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Iodine-123 Metaiodobenzylguanidine Scintigraphic Assessment of Myocardial Sympathetic Innervation in Patients With Familial Amyloid Polyneuropathy

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Objectives. **This study attempted to assess myocardial sympathetic innervation using iodine-123 (I-123) metaiodobenzylguanidine (MIBG) imaging in patients with familial amyloid polyneuropathy.**

Background. **Signs and symptoms of cardiac autonomic dysfunction are commonly seen in patients with cardiac amyloidosis. However, the incidence and magnitude of abnormalities in myocardial sympathetic nerve function by means of I-123 MIBG imaging and their relation to clinical findings, cardiac function and the results of thallium-201 (Tl-201) and technetium-99m pyrophosphate (Tc-99m PYP) myocardial scanning have not yet been clarified.**

Methods. **We performed M-mode, two-dimensional and Doppler echocardiography and I-123 MIBG, Tl-201 and Tc-99m PYP imaging of the heart in 12 patients with familial amyloid polyneuropathy and biopsy-proved cardiac amyloidosis.**

Results. **Ten of 12 patients had no clinical evidence of overt heart disease, but left ventricular (LV) wall thickening was observed in 4 of these 10. Left ventricular percent fractional shortening and Doppler transmitral flow velocity patterns were found to be normal in all 12 patients. Eight of 12 patients showed no myocardial MIBG accumulation, with limited uptake in the remaining 4 demonstrated only in the LV anterior wall. Diffuse but mild myocardial uptake of Tc-99m PYP occurred in only 4 of 12 patients, and all 12 had normal results on Tl-201 myocardial scanning. Complete defects on myocardial MIBG scans were found in five of eight patients with negative findings on Tc-99m PYP myocardial scanning. The incidence and magnitude of myocardial uptake of MIBG were independent of clinical findings, extent of endomyocardial amyloid deposition, electrocardiographic QRS voltage and ventricular wall thickness.**

Conclusions. **Patients with familial amyloid polyneuropathy show a high incidence of myocardial adrenergic denervation with viable myocardium that can be identified very early in cardiac amyloidosis, before the development of clinically apparent heart disease, ventricular wall thickening, significant LV systolic and diastolic dysfunction and positive findings on Tc-99m PYP myocardial scanning.**

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Recent studies (1–4) have shown that iodine-123 (I-123) metaiodobenzylguanidine (MIBG), a radiolabeled analog of the adrenergic blocking agent guanethidine, is taken up by myocardial sympathetic nerves and behaves quantitatively similar to norepinephrine. Because myocardial accumulation of MIBG and its relation to myocardial tissue norepinephrine content have been extensively studied and validated (5,6), MIBG scintigraphy is widely used to assess cardiac adrenergic nerve function. Alterations in MIBG concentrations reflect integrity and function of adrenergic nerves. Decreased cardiac uptake of MIBG has been identified in diseases or pathologic conditions in which norepinephrine content or uptake, or both, is reduced, such as cardiomyopathies (7–10), myocardial infarction (11–14), congestive heart failure (8,15,16), generalized autonomic neuropathies associated with diabetes mellitus (17–19) and Shy-Drager syndrome (17,20), transplanted heart (21,22), idiopathic long QT syndrome (23) and neuromuscular disease (24).

Familial amyloid polyneuropathy is a hereditary systemic amyloidosis with polyneuropathy that shows chronic progression and variable degrees of amyloid infiltration into the heart (25–27). One of the most common symptoms is related to autonomic dysfunction involving the cardiovascular, gastrointestinal and urogenital systems (26,27), and several investigators (28) have demonstrated involvement of the cardiac autonomic nervous tissues innervating the sinoatrial and atrioventricular (AV) nodes secondary to extensive amyloid deposition. However, there have been no precise reports on myo-

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Abbreviations and Acronyms

AV	=	atrioventricular
ECG	=	electrocardiogram, electrocardiographic
I-123 MIBG	=	iodine-123 metaiodobenzylguanidine
LV	=	left ventricle, left ventricular
RV	=	right ventricular
SPECT	=	single-photon emission computed tomography
Tc-99m PYP	=	technetium-99m pyrophosphate
Tl-201	=	thallium-201

cardial sympathetic nervous activity in this disorder by I-123 MIBG scintigraphy.

