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The Detection of Myocardial Ischemia by Thallium-201 Myocardial Scintigraphy in Patients with Multiple Coronary Arterioventricular Connections

KOICHI KAWAKAMI, M.D., TOSHIO SHIMADA, M.D., SACHIKO YAMADA, M.D., RINJI MURAKAMI, M.D., SHIGEFUMI MORIOKA, M.D., KATSUTOSHI MORIYAMA, M.D.

The Fourth Department of Internal Medicine, Shimane Medical University, Izumo, Japan

Summary: The question of whether myocardial ischemia could be induced in 5 patients with multiple coronary arterioventricular connections by thallium-201 (^{201}Tl) exercise stress myocardial scintigraphy was investigated. Both ST-T changes on ECG and transient myocardial perfusion defects in myocardial scintigrams were observed in 2 patients (40%). In previous reports, all multiple coronary arterioventricular connections, which were shown in angiograms, have been regarded as either Thebesian veins or embryonic sinusoids. However, it is unlikely that Thebesian veins cause myocardial ischemia judging from anatomy. If the vessels cause myocardial ischemia, they should be regarded as multiple coronary arterioventricular fistula. Angiography itself cannot differentiate multiple coronary arterioventricular fistula from Thebesian veins or remnants of embryonic sinusoids. Exercise stress myocardial scintigraphy has a high potential to detect myocardial ischemia due to intracoronary steal. Exercise stress myocardial scintigraphy was used to demonstrate myocardial ischemia in multiple coronary arterioventricular connections. It is concluded that exercise stress myocardial scintigraphy is a reliable test to differentiate multiple coronary arterioventricular fistula from Thebesian veins or remnants of embryonic sinusoids in clinical practice.

Key words: multiple coronary arterioventricular connections, myocardial ischemia, ^{201}Tl myocardial scintigraphy

Address for reprints:

Koichi Kawakami, M.D.
The Fourth Department of Internal Medicine
Shimane Medical University
89-1 Enya-cho, Izumo-shi
Shimane-ken, Japan 693

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Introduction

Multiple coronary arterioventricular connections are relatively rare anomalies, and they were first described as Thebesian veins by Kinard[1] angiographically. Since their report, this anomaly has been regarded as so-called Thebesian venous system. Sheikhazadeh *et al.* reported myocardial ischemia in this cardiac anomaly.[2] Thebesian veins themselves are within the venous system[3] and so are unlikely to cause myocardial ischemia. Lovitt and Lutz also proposed that these vessels were embryological aneurysms of the myocardial vessels.[4] Duckworth *et al.* reported a case with myocardial ischemia detected by exercise myocardial scintigraphy in patients with remnants of embryonic sinusoids.[5] If some multiple coronary arterioventricular connections cause myocardial ischemia, they should be classified as arterioluminal vessels[6] which belong to arteriosystemic fistula. We devised this study to confirm whether these vessels really can cause myocardial ischemia. We speculate that these connections which cause myocardial ischemia should not be regarded as part of the venous system, such as Thebesian veins or as aneurysms, such as remnants of embryonic sinusoids. Exercise stress myocardial scintigraphy is commonly used to detect myocardial ischemia in patients with coronary heart disease.[7] Therefore exercise stress myocardial scintigraphy can be a useful method to detect myocardial ischemia in this heart anomaly in clinical evaluation.

Method

Patients

This study consisted of 5 patients at our university hospital, 2 men and 3 women 51 to 68 years in age (mean 59±6 years) (Table I). Coronary arteriography revealed normal coronary arteries except for multiple arterioventricular connections in all of them. Three patients (60%) had episodes of chest discomfort, but they were atypical rather than exertional or spastic angina pectoris. On ECG at rest, ST-T abnormalities were found in 3 patients (60%).

