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Clinical significance of reverse redistribution on resting thallium-201 imaging in patients with vasospastic angina

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To evaluate the clinical significance of reverse redistribution (RR) of resting ^{201}Tl single photon emission computed tomography (SPECT) in patients with vasospastic angina (VSA), we performed left ventriculography, coronary angiography and resting ^{201}Tl-SPECT in 22 patients with VSA. Left ventriculography showed abnormal wall motion in 17 of 22 patients (77%) and 37 of 154 segments. Thirty-one of these 37 segments (84%) were within the area perfused by coronary arteries showing acetylcholine-induced vasospasm. On ^{201}Tl images, abnormal findings were observed in 11 of 22 patients (50%), and among them, 7 patients (32%) had RR. Seven of 37 segments (19%) having abnormal regional wall motion had RR of ^{201}Tl, and in 6 of these 7 segments (86%), accumulation of ^{123}I-BMIPP was found to be reduced.

We conclude that repetitive brief myocardial ischemia may cause myocardial injuries in patients with VSA, and that the presence of RR of ^{201}Tl indicates the presence of myocardial injury in these patients.

Key words: thallium-201, reverse redistribution, vasospastic angina

INTRODUCTION

IT IS WELL KNOWN that patients with vasospastic angina (VSA) having normal coronary arteries often have abnormal left ventricular wall motion,[1] abnormal myocardial free fatty acid utilization,[2] and regional myocardial sympathetic dysinnervation[3] even during attack-free periods, all suggesting myocardial stunning. In fact, some authors have described myocardial stunning after coronary vasospasm.[4–6]

Nevertheless, little is known about the relationship between abnormal left ventricular wall motion and reverse redistribution (RR) on resting ^{201}Tl imaging in patients with VSA, although the latter is another important phenomenon in cases of myocardial stunning.[7–9] In this study, we performed resting single photon emission computed tomography (SPECT) with ^{201}Tl and ^{123}I-β-methyl-p-iodophenyl pentadecanoic acid (BMIPP), and left ventriculography (LVG) to clarify the clinical implication of RR on resting ^{201}Tl in patients with VSA.

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MATERIALS AND METHODS

Recruitment of patients

Twenty-two patients with VSA (19 men and 3 women; 46 to 80 years old, mean age 64 ± 9) were recruited (Table 1). All patients had chest pain which appeared at rest rather than on exertion. None showed an increase in the serum creatine kinase level after anginal attack or an abnormal Q wave on a 12-lead Electrocardiogram (ECG). Thirteen patients were current smokers, 4 had diabetes, 2 had hypertension and 2 had hypercholesterolemia. Patients with prior myocardial infarction, significant coronary stenosis (> 50%), left ventricular hypertrophy, right or left bundle-branch block or any other systemic disorder known

to affect left ventricular function or metabolism were excluded. Written informed consent was obtained from all subjects.

LVG and coronary angiography

Biplane LVG and coronary angiography were performed in all subjects prior to radionuclide studies after discontinuation of antianginal drugs for several days, except for sublingual nitroglycerin. The mean interval from the last anginal attack to angiography was 15.5 days (range 2 to 25 days). On LVG, left ventricular silhouette was divided into 7 segments (Fig. 1) and regional wall motion was visually scored on a 5-point scale (0: normal, 1: mild hypokinesis, 2: severe hypokinesis, 3: akinesis, 4: dyskinesis) by two experienced observers.[10] VSA was confirmed by coronary artery spasm, defined as total or subtotal coronary occlusion associated with chest pain and ischemic ST-segment deviations, induced by intracoronary injection of acetylcholine.[11] Fixed coronary stenosis was measured with quantitative cardiovascular angiographic software (Automated Coronary Analysis D.C.I. Philips, USA) after nitroglycerin administration. Significant stenosis was defined as luminal narrowing of > 50%.

SPECT imaging and analysis

In all subjects, ^{201}Tl and ^{123}I-BMIPP dual SPECT imaging were performed within two weeks after coronary angiography and LVG. None had anginal attacks between angiography and SPECT studies. After overnight fasting, ^{123}I-BMIPP-SPECT images were acquired at rest, 20 min after administration of 111 MBq of ^{123}I-BMIPP. 111 MBq of ^{201}Tl was then injected, followed by SPECT acquisition 10 min (rest imaging) and 3 hours later (redistribution imaging).[12] The reconstructed SPECT images of the left ventricular slice (1 vertical long axial slice and 1 horizontal long axial slice) were divided into 7 segments to compare the regional uptake of tracer to regional wall motion on LVG (Fig. 1). The myocardial accumulation of ^{123}I-BMIPP and ^{201}Tl were assessed visually by 2 independent observers using a 4-point defect score (0; normal uptake, 1; mildly reduced uptake, 2; moderately reduced uptake, 3; severely reduced uptake). The abnormal tracer uptake was a defect score of 2 or 3, and normal was 0 or 1. Furthermore, on rest and redistribution ^{201}Tl images, we defined 3 patterns of abnormal findings as follows. Redistribution (RD): abnormal uptake of ^{201}Tl on rest images altered normal uptake on redistribution images. Reverse redistribution (RR): normal uptake of ^{201}Tl on rest images altered abnormal uptake on redistribution images. Fixed defect (FD): abnormal uptake of ^{201}Tl is observed on both rest and redistribution images. In each patient, regional left ventricular wall motion and tracer uptake were compared.

