmful, diagnostic or therapeutic procedures.

Striatal dopamine transporter (DAT) imaging provides information about nigrostriatal neuronal integrity and can separate neurodegenerative Parkinsonism with decreased striatal tracer uptake from Parkinsonism without dopaminergic terminals loss and normal DAT imaging findings as occurs in PsyP.[4–6] The aim of this work is to report the clinical features, ^{123}I-Ioflupane single-photon emission computed tomography (SPECT) findings, and long-term follow-up in 9 patients with Parkinsonism suspected to be of psychogenic origin.

PATIENTS AND METHODS

Patients with suspected PsyP seen at our Movement Disorders Unit from January 2003, to December 2004, were assessed with ^{123}I-Ioflupane SPECT. All patients presented at least two of the three cardinal parkinsonian signs of rest tremor, increased muscular tone, and slowness of movement. The suspicion of PsyP was raised in

*Correspondence to: Maria José Martí, Hospital Clínic, Service of Neurology. Villarroel 170, Barcelona 08036, Spain.
E-mail: mjmarti@clinic.ub.es

Received 18 November 2005; Revised 7 April 2006; Accepted 15 April 2006

Published online 28 August 2006 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21062