TABLE I Patient profiles

Case no.	Sex	Age (years)	Resting ECG	Origin of fistula	Site of drainage	Episode of chest discomfort
1	M	51	Flat T wave (II,III, aVF, V_6) AF	LAD,LCx RCA	LV, RV	(−)
2	M	63	Negative T wave (II, III, aVF, V_{3-5})	LAD, LCx RCA	LV	(+)
3	F	57	Negative T wave (II, III, aVF, V_{3-6})	LAD	LV	(−)
4	F	58	WNL	LAD, RCA	LV	(+)
5	F	68	WNL	LAD, LCx	LV	(+)
Mean ± SD		59 ± 6				

Abbreviations: AF = atrial fibrillation; LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery; LV = left ventricle; RV = right ventricle; WNL = within normal limits.

Atrial fibrillation was detected in 1 patient (20%). Two patients (40%) were diagnosed with essential hypertension and had taken drugs. Medication such as beta-adrenergic receptor-blocking agents, calcium-channel blockers, or other drugs which might affect cardiac performance were stopped 3 days before the study. Patients were adequately informed about radiation exposure, potential risks of thallium-201 (^{201}Tl), and exercise stress tests before the study.

Left Ventriculography and Coronary Angiography

Left ventriculograms (LVG) were taken in the 30 degree right anterior oblique and 60 degree left anterior oblique positions. One patient had marked left ventricular hypertrophy which was probably due to hypertension, but her left ventriculogram showed normal wall motion. Other patients had normal left ventricular cavities and normal wall motion. Selective coronary angiogram (CAG) did not show any coronary arterial stenosis. However, in their distal portions, some of the coronary arteries formed a plexus of fine channels in the subendocardial regions of the ventricular wall, emptying directly into the ventricular cavities (Fig. 1). These abnormal vessels arose from one to three coronary arteries. One-vessel involvement was seen in only 1 case (20%), in which the vessel originated from the left anterior descending coronary artery (LAD). In 2 patients, these abnormal vessels arose from 2 different coronary arteries (40%). The LAD and right coronary arteries (RCA) were involved in Case 4. In Case 5, abnormal vessels arose from the LAD and the left circumflex coronary arteries (LCx). Connections involving all three major coronary arteries were found in 2 other patients (40%, Cases 1 and 2).

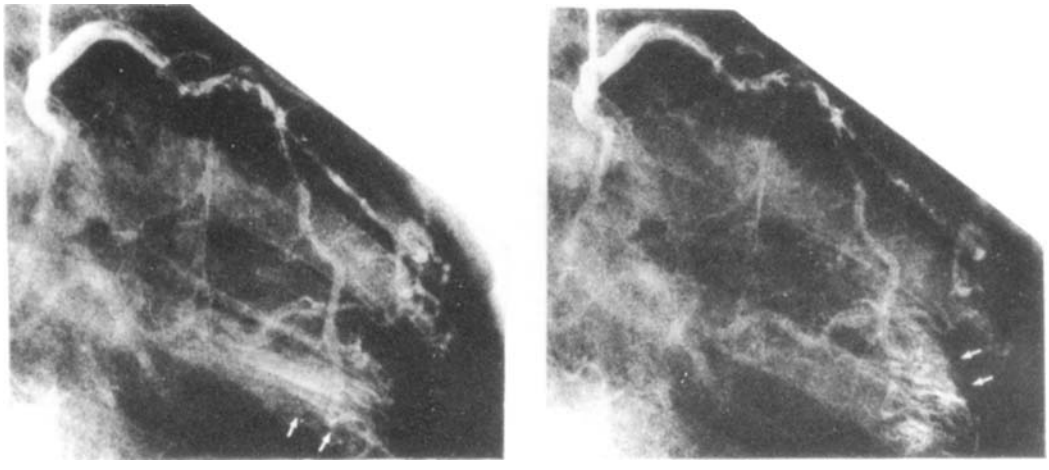

FIG. 1 Selective left coronary arteriogram in Case 1. Contrast medium fills the left ventricle (arrows) via multiple connections (arrows) arising from branches of the anterior descending coronary artery.

