Reduced Cardiac Uptake and Enhanced Washout of $^{123}$I-MIBG in Pure Autonomic Failure Occurs Conjointly with Parkinson’s Disease and Dementia with Lewy Bodies

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The purpose of this study was to investigate myocardial uptake of $^{123}$I-metaiodobenzylguanidine (MIBG) in patients with pure autonomic failure (PAF), which has pathologic features in common with idiopathic Parkinson’s disease (IPD) and dementia with Lewy bodies (DLB). **Methods:** Six patients with PAF, 130 with IPD, 21 with DLB, 9 with corticobasal degeneration (CBD), 11 with progressive supranuclear palsy (PSP), and 11 with multiple-system atrophy (MSA) underwent myocardial $^{123}$I-MIBG scintigraphy, as did 16 control patients. **Results:** Resulting heart-to-mediastinum (H/M) ratios were significantly lower in patients with PAF, IPD, or DLB than in patients with CBD, PSP, or MSA and in the controls. H/M ratios were lower for delayed images than for early ones in patients with PAF, IPD, or DLB, whereas the ratios were higher for delayed images in patients with CBD and in the controls. **Conclusion:** Cardiac sympathetic denervation and enhanced washout of $^{123}$I-MIBG from sympathetic nerve terminals may develop in parallel in patients with PAF, IPD, or DLB.

**Key Words:** Parkinson’s disease; myocardial MIBG scintigraphy; dementia with Lewy bodies; pure autonomic failure


Evidence indicates that cardiac uptake of $^{123}$I-metaiodobenzylguanidine (MIBG) is reduced in patients with Parkinson’s disease (PD) or dementia with Lewy bodies (DLB) (1–4). Reduced cardiac uptake may occur even during the early stage and offers a sensitive tool with which to differentiate PD and DLB from other disorders with rigid akinesic symptoms and dementia (2–4). PD, DLB, and pure autonomic failure (PAF) have Lewy bodies as a common pathologic feature (5,6) and are considered to be 3 phenotypes of a single disorder that may be called Lewy body disease. Yoshida et al. (7) reported 2 patients with PAF who had reduced myocardial $^{123}$I-MIBG uptake. We performed myocardial $^{123}$I-MIBG scintigraphy on 6 patients with PAF and compared the results with those for patients with PD, DLB, or other neurodegenerative disorders presenting extrapyramidal symptoms and with those for the control patients.

**MATERIALS AND METHODS**

With their informed consent, we studied 130 patients with idiopathic PD (IPD), 21 with DLB, 6 with PAF, 9 with corticobasal degeneration (CBD), 11 with progressive supranuclear palsy (PSP), and 11 with multiple-system atrophy (MSA) who had visited our hospital and undergone $^{123}$I-MIBG myocardial scintigraphy from August 1, 2002, to December 31, 2005. The probable-PD diagnosis was based on the criteria of the United Kingdom Brain Bank (8). If patients with PD had no family history of that disease, they were categorized in the IPD group. The respective diagnoses of probable DLB, CBD, PSP, and MSA were based on the criteria of McKeith et al. (6), Kumar et al. (9), Litvan et al. (10), and Gilman et al. (11). PAF was diagnosed when patients presented with orthostatic hypotension combined with repeated fainting spells and severe reduction of systolic blood pressure (>30 mm Hg) within 3 min after standing and showed no sign of central nervous system degeneration. The controls were 16 patients with neurologic diseases who had no neurodegenerative disorder. None of these patients had a previous history of a heart disease detectable on electrocardiography or of diabetes mellitus, and none had been taking tricyclic antidepressant medication. This study was approved by the Ethical Committee of Okayama Kyokuto Hospital.

The severity of patients’ motor impairment was assessed by Hoehn and Yahr staging. Patients’ cognitive functions were measured by the Mini-Mental State Examination (MMSE). Head-up tilt tests were performed on a motor-driven tilt table, and maximum reduction of systolic blood pressure (ΔSBP) was determined within 3 min after standing.

**$^{123}$I-MIBG Myocardial Imaging**

After a 30-min resting period, patients and controls received an intravenous injection of 111 mBq of $^{123}$I-MIBG (Daichi Radioisotope Laboratories Co.). A planar image of the chest was obtained in an anterior view for 5 min with a double-head Starcam 400AC/T γ-camera (GE Healthcare) after 15 min for the early image and after 4 h for the delayed one (Fig. 1). Photopacb energy...
RESULTS

Statistical Analysis

Intergroup differences in age, disease duration, H/M ratio, and δBP on the head-up tilt test were evaluated by 1-way ANOVA followed by the Scheffe’ test post hoc. Intergroup differences in the Hoehn and Yahr stages and MMSE scores were determined by the Kruskal–Wallis and Mann–Whitney U tests. The paired t test was used to evaluate differences in H/M ratios obtained from early and delayed images of the same group.

DISCUSSION

Our findings clearly show that patients with PAF had the same degree of reduced myocardial $^{123}$I-MIBG uptake as did those with IPD or DLB. Taking into account the shorter disease duration for patients with PAF than for those with IPD, the PAF H/M ratio may decrease earlier during the disease. Sympathetic dysfunction determined from the
disease duration was significantly shorter in patients with PAF and DLB than in those with IPD. Hoehn and Yahr stages were the same for IPD and DLB. The mean MMSE score was lower for patients with DLB than for those with IPD and was lower for patients with IPD than for those with PAF. Reduction of systolic blood pressure on standing was more marked in patients with PAF than in those with IPD or DLB.