Table 1 Characteristics of the patients

Patrent	Age	Sex	Vasoconstriction	LVG	Tl	BMIPP
1	65	M	LAD	2 (MH) 3 (SH)	3 (RR)	normal
2	70	M	LAD/Cx	2 (MH)	normal	normal
3	71	M	Cx	2, 7 (MH)	7 (FD)	4 (MR) 7 (SR)
4	60	M	LAD/Cx	2 (SH) 3 (MH)	2 (FD)	2 (SR)
5	65	M	Cx	4 (MH) 7 (SH)	4 (RR) 7 (RD)	4, 7 (MR)
6	76	M	Cx	7 (MH)	normal	7 (MR)
7	69	F	LAD	1, 2, 3, 6 (MH)	normal	2, 3 (MR)
8	48	M	LAD	normal	normal	normal
9	59	F	LAD	2, 3, 6 (MH)	2 (RR)	2 (MR) 6 (SR)
10	65	M	RCA/LAD	7 (MH)	normal	normal
11	70	F	RCA/LAD/Cx	normal	normal	2 (MR)
12	53	M	Cx	4 (SH) 5, 7 (MH)	4 (FD) 5 (RR)	4 (SR) 5 (MR)
13	74	M	RCA/LAD/Cx	2 (SH) 3 (MH)	2, 3 (RR)	2, 3, 4 (MR)
14	66	M	LAD	2, 3, 6 (MH)	normal	normal
15	46	M	LAD	2 (SH) 3, 4 (MH)	2 (RR)	2, 3 (MR)
16	79	M	LAD	2 (SH) 6 (MH)	2 (RD)	2 (MR)
17	80	M	RCA/LAD	normal	4, 5 (RR)	normal
18	60	M	Cx	3, 4, 7 (MH)	normal	4, 5 (MR)
19	59	M	Cx	2 (MH) 7 (SH)	7 (FD)	2, 4 (MR) 7 (SR)
20	62	M	RCA	normal	normal	normal
21	54	M	RCA	2 (MH)	normal	normal
22	54	M	RCA/LAD	normal	normal	normal

LVG; left ventriculography, RCA; right coronary artery, LAD; left anterior descending artery, Cx; left circumflex artery, MH; mild hypokinesis, SH; severe hypokinesis, RR; reverse redistribution, FD; fixed defect, RD; redistribution, MR; moderately reduced uptake, SR; severely reduced uptake. Numbers of LVG, Tl and BMIPP were expressed according to Figure 1.

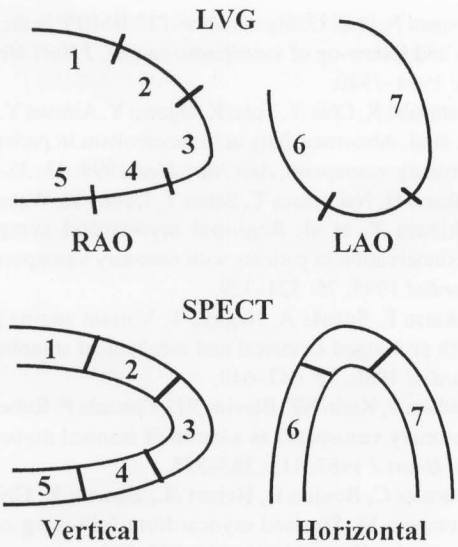

Fig. 1 Schematic representation of LVG and SPECT.

Statistical analysis

All data are presented as the mean value ± SD. Fisher exact test was used to compare proportions. A p value < 0.05 was considered significant.

RESULTS

LVG and coronary angiography

LVG showed abnormal wall motion in 17 of 22 patients (77%), although none showed signs of akinesis or dyskinesis on LVG. On segment-based analysis, abnormal wall motion was found in 37 of 154 segments consisting of 29 segments showing mild hypokinesis and 8 showing severe hypokinesis. Thirty-one of these 37 segments (84%) were within the area perfused by coronary arteries showing acetylcholine-induced vasospasm (Table 1). On ECG during acetylcholine-induced vasospasm, ST-segment elevation was found in 19 patients and ST-segment depression in 3 patients.

