

## Thallium-201 myocardial scintigraphic evidence of ischemia in a patient with angina pectoris and normal coronary arteriogram: significance of thallium-201 washout analysis

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We present a patient who had anginal pain and an abnormal exercise electrocardiogram but a normal coronary arteriogram. We thought that myocardial ischemia was responsible for this symptom in view of the exercise left ventriculogram, exercise thallium-201 myocardial scintigraphy and effect of nitroglycerin on the anginal pain. The left ventriculogram at rest was normal but exercise worsened the entire left ventricular wall motion. Exercise thallium-201 myocardial images showed minimal reduction of radio-activity in the anterior, apical, antero-lateral and postero-lateral wall. Myocardial thallium-201 washout analysis revealed washout abnormalities all over the left ventricular myocardium similar to those of triple vessel disease, supporting the exercise left ventriculographic finding. Myocardial thallium-201 washout analysis as well as the visual method should be performed in patients with angina pectoris and normal coronary arteriograms.

**Key words:** Angina pectoris, Normal coronary arteriogram, Thallium-201 myocardial scintigraphy

### INTRODUCTION

THE EXACT CONDITION of patients with angina pectoris but normal coronary arteriograms is unknown, and it has also been called syndrome X.<sup>1</sup> Some investigators reported that the causes of this disease were myocardial ischemia caused by an abnormal oxyhemoglobin dissociation, coronary arterial spasm or small vessel disease.<sup>1-3</sup> However, it is difficult to demonstrate this myocardial ischemia. We report a patient with a normal coronary arteriogram and exercise-induced myocardial ischemia, and discuss the significance of the thallium-201 (Tl-201) exercise test in this disease.

### CASE REPORT

A 40-year-old housewife presented with a 10-year history of exertional angina and systemic hypertension. The onset of pain invariably occurred when the

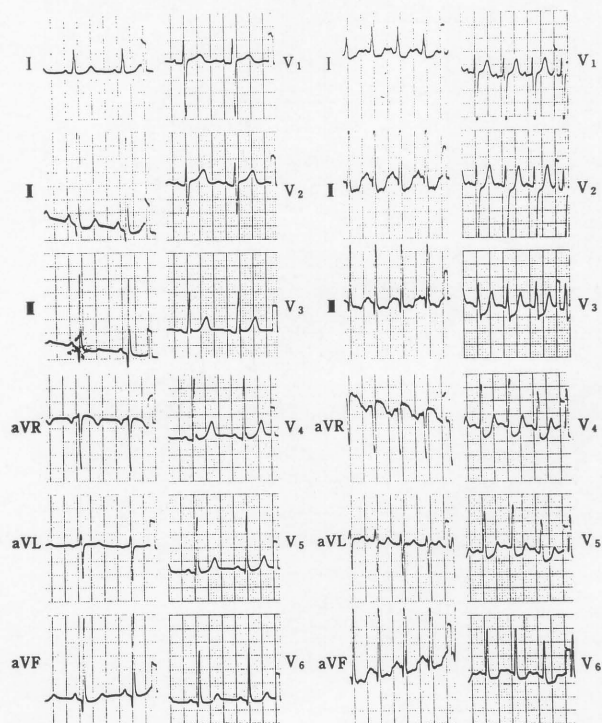
patient was physically active. Then, upon cessation of the activity, the pain subsided within 5 minutes. Sublingual nitroglycerin relieved the pain within a few minutes. She had no risk factor for coronary atherosclerosis except systemic hypertension. Both parents had systemic hypertension. Physical examination disclosed the following: height 149 cm, weight 48 kg, pulse 70/min, blood pressure 196/104 mmHg. There were no abnormal findings on cardiac examination. Laboratory findings were normal. Chest X ray was normal. The resting electrocardiogram was normal, but a bicycle ergometer exercise test in the morning caused clearly abnormal ST segment depression in precordial leads V3-V6 and in limb leads I, II, III and aVF (Fig. 1), associated with anginal pain. Likewise in the afternoon, a repetitive identical exercise test induced angina and ECG changes. Circadian variation in her exercise capacity is hardly probable.

The patient underwent a Tl-201 exercise test, stopping for angina and ST segment depression. One minute before the termination of exercise, 3.0 mCi Tl-201 was injected intravenously. At the time of the injection of Tl-201, her heart rate was 82 percent of her age-predicted maximal heart rate (148/min).