The present study was designed to assess the incidence and magnitude of abnormalities in myocardial sympathetic nerve dysfunction by means of I-123 MIBG imaging and to determine their relation to clinical findings, cardiac function and the results of myocardial thallium-201 (Tl-201) and technetium-99m pyrophosphate (Tc-99m PYP) scanning in patients with familial amyloid polyneuropathy.

Methods

Patients. We studied 12 patients with familial amyloid polyneuropathy (six men, six women; 17 to 44 years old, mean [±SD] age 38.3 ± 8.1) who were referred to us from several locations in Nagano Prefecture in the central part of Japan (26,27). The diagnosis was based on neurologic findings and pedigrees and confirmed by amyloid deposition in biopsy specimens obtained from the stomach, rectum, sural nerve or abdominal fat tissue. Right ventricular (RV) endomyocardial biopsy was performed in 10 of the 12 patients, and histologic evidence of amyloid deposition was found in all 10. All patients had a complete history taken, physical examination and autonomic function tests examining blood pressure response to standing, heart rate variability at rest using the RR interval coefficient of variation on the electrocardiograms (ECG) (29) and plasma norepinephrine levels. They also underwent chest roentgenographic; ECG; M-mode, two-dimensional and Doppler echocardiographic studies; and I-123 MIBG, Tl-201 and Tc-99m PYP scintigraphic examinations. No patient had any other disease, such as diabetes mellitus, that could contribute to a cardiac adrenergic neuropathy, and none were taking medications that could interfere with MIBG uptake and assessment of autonomic function. Correlations between I-123 MIBG scintigraphic findings and the degree of neurologic disabilities, duration of illness, extent of endomyocardial amyloid deposition, ECG QRS voltage, echocardiographic findings and the results of Tl-201 and Tc-99m PYP myocardial scanning were then examined. Neurologic disabilities were classified according to the criteria of Coutinho et al. (30) as follows: *stage I* = peripheral neuropathy limited to the lower limbs; *stage II* = neuropathy involving both the lower and upper limbs; and *stage III* = bedridden because of extensive progressive neuropathy.

In addition, we examined 15 normal volunteers (eight men, seven women; 24 to 47 years old, mean age 39.8 ± 9.3) without evidence of cardiovascular disease. All had normal findings on their physical examination, chest roentgenograms and ECGs, and they served as normal control subjects. They also underwent autonomic function tests. Written informed consent was obtained from each subject included in the study.

Echocardiographic examinations. M-mode echocardiograms derived from two-dimensional images were obtained, and the measurements included left ventricular (LV) internal end-diastolic and end-systolic dimensions and ventricular septal wall thickness and LV posterior wall thickness at end-diastole (31). Left ventricular percent fractional shortening was then calculated. Doppler recordings of transmitral flow velocity were obtained through an apical four-chamber view with a Doppler cursor oriented parallel to the long-axis plane of the LV, and the sample volume was carefully placed at the tip of the mitral leaflets (32).

Scintigraphic examinations. Iodine-123 MIBG scanning was carried out within 1 week of the ECG, echocardiographic and Tl-201 and Tc-99m PYP scintigraphic examinations. The scintigraphic studies were performed with a scintillation camera (ZLC 7500, Siemens, Solana, Sweden) with a parallel-hole general-purpose collimator (low energy, high resolution type). The camera was interfaced to a digital data acquisition system (Scintipac 2400, Shimazu, Kyoto, Japan). The images were independently examined by two experienced nuclear cardiologists (M.T., T.F.) without knowledge of the clinical findings.