^{201}Tl images and left ventricular wall motion

Abnormal ^{201}Tl images were found in 11 of 22 VSA patients (50%) including 10 of 17 patients (59%) with abnormal left ventricular wall motion. RR of ^{201}Tl was observed in 6 of these 10 patients (Table 1, Fig. 2). In contrast, only 1 of 5 patients (20%) with normal left ventricular wall motion had abnormal findings in ^{201}Tl images. The incidence of abnormal ^{201}Tl images in patients with and without abnormal left ventricular wall motion was significantly different ($p < 0.05$).

On segment-based analysis, abnormal ^{201}Tl images were found in 15 of 154 segments including 13 of 37 segments (35%) having abnormal left ventricular wall motion (including 7 segments showing RR; Table 1). On the other hand, only 2 of 117 segments (2%) with normal left ventricular wall motion showed signs of abnormal ^{201}Tl uptake. The incidence of abnormal ^{201}Tl findings for segments with and without abnormal left ventricular wall motion also differed significantly ($p < 0.05$).

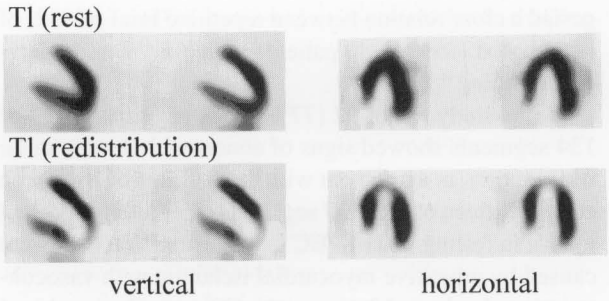

Fig. 2 Representative SPECT images with resting ^{201}Tl (Patient 1 in Table 1). RR of ^{201}Tl is observed at the apical portion of left ventricle.

^{123}I-BMIPP images and left ventricular wall motion

^{123}I-BMIPP images were abnormal in 13 of 22 patients (59%) including 12 of 17 patients (71%) with abnormal left ventricular wall motion, but only 1 of 5 patients (20%) with normal left ventricular wall motion had abnormal ^{123}I-BMIPP images (Table 1). The incidence of reduced ^{123}I-BMIPP uptake in patients with and without abnormal left ventricular wall motion differed significantly ($p < 0.05$).

On segment-based analysis, 24 of 154 segments including 19 of 37 segments (51%) with abnormal wall motion had reduced ^{123}I-BMIPP uptake, but only 5 of 117 segments (4%) with normal left ventricular wall motion had reduced accumulation of ^{123}I-BMIPP. The incidence of reduced ^{123}I-BMIPP uptake in segments with and without abnormal left ventricular wall motion also differed significantly ($p < 0.05$).

Relation between ^{201}Tl and ^{123}I-BMIPP images

Accumulation of ^{123}I-BMIPP was reduced in 12 of 15 segments (80%) showing abnormal findings in ^{201}Tl-SPECT. Moderately reduced ^{123}I-BMIPP uptake was observed in 6 of 9 RR segments (Table 1), but 12 segments without abnormal findings in ^{201}Tl images also showed reduced accumulation of ^{123}I-BMIPP. Of these, 7 segments showed signs of mild hypokinesis and 5 showed normal wall motion.

DISCUSSION

Previous reports have well documented that RR pattern on resting ^{201}Tl image is often observed in patients with acute myocardial infarction, and that the phenomenon is related to myocardial stunning after successful reperfusion.[7–9] Nevertheless, the relationship between abnormal left ventricular wall motion and RR on resting ^{201}Tl-SPECT has not been examined systematically in patients with VSA, although several authors have sug-

gested a close relation between repetitive brief periods of myocardial ischemia in patients with VSA and myocardial stunning.[4–6]

In this study, 17 of 22 (77%) VSA patients and 37 of 154 segments showed signs of abnormal left ventricular wall motion, in agreement with the findings of Nakajima et al.[1] Thirteen of these 37 segments (35%) had abnormal uptake in resting ^{201}Tl-SPECT, suggesting that they were caused by repetitive myocardial ischemia with vasoconstriction. In these 13 segments, FD was observed in 4 segments, RD in 2 segments and RR in 7 segments. Geft et al. reported that brief intermittent periods of myocardial ischemia, which when single did not cause necrosis, had a cumulative effect and caused myocardial necrosis.[13] Since this mechanism of necrosis may be relevant clinically in patients with frequent anginal episodes, FD of ^{201}Tl is considered to reflect myocardial necrosis. On the other hand, Weiss et al.[7] reported that the pattern of RR in resting ^{201}Tl images represented an admixture of viable and nonviable myocardium. Therefore, both necrotic and stunned (viable) myocardium might exist in the region threatened by repeated transient ischemia in patients with VSA.