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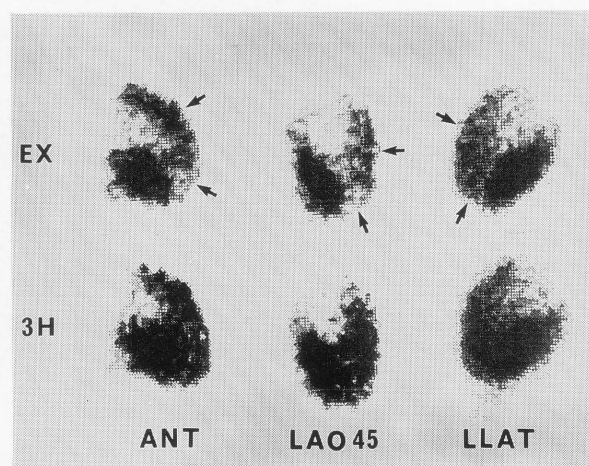
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Images were obtained immediately after exercise and 3 hours later in anterior, left anterior oblique and left lateral projections with an Anger camera equipped with a high resolution parallel hole collimator. A 20 percent energy window centered on the 80 KeV X ray peak was used and 500,000 counts were acquired in each view. All images were enhanced

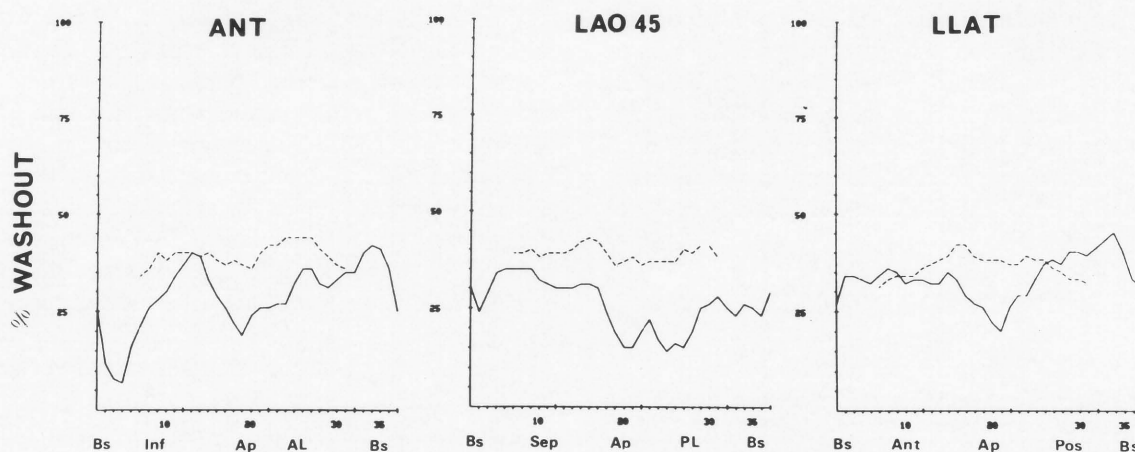


**Fig. 1** Electrocardiograms at rest (left panel) and during exercise (right panel). The resting tracing is normal. During exercise on a bicycle ergometer, ST segment depression occurred in leads I, II, III, aVF and V3 to V6. The subject felt chest pain during exercise.