Thallium-201 imaging. Three millicuries of Tl-201 chloride was administered intravenously at rest. Scintigrams were obtained in the anterior, 45° left anterior oblique and left lateral views 10 min after the injection, and 500,000 counts/view were acquired. In each Tl-201 study, single-photon emission computed tomography (SPECT) was applied. Thirty-two projections were acquired over a 180° arc from right anterior oblique to left posterior oblique views with 30 s/step. Oblique-angle myocardial tomograms were reconstructed using a filtered backprojection algorithm and a Hamming/Hann filter. The reconstructed tomographic data were displayed in three planes, including the horizontal long axis, vertical long axis and short axis. A 20% energy window was centered at 72 and 169 keV.

Iodine-123 MIBG imaging. Four millicuries of I-123 MIBG was injected as an intravenous bolus with patients in a relaxed supine position. Scintigrams were obtained in the anterior, 45° left anterior oblique and left lateral views at 30 min (early images) and 3 h (delayed images) after the injection. A 20% window centered at 159 keV was used, and 500,000 counts/view were collected. The SPECT studies were carried out in the same manner as in the Tl-201 SPECT methods, including the settings of the cardiac axes.

Technetium-99m PYP imaging. Scintigrams were recorded 3 h after intravenous injection of 20 mCi of Tc-99m PYP. A 20% window centered at 140 keV was used, and 500,000 counts/image were acquired. Four images, including anterior, 45° left anterior oblique, left lateral and 30° right anterior oblique views, were obtained. The images were graded accord-

Table 1. Clinical, Echocardiographic and Myocardial Scintigraphic Findings in 12 Patients With Familial Amyloid Polyneuropathy

Pt No./ Gender	Age (yr)	Disease Stage*	Duration of Disease (yr)	Endomyocardial Amyloid Deposition	VST (mm)	PWT (mm)	FS (%)	TMFV Pattern	Myocardial Uptake		
									I-123 MIBG	Tl-201	Tc-99m PYP†
1/F	42	II	7	Moderate	8	10	52	Normal	0	Normal	2
2/F	44	I	3	Mild	10	10	40	Normal	0	Normal	1
3/F	42	III	6	Moderate	9	8	50	Normal	Anterior	Normal	2
4/M	38	II	10	Moderate	10	11	43	Normal	Anterior	Normal	1
5/M	34	III	4	Severe	14	13	44	Normal	0	Normal	0
6/M	17	I	1	Moderate	10	9	38	Normal	Anterior	Normal	0
7/M	49	II	12	Moderate	14	12	34	Normal	0	Normal	2
8/F	38	I	0.6	Mild	10	9	38	Normal	0	Normal	1
9/M	39	I	5	Moderate	11	10	40	Normal	0	Normal	1
10/F	34	I	5	Mild	11	10	32	Normal	Anterior	Normal	0
11/M	36	III	6	NA	13	13	31	Normal	0	Normal	2
12/F	46	II	4	NA	13	12	33	Normal	0	Normal	1

*See Methods for definition of disease stages. †See Methods for explanation of uptake grades. Anterior = left ventricular anterior wall; FS = fractional shortening; I-123 MIBG = iodine-123 metaiodobenzylguanidine; NA = not available; Pt = patient; PWT = posterior wall thickness; Tc-99m PYP = technetium-99m pyrophosphate; Tl-201 = thallium-201; TMFV = transmitral flow velocity; VST = ventricular septal wall thickness; 0 = absent.

ing to level of radioactivity in the cardiac region as follows: 0 = negative; 1 = faint activity in the heart; 2 = definite activity but less intense than that in the ribs; 3 = intensity equal to that in the ribs but less than that in the sternum; and 4 = intensity equal to or greater than that in the sternum. Diffuse myocardial uptake of grade ≥2 were considered positive scans according to the criteria of Parkey et al. (33). SPECT studies were then performed in all patients. The gantry was rotated 180° around the long-axis of the patient, collecting data from 32 views. These images were reconstructed into 12-mm thick multiple slices in the transaxial plane (34).

Statistical analysis. Results are expressed as mean value ± standard deviation. The chi-square test was used to compare the incidence of the variables, and the unpaired *t* test was performed to analyze the differences in the results of the autonomic function tests and ECG QRS voltage. A probability value <0.05 was considered statistically significant.