Protocol for the Stress Exercise

All exercise studies were performed in the morning on a motorized ergometer machine at supine position using the standard multistage method. Exercise load started at 20 W and was increased incrementally by 20 W at 1 minute intervals. At peak exercise, 111 MBq of ^{201}Tl was injected into a peripheral arm vein and the patients exercised for 1 additional minute. The exercise test was terminated by either ischemic change on the ECG or fatigue. A 12-lead ECG was continuously monitored and recorded at 1 minute intervals, at peak exercise, and 1, 2, and 3 minutes after exercise. The ST-segment displacement was quantified as the vertical distance from the baseline (TP segment) at 80 ms after the J point. The first displacement of ST segment in ECG was computed from the average of 5 consecutive beats; and the second displacement was calculated in the same manner. Blood pressure and heart rate were measured when the ECG was recorded.

Single-Photon Emission Computed Tomography (SPECT)

Stress imaging began at 4 minutes after the injection of ^{201}thallium. To make the SPECT images, the gantry was rotated 180 degrees from a 60° left posterior oblique to a 30° right anterior oblique angle around the long axis of the patient. Thirty images were obtained for 25 seconds each at 6° intervals. Delayed images were recorded 240 minutes after the infusion of ^{201}Tl, in the exact same manner as the initial images. Starcam 400-ACT scintillation camera (General Electric) equipped with a low-energy, all-purpose, parallel-hole collimator, was interfaced to a Starcam computer system. Data were collected in a 128 × 128 matrix. Images were reconstructed into 10-mm thick multiple slices in the transaxial planes by a filtered back-projection method with a Butterworth spatial filter (power factor: 10, cut-off frequency: 0.4 cycles/cm) as a prefilter and a Ramp filter to reconstruct images. Each reconstructed image contained 200,000 to 800,000 counts. The vertical short-axial (frontal), long-axial (sagittal), and transaxial (horizontal) sections of the heart were reconstructed by the method described by Borrello *et al.*[8]

Visual Analysis of SPECT

The SPECT images were visually analyzed by consensus interpretation of two experienced observers who did not have any information of the clinical diagnosis or the angiographic findings. The vertical long axial slices were divided into anterior, apical, and inferior/posterior regions. The short axial slices were divided into anterior, septal, inferior/posterior, and lateral regions. The transaxial slices were divided into septal, apical, and lateral regions. In comparison with myocardial regions of the most intense uptakes on the images, myocardial segment was judged by a 4-point scoring system for each wall: 0 = normal (100–76% of the most intense uptakes), 1 = mildly reduced tracer concentration (75–51% of the most intense uptakes), 2 = moderately reduced tracer concentration (50–26% of the most intense uptakes), 3 = markedly reduced tracer concentration (25–0% of the most intense uptakes).

Results

Exercise Stress Test

Patient profiles on exercise tests are summarized in Table II. Heart rate increased from 67 ± 6 at rest to 128 ± 36 beats/min at peak exercise. Systolic blood pressure also increased from 151 ± 23 to 198 ± 16 mmHg. Maximal exercise load was 99 ± 37 W and exercise capacity of the patients was 403 ± 227 W. These patients had neither chest pain nor other symptoms on exercise. The end point of the study was fatigue in all patients. Electrocardiographic ST-segment depression on exercise was observed in two patients (Cases 1 and 2) (Fig. 2). There was no complica-

TABLE II Summary of the exercise stress test

	HR (beats/min)		SBP (mmHg)			EC(watts)			
Case	R	Ex	R	Ex	DP	Max	Total	ECG changes	Sx
1	82	190	122	176	33,440	125	550	ST depression (II, III, aVF, V_{3-6})	(−)
2	56	116	142	210	24,360	150	725	ST depression (II, III, aVF, V_{4-6})	(−)
3	65	97	178	214	20,758	80	280	(−)	(−)
4	66	122	170	190	23,180	80	280	(−)	(−)
5	66	117	142	202	23,634	60	180	(−)	(−)
Mean ± SD	67 ± 6	128 ± 36	151 ± 23	198 ± 16	25,074 ± 4868	99 ± 37	403 ± 227		

Abbreviations: HR = heart rate; SBP = systolic blood pressure; DP = double products (HR on Ex × BP on Ex); EC = exercise capacity; ECG = electrocardiographic; R = rest; Ex = exercise; Max = maximal; Sx = symptom.