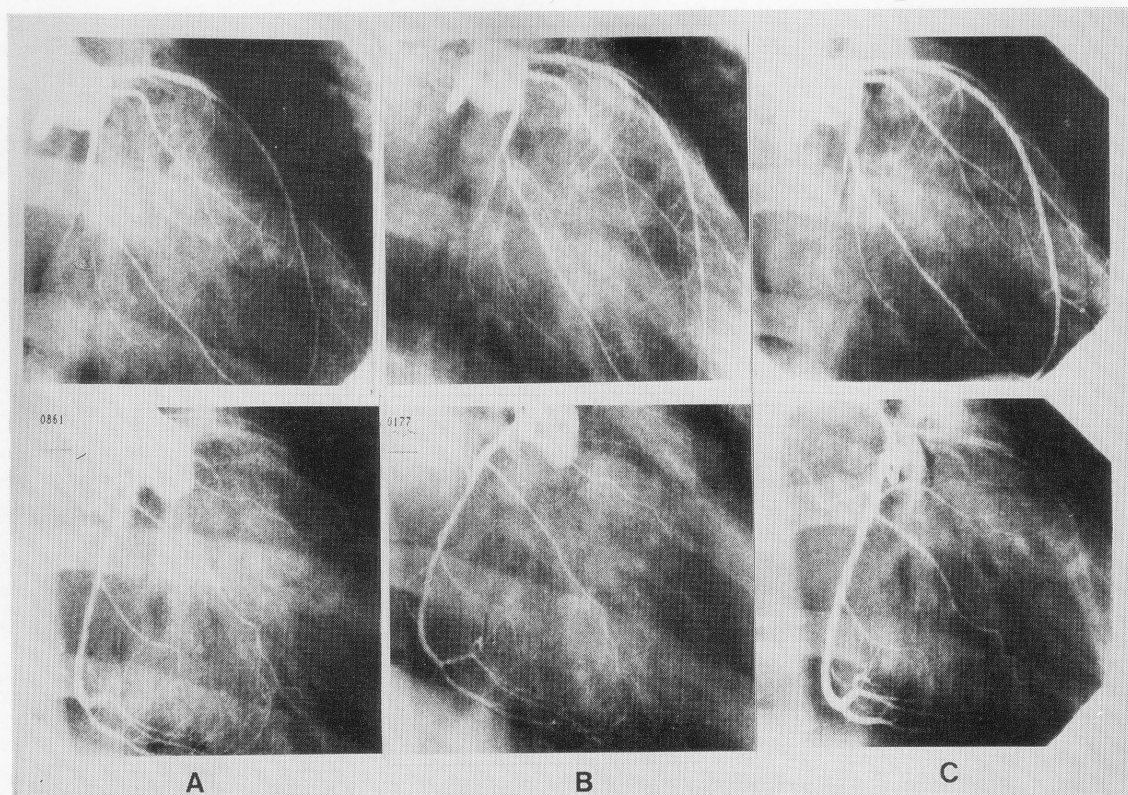
by computer processing and were displayed with a  $128 \times 128$  matrix. The immediate post-exercise images demonstrated the decreased tracer accumulation in the anterior, apical, anterolateral and postero-lateral portions, and the redistribution images normalization of distribution of radioactivity throughout the left ventricular myocardium (Fig. 2). For quantitation of the images, we adopted the TI-201 washout analysis according to the technique described by Garcia et al.<sup>4</sup>: 1) each image was processed by performing interpolative background subtraction and 9-point smoothing. 2) circumferential maximal



**Fig. 2** Thallium-201 myocardial images enhanced by computer processing. (Upper panels) The immediate post-exercise images demonstrate the minimal reduction of radioactivity in the anterior, apical, antero-lateral and postero-lateral wall (arrows). (Lower panels) The redistribution images showed the normalization of distribution of radioactivity throughout the left ventricular myocardium.



**Fig. 3** Myocardial thallium-201 percent washout circumferential profiles. Segments of these profiles (solid line) falling below the lower limits of normal in our laboratory (plotting lines) indicate the multiple washout abnormalities. Bs=base, Inf=inferior wall, Ap=apical wall, AL=antero-lateral wall, Sep=intraventricular septum, PL=postero-lateral wall, Ant=anterior wall, Pos=posterior wall.



**Fig. 4** Selective coronary arteriograms under basic circumstances (A). All three vessels are slender. During an attack of angina induced by exercise, coronary arteriograms are the same (B). After the injection of nitroglycerin, coronary arteries dilated generally and no narrowing was seen (C). Upper panels show left coronary arteriograms. Lower panels show right coronary arteriograms.

counts per pixel were calculated along 36 radii at 10 degree intervals generated from the center of the left ventricle. 3) on the basis of these counts corrected for collection time, 3-hour percent washout (initial counts minus 3-hour counts divided by initial counts as percentage) circumferential profiles were obtained. Multiple washout abnormalities indicated by segments of these profiles falling below the lower limits of normal in our laboratory (mean-2SD in 15 normal subjects) were similar to those with triple vessel disease (Fig. 3).

Echocardiographic study demonstrated the mild concentric left ventricular myocardial hypertrophy.