Results

Clinical presentation. All patients had one or more of the autonomic symptoms, including alternating constipation and diarrhea, nausea and vomiting, hypotension, impotence, dysuria and urinary incontinence, and trophic changes of the skin and anhydrosis. Patients were classified neurologically as follows: stage I in five patients; stage II in four; and stage III in three (Table 1). Duration of the illness from the onset of symptoms ranged from 1 to 10 years (0 to 5 years in seven patients, >5 years in five; mean 5.3 ± 3.3 years) (Table 1). Right ventricular endomyocardial amyloid deposition was found to be mild in 3 of 10 patients, moderate in 6 and severe in 1 (Table 1). Two patients (Patients 4 and 5) had had a permanent pacemaker implanted because of Adams-Stokes syndrome due to severe sinus node dysfunction and complete AV block, respectively, and the remaining 10 had no clinical evidence of overt heart disease, such as congestive heart failure and restrictive cardiomyopathy. Chest roentgenographic examination revealed cardiac enlargement in none of the 12 patients. One or more 12-lead ECG abnormalities were present in eight patients, but low voltage in either limb or precordial leads (35) was absent in all.

All patients had postural hypotension with a systolic blood pressure difference >10 mm Hg. The pressure difference in response to standing was significantly greater in patients than in normal control subjects (19.7 ± 6.6 vs. 1.3 ± 2.9 mm Hg, $p < 0.001$). The coefficients of variation of the RR interval on the rest ECG averaged 1.78 ± 0.31 in patients 30 to 39 years old and 1.17 ± 0.25 in those 40 to 49 years old, compared with the coefficients in normal subjects (5.23 ± 2.58 for 30 to 39 years old, $p < 0.05$, and 4.22 ± 1.71 for 40 to 49 years old, $p < 0.05$). Basal plasma norepinephrine levels in eight patients in whom these could be measured were within normal range in all eight.

Echocardiographic findings. Thickened ventricular walls were present in only 4 (33%) of 12 patients, whereas LV chamber size, percent fractional shortening and Doppler transmitral flow velocity patterns were normal in all 12 (Table 1).

Myocardial scintigraphic findings. *Thallium-201 imaging.* Both plannar and SPECT images showed completely normal myocardial perfusion in all 12 patients (Table 1).

Technetium-99m PYP imaging. Diffuse positive myocardial uptake of Tc-99m PYP, which was judged to be mild (grade 2), was observed in 4 (33%) of 12 patients, whereas scan results were negative in the remaining 8 (Table 1).

Iodine-123 MIBG imaging. Eight (67%) of 12 patients had no LV myocardial localization of MIBG on either the early or delayed images (Fig. 1); the remaining 4 patients showed myocardial uptake of MIBG in the LV anterior wall only (Table 1). No patient exhibited RV MIBG uptake. Age, gender distribution, duration of the illness, neurologic disabilities, ventricular chamber size, ventricular wall thickness, results of autonomic function tests, basal plasma catecholamine levels and ECG QRS voltage did not differ significantly

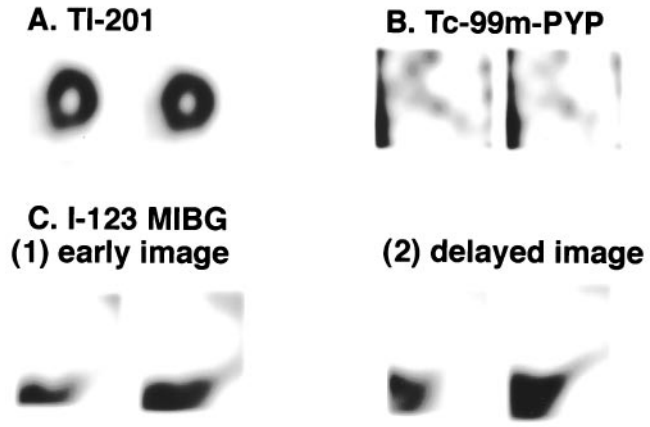

Figure 1. Myocardial scintigraphic images from a 42-year old woman (Patient 2) with biopsy-proved cardiac amyloidosis. **A,** Short-axis images with Tl-201 scintigraphy: myocardial perfusion is completely normal. **B,** Transaxial images with Tc-99m PYP scanning show diffuse but faint myocardial uptake (grade 1). **C,** Both early (**1**) and delayed (**2**) short-axis images with I-123 MIBG scintigraphy demonstrate no myocardial localization.