Reduced ^{123}I-BMIPP accumulations were also found in 13 of 22 (59%) patients and in 19 of 37 segments (51%) showing signs of abnormal left ventricular wall motion. Reduced ^{123}I-BMIPP accumulation was observed in segments showing not only FD and RD, but also in segments showing RR of ^{201}Tl. Since Nakajima et al. observed serial improvement in ^{123}I-BMIPP uptake in VSA patients whose anginal attacks were controlled completely by medical treatment,[1] it is quite likely that RR of ^{201}Tl in our patients also represented stunned but viable segments. Our point of view was also supported by the fact that 6 of 7 segments exhibiting both abnormal left ventricular wall motion and RR of ^{201}Tl showed signs of discordant uptake between ^{201}Tl and ^{123}I-BMIPP (reduced uptake of ^{123}I-BMIPP relative to ^{201}Tl) that has been reported to reflect ischemic but viable myocardium.

We therefore conclude that repetitive brief periods of myocardial ischemia due to coronary spasm could cause myocardial necrosis[13] as well as myocardial injury (stunned but viable), and that RR on ^{201}Tl-SPECT indicates regions with myocardial injury in patients with VSA.

REFERENCES

1. Nakajima K, Shimizu K, Taki J, Uetani Y, Konishi S, Tonami N, et al. Utility of iodine-123-BMIPP in the diagnosis and follow-up of vasospastic angina. *J Nucl Med* 1995; 36: 1934–1940.
2. Watanabe K, Ohta Y, Toba K, Ogawa Y, Aizawa Y, Tanabe N, et al. Abnormal fatty acid metabolism in patients with coronary vasospasm. *Ann Nucl Med* 1999; 13: 33–41.
3. Takano H, Nakamura T, Satou T, Uetani K, Watanabe A, Ishihara T, et al. Regional myocardial sympathetic dysinnervation in patients with coronary vasospasm. *Am J Cardiol* 1995; 75: 324–329.
4. Takatsu F, Suzuki A, Nagaya T. Variant angina pectoris with prolonged electrical and mechanical stunning. *Am J Cardiol* 1986; 58: 647–649.
5. Mathias P, Kerin NZ, Blevins RD, Cascade P, Rubenfire M. Coronary vasospasm as a cause of stunned myocardium. *Am Heart J* 1987; 113: 383–385.
6. Fournier C, Boujon B, Hebert JL, Zamani K, Grimon G, Blondeau M. Stunned myocardium following coronary spasm. *Am Heart J* 1991; 121: 593–595.
7. Weiss AT, Maddahi J, Lew AS, Shah PK, Ganz W, Swan HJ, et al. Reverse redistribution of thallium-201: a sign of nontransmural myocardial infarction with patency of the infarct-related coronary artery. *J Am Coll Cardiol* 1986; 7: 61–67.
8. Fukuzawa S, Ozawa S, Nobuyoshi M, Inagaki Y. Reverse redistribution on Tl-201 SPECT images after reperfusion therapy for acute myocardial infarction: possible mechanism and prognostic implications. *Heart Vessels* 1992; 7: 141–147.
9. Yamagishi H, Itagane H, Akioka K, Ohmura T, Iida H, Tahara A, et al. Clinical significance of reverse redistribution on thallium-201 single-photon emission computed tomography in patients with acute myocardial infarction. *Jpn Circ J* 1992; 56: 1095–1105.
10. Nakano A, Lee J-D, Shimizu H, Tsuchida T, Yonekura Y, Ishii Y, et al. Reciprocal ST-segment depression associated with exercise-induced ST-segment elevation indicates residual viability after myocardial infarction. *J Am Coll Cardiol* 1999; 33: 620–626.
11. Miwa K, Goto M, Lee J-D, Matsuyama F, Shimizu H, Kato T, et al. Supersensitivity of coronary arteries in variant angina to spasm induced by intracoronary acetylcholine. *Am J Cardiol* 1988; 61: 77–82.
12. Yang JT, Yamamoto K, Sadato N, Tsuchida T, Takahashi N, Hayashi N, et al. Clinical value of triple-energy window scatter correction in simultaneous dual-isotope single-photon emission tomography with ^{123}I-BMIPP and ^{201}Tl. *Eur J Nucl Med* 1997; 24: 1099–1106.
13. Geft IL, Fishbein MC, Ninomiya K, Hashida J, Chaux E, Yano J, et al. Intermittent brief periods of ischemia have a cumulative effect and may cause myocardial necrosis. *Circulation* 1982; 66: 1150–1153.