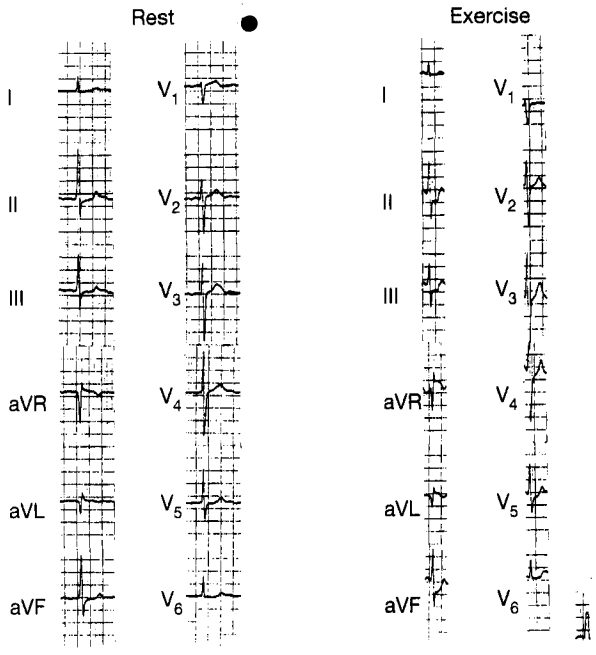

FIG. 2 Electrocardiogram at rest and on exercise in Case 1. Although there are no accurate myocardial ischemic changes at rest electrocardiographically, ischemic ST-T depression was detected in the leads II, III, aVF, and V_{3-6} on exercise.

tion of myocardial infarction, angina pectoris, or death related to this stress test.

Visual Analysis of SPECT (Fig. 3)

In Case 1, moderate tracer reduction on exercise image in the anterior wall became mild on delayed image. Moderate reduction in the septal wall became normal. Mildly depressed counts in inferior/posterior walls did not change.

In Case 2, moderately reduced inferior counts in the exercise image became normal and mildly reduced septal wall counts in the exercise image became normal in the delayed image. Mildly reduced anterior wall counts were unchanged (Fig. 4).

In Case 3, marked septal hypertrophy in both exercise and delayed images was detected, but no obvious perfusion reductions were shown.

In Case 4, mildly reduced anterior and inferior/posterior tracer counts in the exercise image became normal in the delayed image.

In Case 5, mildly reduced posterior/inferior counts in the exercise image unchanged in the delayed image.

As we have previously reported, we consider the perfusion defects as the counts less than 50% of the most intense uptakes (grades 2 and 3).[9] In this manner, myocardial ischemia was found in two patients (Cases 1 and 3, 40%) by exercise myocardial scintigraphy.

Discussion

Congenital coronary artery fistula is an uncommon anomaly.[8] Most cases of coronary artery fistula drain into the right side of the heart, such as the right ventricle, right atrium, pulmonary artery, or coronary sinus. Coronary artery fistula communicating to the left ventricle is rare. Chia *et al.* described that in some cases a large major coronary artery drained directly into left ventricle.[11] Reddy *et al.* first described a case with multiple arteriosystemic fistula.[12] Kinard[1] and Rose[13] speculated that these vessels were Thebesian veins. Since these reports, many multiple coronary arterioventricular connections, which are shown