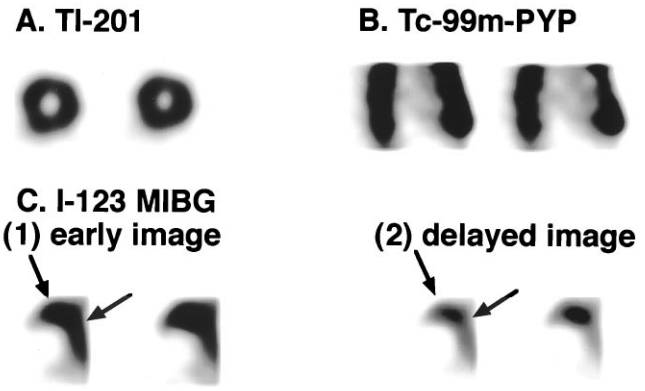

Figure 2. Myocardial scintigrams from a 17-year old man (Patient 6) with biopsy-proved amyloid heart disease. **A,** Short-axis images with Tl-201 scintigraphy reveal normal myocardial perfusion. **B,** Myocardial uptake is not visualized (grade 0) with transaxial images with Tc-99m PYP scanning. **C,** Early (**1**) and delayed (**2**) short-axis images with I-123 MIBG scintigraphy. Myocardial uptake of I-123 MIBG is observed only at left ventricular anterior wall (**arrows**) on both the early and delayed images.

between patients with and without absent myocardial uptake of MIBG. The sum of $SV_1 + RV_6$ in precordial leads in eight patients with complete defects on myocardial MIBG scans was 28.8 ± 6.5 mm versus 29.6 ± 4.7 mm ($p = NS$) in the remaining four patients with limited but positive myocardial uptake of MIBG. There were no significant differences in the incidence of myocardial defects on MIBG scans in relation to neurologic disabilities (three of five patients in neurologic stage I; three of four in stage II; two of three in stage III), duration of the illness (five of seven patients with duration 0 to 5 years; three of five with duration >5 years) and extent of amyloid deposition in the RV endomyocardium (two of three patients with mild, three of six with moderate, one of one with severe deposition). No significant correlations were found between the prevalence of decreased myocardial uptake of MIBG and ventricular wall thickness and the results of Tc-99m PYP scanning. Loss of myocardial uptake of MIBG was found in all patients with ventricular wall thickening and in four of eight without increased wall thickness. Complete defects on myocardial MIBG scans were present in five of eight patients with negative findings on Tc-99m PYP myocardial scanning and in three of four who showed positive myocardial uptake of PYP (Table 1, Fig. 1 and 2). Patient 4 (one of the two patients with permanent pacemaker) had limited myocardial uptake of MIBG, and Patient 5 showed absent myocardial uptake (Table 1).

Clinical course. All patients were followed up for a mean of 15.5 ± 5.8 months (range 9 to 35). No patient died of cardiovascular disease during the follow-up period. However, two patients (Patients 3 and 12) developed severe sinus node dysfunction 5 and 12 months, respectively, after the scintigraphic studies and had a permanent pacemaker implanted. Both patients had shown loss of myocardial uptake of MIBG (Table 1), but neither developed lethal cardiac arrhythmias, and clinical and echocardiographic findings in these two patients were similar to those in the other eight patients without clinically significant bradyarrhythmias.