Cardiac catheterization was performed without premedication. The left ventriculogram at rest was normal. Exercise worsened the entire left ventricular wall motion, associated with angina and ST segment depression. Selective coronary arteriograms showed no segmental narrowing. However, all three vessels were slender (Fig. 4A). After immediately following the onset of angina and ST segment depression induced by exercise, coronary arteriograms were the same (Fig. 4B). Intravenous ergonovine maleate did not induce segmental spasm of the coronary arteries. After the injection of nitroglycerin, the coronary

arteries dilated generally and no coronary arterial narrowing was seen (Fig. 4C).

When the patient received oral nitroglycerin, exercise test caused neither angina nor ST segment depression until the arrival of 85 percent of age predicted maximal heart rate. Exercise Tl-201 myocardial scintigraphy with oral nitroglycerin were normal visually and quantitatively (washout analysis).

## DISCUSSION

The paradox of patients having typical exercise-induced angina but normal coronary arteriograms has been discussed. In some of these patients, myocardial ischemia caused by an abnormal oxyhemoglobin dissociation, coronary arterial spasm or occlusive disease of the small coronary arteries not visualized by coronary arteriography have been suggested.<sup>1-3</sup> In the other, however, the nature of this disease is unknown.

In our case, it is strongly suggested that myocardial ischemia is the cause of symptom because of the worsening left ventricular wall motion during exercise, decreased tracer accumulation on the exercise

Tl-201 myocardial scintigram and relief of anginal pain with nitroglycerin. The small vessel lesions or slender major coronary arteries are the most probable causes of myocardial ischemia in this case. It is possible that the slender vessels result from diffuse spasm because of the vasodilating action of nitroglycerin on the coronary arteries in this case. But even during the attack of angina, coronary narrowing did not increase. The definition of coronary spasm is confused but we have no good reason for interpreting these coronary arteriograms without a progression of focal or diffuse coronary narrowing during the attack of angina as spasm. Therefore, we could not help interpreting these coronary arteriograms as normal. An abnormal oxyhemoglobin dissociation is unlikely. If an abnormal oxyhemoglobin dissociation is responsible for myocardial ischemia, the anginal pain should not be relieved by nitroglycerin, and myocardial Tl-201 washout should not be reduced. Liu et al reported that hypoxia without coronary flow reduction increased myocardial Tl-201 washout.<sup>5</sup> Massie et al reported that myocardial Tl-201 washout was underestimated at a low level of exercise.<sup>6</sup> However, they also observed that patients who exercised to ischemia or to near-maximal heart rate displayed normal washout in uninvolved regions. Our case was exercised to near maximal heart rate (82 percent of age-predicted maximal heart rate).

Our myocardial Tl-201 washout analysis indicated myocardial ischemia not only in the portions interpreted visually as abnormal but also in the other portions. This finding is supported by the entire left ventricular wall motion abnormalities during

exercise. When the myocardial Tl-201 uptake is uniformly decreased, it often happens that images are visually interpreted as normal. The myocardial Tl-201 washout analysis can compensate for this fault in the visual method. Some patients with angina pectoris and visually normal exercise Tl-201 myocardial scintigrams may demonstrate Tl-201 washout abnormalities.

As mentioned above, exercise Tl-201 myocardial scintigraphy and its washout analysis should be performed in patients with angina pectoris and normal coronary arteriograms.

## REFERENCES

1. Kemp HG: Left ventricular function with anginal syndrome and normal coronary arteriograms. *Am J Cardiol* 32: 375-376, 1973
2. Eliot RS, Bratt G: The paradox of myocardial ischemia and necrosis in young women with normal coronary arteriograms. *Am J Cardiol* 23: 633-638, 1969
3. James TN: Small arteries of the heart. *Circulation* 56: 2-14, 1977
4. Garcia E, Maddahi J, Berman D, et al: Space/time quantitation of thallium-201 myocardial scintigraphy. *J Nucl Med* 22: 309-317, 1981
5. Liu P, Lutrario D, Boucher AC, et al: The effect of hypoxia alone without flow reduction on myocardial thallium kinetics. *Circulation* 70: Suppl. II, 449, 1984 (abst)
6. Massie BM, Wisneski J, Kramer B, et al: Comparison of myocardial thallium-201 clearance after maximal and submaximal exercise. *J Nucl Med* 23: 381-385, 1982