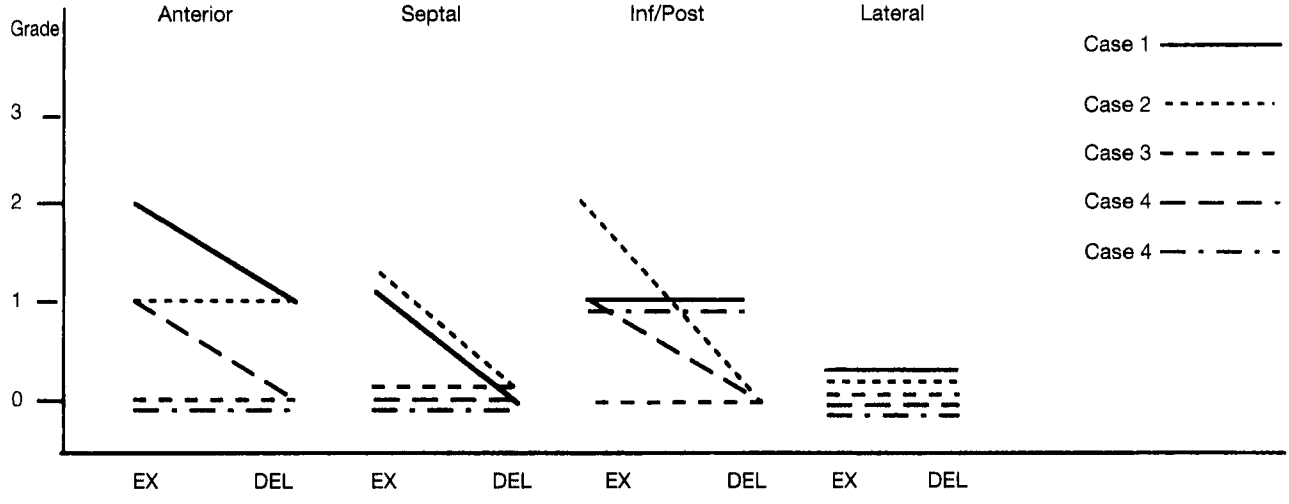

FIG. 3 Visual analysis of SPECT. Comparison of the perfusion defects between the SPECT images 3 minutes after exercise and those of 4 hours later. Myocardial ischemia was detected in Case 1 (anterior), and Case 3 (Inf/Post). Ex = exercise; DEL = delay; Inf = inferior; Post = posterior.

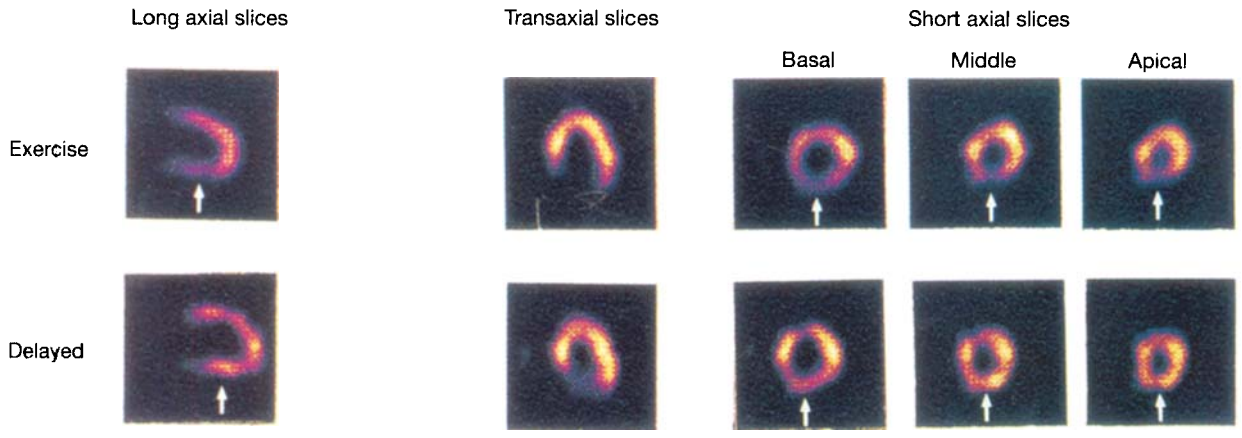

FIG. 4 Exercise Tl-201 myocardial scintigraphy in Case 2. Moderately reduced tracer counts in the inferior wall on exercise image became normal at delayed image (arrow). Mildly reduced anterior wall counts unchanged throughout the exercise.