Discussion

To our knowledge, the present study is the first to use I-123 MIBG scintigraphy to analyze myocardial sympathetic nervous activity in patients with familial amyloid polyneuropathy and biopsy-proved cardiac amyloidosis. Although some of the bedside autonomic function tests, such as sinus arrhythmia during deep breathing, reflect cardiac parasympathetic nervous activity, direct noninvasive methods to assess cardiac sympathetic nervous function are not yet available. The major advantage of I-123 MIBG myocardial scintigraphy is its ability to directly and noninvasively assess cardiac adrenergic innervations in specific anatomic regions, which cannot be accomplished by the traditional autonomic function tests.

Iodine-123 MIBG scintigraphic findings in patients with autonomic dysfunction. Several investigators have reported abnormal myocardial localization and washout of I-123 MIBG in patients with systemic diseases associated with autonomic dysfunction or neuropathies. Nakajo et al. (20) found rapid clearance of MIBG from the heart in patients with severe autonomic dysfunction compared with that in normal subjects. Sisson et al. (17) noted little or no myocardial uptake of MIBG despite normal Tl-201 myocardial perfusion in patients with autonomic neuropathies due to diabetes mellitus, Shy-Drager syndrome and unknown origin, which was strikingly different from the uptake in normal subjects. All patients had severe autonomic dysfunction assessed by the simple bedside tests. The other investigators (18,19) pointed out greatly diminished accumulation of MIBG in the heart of patients with diabetes

mellitus and apparent autonomic dysfunction. The results were consistent with those of a previous postmortem study (36) that demonstrated reduced concentration of myocardial norepinephrine in these patients. However, the investigators failed to find strong correlations between the results of clinical assessment of autonomic dysfunction and the magnitude of abnormalities in myocardial MIBG uptake (19).

Involvement of cardiac autonomic nervous system in familial amyloid polyneuropathy. In contrast to other forms of cardiac amyloidosis, such as primary amyloidosis, in patients with familial amyloid polyneuropathy, LV systolic function is generally preserved, and congestive heart failure rarely occurs until late in the course of the disease (32,37,38). One of the most important cardiac manifestations in this disease is a high incidence of cardiac conduction disturbances (39–41). In general, previous studies have attributed these abnormalities only to direct amyloid infiltration into the cardiac conduction system. However, accumulating evidence suggests that cardiac autonomic denervation is another contributory factor accounting for various kinds of conduction disturbances seen in patients with familial amyloid polyneuropathy. Some investigators (28) demonstrated in an autopsy study that in addition to the involvement by direct amyloid deposition, autonomic innervation to the cardiac conduction system was severely impaired due to marked degeneration of the autonomic nerves secondary to amyloid infiltration and that these pathologic changes were most striking at the sinoatrial node and less so at the AV node. Furthermore, pathologic findings of the conduction system corresponded well with the ECG conduction disturbances during life (28).

Myocardial uptake of I-123 MIBG in familial amyloid polyneuropathy. In the present study, we found complete defects on MIBG myocardial scans in 8 of 12 patients and limited uptake in the remaining 4 in association with severe systemic autonomic dysfunction. The incidence and magnitude of myocardial accumulation of MIBG were independent of clinical findings, including neurologic disabilities, duration of the illness, extent of endomyocardial amyloid deposition, ECG QRS voltage and ventricular wall thickness. These findings strongly suggest that cardiac adrenergic denervation due to autonomic nervous degeneration (28) accounts for alterations in I-123 MIBG myocardial imaging in patients with familial amyloid polyneuropathy. The presence of small localized concentrations of MIBG in the LV anterior wall in some patients indicates that myocardial sympathetic innervation is not equally impaired in this disease.

As we have previously reported (34), Tc-99m PYP scintigraphy may have the potential to detect early myocardial amyloid infiltration in patients with familial amyloid polyneuropathy because positive findings on myocardial pyrophosphate scans can be seen even in the absence of identifiable heart disease, ventricular wall thickening or abnormal LV systolic function. Most of our patients lacked these clinical features. Thus, the majority of them were considered to be in the early stage of cardiac amyloidosis (32,34,37,38), and we confirmed the ability of Tc-99m PYP scanning to detect early myocardial amyloid infiltration in some patients. Furthermore, we demonstrated complete loss or limited uptake of MIBG by the heart in five of eight patients with negative findings on Tc-99m PYP scans whose myocardial amyloid deposition was considered to be mild to moderate. These findings indicate that myocardial sympathetic denervation may occur in the very early stages of cardiac amyloidosis in familial amyloid polyneuropathy.