Patients’ H/M ratios for each disease are listed in Table 1 and Figure 2. Patients with PAF, IPD, or DLB had a significantly lower H/M ratio for both the early and the delayed images than did those with CBD, PSP, or MSA and the controls. H/M ratios for the controls were considered to be normal, and the lower limits (mean – 2 SDs) were set at 1.84 and 1.78 for the early and delayed images, respectively. Thus, no decrease was found for patients with CBD, PSP, or MSA.

In each type of Lewy body disease, the H/M ratio was significantly lower for the delayed images than for the early one (PAF, value of $t = 4.3$; IPD, $t = 19.7$; DLB, $t = 7.9$; $P < 0.01$). This tendency was preserved in all 27 patients with Lewy body diseases (IPD, 21; DLB, 6) who showed early H/M ratios higher than 1.84. The mean ± SD of their early and delayed H/M ratios were 2.16 ± 0.25 and 1.86 ± 0.25, respectively. The decrease also was significant ($t = 9.1$, $P < 0.01$). Patients with CBD and the controls had significantly higher H/M ratios for the delayed image than for the early image (CBD, $t = -2.6$; controls, $t = -4.0$; $P < 0.05$).

### Table 1

**Patients’ Clinical Characteristics and Myocardial $^{123}$I-MIBG Scintigraphy Results**

<table>
<thead>
<tr>
<th>Patient group</th>
<th>n</th>
<th>Age (y)</th>
<th>Disease duration (y)</th>
<th>Hoehn and Yahr stage On</th>
<th>Off</th>
<th>MMSE</th>
<th>δBP</th>
<th>H/M ratio Early</th>
<th>Delayed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16</td>
<td>75.4 ± 6.8</td>
<td>7.0 ± 5.9</td>
<td>3.1 ± 1.0</td>
<td>3.4 ± 1.1</td>
<td>22.5 ± 6.5</td>
<td>27.5 ± 23.2</td>
<td>2.26 ± 0.21</td>
<td>2.48 ± 0.35</td>
</tr>
<tr>
<td>IPD</td>
<td>130</td>
<td>72.3 ± 8.2</td>
<td>2.8 ± 2.8*</td>
<td>3.3 ± 1.2</td>
<td>3.4 ± 1.3</td>
<td>17.7 ± 6.1*</td>
<td>21.6 ± 23.3</td>
<td>1.69 ± 0.44*</td>
<td>1.47 ± 0.37*</td>
</tr>
<tr>
<td>DLB</td>
<td>21</td>
<td>75.3 ± 6.0</td>
<td>1.1 ± 1.1*</td>
<td>0*</td>
<td>0*</td>
<td>28.5 ± 1.9*</td>
<td>63.5 ± 18.8*</td>
<td>1.47 ± 0.19*</td>
<td>1.32 ± 0.16*</td>
</tr>
<tr>
<td>PAF</td>
<td>6</td>
<td>71.3 ± 6.6</td>
<td>3.1 ± 3.1</td>
<td>3.4 ± 1.0</td>
<td>3.4 ± 1.0</td>
<td>22.9 ± 6.9</td>
<td>ND</td>
<td>2.51 ± 0.44</td>
<td>2.75 ± 0.51</td>
</tr>
<tr>
<td>CBD</td>
<td>9</td>
<td>66.2 ± 7.4</td>
<td>2.5 ± 1.7</td>
<td>3.3 ± 0.6</td>
<td>3.3 ± 0.6</td>
<td>25.8 ± 3.0</td>
<td>ND</td>
<td>2.45 ± 0.37</td>
<td>2.57 ± 0.38</td>
</tr>
<tr>
<td>PSP</td>
<td>11</td>
<td>74.6 ± 4.6</td>
<td>2.3 ± 1.3</td>
<td>3.0 ± 1.0</td>
<td>3.0 ± 1.0</td>
<td>29.3 ± 1.0</td>
<td>20.7 ± 25.7</td>
<td>2.54 ± 0.29</td>
<td>2.53 ± 0.41</td>
</tr>
<tr>
<td>MSA</td>
<td>11</td>
<td>67.8 ± 7.8</td>
<td>2.5 ± 1.7</td>
<td>3.3 ± 0.6</td>
<td>3.3 ± 0.6</td>
<td>25.8 ± 3.0</td>
<td>ND</td>
<td>2.45 ± 0.37</td>
<td>2.57 ± 0.38</td>
</tr>
</tbody>
</table>

*Values for IPD, DLB, and PAF differ significantly from values for IPD ($P < 0.05$).
†Values for IPD, DB, and PAF differ significantly from values for IPD and DB ($P < 0.05$).
‡Values for IPD, DB, PAF, CBD, PSP, MSA, and controls differ significantly from values for CBD, PSP, MSA, and controls ($P < 0.05$).
δBP = maximum reduction of systolic blood pressure within 3 min of standing after motor-driven tilt-table test; ND = not determined.

Data are mean ± SD.
sympathetic nerve terminals may therefore precede their loss. An enhanced washout of $^{123}$I-MIBG on the delayed image may be more sensitive than a reduced uptake of $^{123}$I-MIBG for differentiating Lewy body disorders from other neurodegenerative diseases.

**CONCLUSION**

Myocardial $^{123}$I-MIBG uptake is reduced, and washout enhanced, from sympathetic nerve terminals in PAF and in other Lewy body diseases, including IPD and DLB. Because this reduction and enhanced washout occur earlier during these diseases, their time of appearance may prove a sensitive way to differentiate PAF and other Lewy body diseases from MSA and other neurodegenerative disorders that present with extrapyramidal or autonomic dysfunction.

**REFERENCES**