in angiograms, have been regarded as Thebesian veins. The Thebesian vein system was thought to be a major venous channel for the right heart only by Wearn *et al.*[6] Only 2% of the coronary blood flow pours into the canine left atrium through the Thebesian venous system.[14] Some investigators considered these channels as the nutrient supply of the myocardium.[15] Some of the reports described an absence of chest pains or other symptoms such as angina pectoris.[12] Some reported abnormal ECG at rest[10, 16, 17] without any symptoms. Angina pectoris and positive exercise stress test on ECG were reported in some heart anomalies.[1, 16, 18, 19, 20] Cha *et al.* regarded the fistula channels as an unusual, prominent Thebesian system which seems to be the embryological etiology of this condition.[16] Their patients did not show any exertional myocardial ischemia, but they considered the well-developed sinusoidal channels (with a possible large amount of fistula flow) as a probable cause of coronary steal, and subsequent coronary ischemia. Because blood flow from Thebesian veins passes through capillary networks in the same manner as through normal coronary veins, it is unlikely that myocardial ischemia results from coronary steal. Duckworth *et al.* reported a case of myocardial ischemia detected by exercise stress myocardial scintigraphy.[5] They regarded these vessels as remnants of embryonic sinusoids, which were described by Lovitt and Lutz.[4] Remnants of embryonic sinusoids also have very little opportunity to cause myocardial ischemia for the same reason as described above. Wearn *et al.* described three types of intracardiac coronary artery termination: into the conventional capillary plexus, into a myocardial sinusoid, or directly into a lumen of ventricle.[6] The latter direct vascular connection between the coronary arteries and ventricular cavities was first described by Viessens[21] and was identified as arterioluminal vessels by Wearn *et al.*[6] Baroldi *et al.*[22] reported that they were frequently seen in the ventricles, but only rarely in the atria. Venous channels, called Thebesian veins are found frequently in the atria and less often in the ventricles. If a vessel causes myocardial ischemia, we speculate that this vessel should not be considered as part of the Thebesian venous system or as remnants of embryonic sinusoids. Rather, it should be defined as multiple coronary arterioventricular fistula. These vessels cannot be differentiated from conventional coronary arteriogram without the aid of stress ^{201}Tl myocardial scintigraphy. Only one previous case report had detected myocardial ischemia in these anomalies by the scintigraphic method. If this anomaly causes myocardial ischemia, regional myocardial perfusion becomes markedly abnormal through increased blood flow levels after potent vasodilator stimuli such as exercise.

Exercise myocardial scintigraphy is commonly used to detect myocardial ischemia in the patients with coronary heart disease.[7] SPECT yields a higher sensitivity than planar imaging in the detection of the myocardial infarction.[23] The sensitivity and specificity of SPECT to detect coronary arterial stenosis have been reported to be about 90%.[24–26] We also have already reported sensitivity as 82% and specificity as 89% in detecting coronary arterial stenosis with SPECT in our institute when myocardial perfusion abnormality is taken as less than 50% of the maximal counts.[7]

In the present study, ECG abnormalities at rest were found in 3 patients (60%). ST depression induced by exercise was found in 2 patients (40%. These ECG changes might indicate some kind of myocardial damages. In SPECT, these 2 patients also had moderate perfusion defects on exercise stress. All of them had redistribution, which indicated myocardial ischemia. Besides the accurate prediction of myocardial ischemia, there also were mildly reduced tracer concentrations in 4 patients (80%). In these patients, 4 segments showed redistribution and 3 segments did not. Theman *et al.* reported myocardial ischemia caused by coronary artery steal in patients with coronary artery fistula.[27] We speculate that patients who

show myocardial ischemia are not representative of the classical Thebesian venous system or remnants of embryonic sinusoids, but are indicative of multiple coronary arterioventricular fistula. We could detect myocardial ischemia in some patients by exercise stress test. We demonstrated that these ischemic changes in multiple coronary arterioventricular connections derived from coronary steal phenomena. We conclude that myocardial ischemia detected by our methods should be diagnosed as multiple coronary arterioventricular fistula, distinguishing such cases from classical Thebesian venous system abnormalities or remnants of embryonic sinusoids.

In summary, exercise stress myocardial scintigraphy can be a good method for identifying myocardial ischemia in multiple coronary arterioventricular fistula and differentiating it from Thebesian venous system abnormalities or remnants of embryonic sinusoids.

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