Before the scintigraphic studies, two patients had had a permanent pacemaker implanted due to the clinically significant bradyarrhythmias. During the follow-up period, an additional two patients developed severe sinus node dysfunction. Three of these four patients exhibited complete defects on MIBG myocardial scans, and the remaining patient showed limited uptake of MIBG. It is not possible to determine from our results why some patients developed clinically significant bradyarrhythmias and others did not because we could not find any differences in the clinical findings and the results of MIBG scanning between them, and our study was limited to a small number of patients.

Clinical implications. Cardiac MIBG scintigraphy has been reported (42) to have prognostic value in patients with congestive heart failure compared with other noninvasive hemodynamic indexes. In addition, a high prevalence of myocardial sympathetic denervation has been described (43) in patients with ventricular tachycardia in the absence of coronary artery disease. Although clinically significant ventricular arrhythmias are not common in patients with familial amyloid polyneuropathy (39–41), some investigators (44) have pointed out an association between complex ventricular arrhythmias and cardiac death in patients with primary amyloidosis. Thus, further investigation is required to assess the role of adrenergic denervation in the development of complex ventricular arrhythmias and the exact prognostic significance of MIBG scanning in other forms of cardiac amyloidosis, such as primary amyloidosis.

Recent reports (45,46) suggest that liver transplantation is becoming a new promising therapeutic approach in patients with familial amyloid polyneuropathy because clinical findings, including neuropathic and autonomic symptoms, generally improve or do not progress after transplantation. This accompanies a decrease in plasma amyloid protein, a variant transthyretin, which is known to be produced in the liver (45,46). However, there have been no reports on the effects of liver transplantation on the cardiac autonomic nervous system. Therefore, it is of great interest to examine whether myocardial sympathetic reinnervation may occur in this disease.

Study limitations. There were several limitations to our study. The incidence and magnitude of myocardial uptake of MIBG were not correlated with clinical findings, especially with the results of the autonomic function tests. However, basal plasma norepinephrine levels, which we measured, are generally insensitive indicators of adrenergic dysfunction, and stimulated levels, obtained by patients standing up, would have been more sensitive. Therefore, a better relation between assessment of autonomic dysfunction and the results of MIBG

imaging might have been obtained if we had performed more comprehensive autonomic function tests, such as examining changes in the RR interval in response to the Valsalva maneuver, deep breathing, standing and sustained hand grip (29,47). Another consideration was related to the dose and activity of MIBG. However, we used a standard method of MIBG scanning, including a dose of MIBG, and the normal subjects who underwent MIBG scanning on the same day showed uniform uptake in the heart. Thus, the dose and activity of MIBG were considered to be appropriate in the present study.

Conclusions. We assessed myocardial sympathetic innervation using I-123 MIBG imaging and its relation to clinical findings, cardiac function and the results of Tl-201 and Tc-99m PYP myocardial scanning in 12 patients with familial amyloid polyneuropathy. Ten of 12 patients had no clinical evidence of overt heart disease and normal ventricular wall thickness, and all 10 showed normal LV systolic and diastolic function, as well as normal Tl-201 myocardial perfusion. Eight of 12 of the patients had absence of myocardial MIBG accumulation, and the remaining 4 showed limited uptake; only 4 of 12 patients exhibited diffuse but mild myocardial uptake of Tc-99m PYP. Complete defects on myocardial MIBG scans were found in 5 of 8 patients with negative findings on Tc-99m PYP myocardial scanning. The incidence and magnitude of myocardial uptake of MIBG were not correlated with clinical findings, extent of endomyocardial amyloid deposition, ECG QRS voltage and ventricular wall thickness. Thus, patients with familial amyloid polyneuropathy show a high incidence of cardiac adrenergic denervation with viable myocardium that can be identified very early in cardiac amyloidosis.

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