Myocardial Infarction in Young Women with Normal Coronary Arteriograms

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SUMMARY

Two women, ages 34 and 36 years, suffered an acute transmural anterior myocardial infarction accompanied by typical ECG and serum enzyme changes. At the time of selective cinecoronary arteriography 29 and 57 months later, however, neither had demonstrable narrowing of any coronary artery. Both have persistent ECG changes of an anterior infarct and markedly diminished contractions of a large segment of the anterior wall and apex on left ventriculogram. Neither before nor after infarction has either patient experienced angina pectoris. Both patients are premenopausal, and neither of them has diabetes, hypertension, obesity, valvular heart disease, a lipoprotein abnormality, or a family history of premature coronary arterial disease. Both smoke cigarettes. At the time of infarction one patient was taking an oral contraceptive and the other was 11-days postpartum. The pathogenesis of the myocardial infarcts in these patients is unknown. Embolization or in situ thrombosis of a previously normal anterior descending coronary artery with subsequent clot lysis would explain the infarcts, the normal coronary arteriograms, and the absence of prior or subsequent angina.

Additional Indexing Words:

Coronary artery

Both necropsy1-6 and arteriographic7-9 studies have demonstrated that with rare exceptions persons with transmural myocardial infarcts have significant narrowing of major coronary arterial branches. We have studied two women, however, one who at 34 and the other who at 36 years of age suffered an acute anterior myocardial infarction accompanied by typical electrocardiographic (ECG) and serum enzyme changes; yet, at the time of selective cinecoronary arteriography 29 and 57 months later, neither had demonstrable narrowing of any coronary artery. The purpose of this report is to describe the clinical and laboratory findings in these patients, neither of whom has ever experienced angina pectoris.

Report of Patients

Patient I.B.

A 34-year-old Puerto Rican woman was well until September 18, 1967, when she was admitted to a hospital in New York City because of severe retrosternal and epigastric pain. Serial ECG changes (fig. 1) were typical of acute transmural anterior myocardial infarction. Serum glutamic oxaloacetic transaminase (SGOT) determinations were: 68 units on the day of admission, 360 on the second hospital day, 108 on the third, and 18 on the fifth day. A 3-week convalescence in the hospital was uncomplicated. For 5 months the patient had been taking an oral contraceptive, and this was discontinued on admission. She smoked one pack of cigarettes per day.

In February 1970 the patient was studied at the National Heart and Lung Institute. She had no family history suggestive of coronary arterial disease, diabetes mellitus, or hypertension. Her only symptoms were mild exertional dyspnea and an occasional sharp inframammary pain unrelated to exertion. She had no symptoms compatible with angina pectoris. Her menstrual periods were
regular. Blood pressure was 115/70 mm Hg, and physical examination was normal except for a diffuse left ventricular apical impulse. Her weight (64 kg) was at the upper limit of normal for her height (162 cm). Plasma cholesterol (159 mg/100 ml) and triglyceride (140 mg/100 ml) concentrations were normal, as were lipoprotein fractionation by ultracentrifugation and lipoprotein electrophoresis on paper. An oral glucose tolerance test was normal. Hemoglobin, hematocrit, total and differential leukocyte count, platelet count, prothrombin time, partial thromboplastin time, protein-bound iodine, total serum protein, serum protein electrophoresis, SCOT, and serum electrolytes were within normal limits. Serum uric acid (7.1 mg/100 ml) was slightly elevated. L.E. cell preparations and a serologic test for syphilis were negative. Chest roentgenogram was normal.

At cardiac catheterization left ventricular pressure was 125/23 mm Hg. There was no pressure gradient across the aortic valve. Selective cinecoronary arteriograms (fig. 2) showed all major branches to be widely patent without luminal narrowing or irregularity, and no intercoronary collateral channels were noted. The anterior descending branch was unusually straight and did not shorten with systole, but the left ventricular cineangiogram provided an explanation for this. The entire anterior wall and apex of the left ventricle were markedly hypokinetic.

**Patient M.H.**

A 36-year-old white woman was well until August 27, 1965, when 11 days after the uncomplicated delivery of her third child she experienced severe pain that began in her back and radiated to her left arm and chest. The pain lasted 30 min and was accompanied by diaphoresis. She was admitted to a hospital in Kabul, Afghanistan, where she was living at the time. Serial ECG changes (fig. 3) were typical of acute transmural anterior myocardial infarction with left anterior hemiblock. SCOT on admission was 20 units. The next day it was 190 units, and serum lactic dehydrogenase was 2,000 units. On the third day her leukocyte count was 11,400/mm³, and her oral temperature had risen from 98.4°F on admission to 100.4°F. Convalescence was uncomplicated. The patient has occasionally had blood pressure measurements as high as 150/95 mm Hg. Most measurements, however, have been 135/80 mm Hg or less despite the fact that she has not been treated for hypertension. She has never smoked more than five cigarettes a day. Her father died of a myocardial infarct at age 66 and her mother has systemic hypertension. There is no family history of diabetes mellitus.
Figure 2

Patient I.B.'s cineangiograms. (A) The left coronary artery in the right anterior oblique (RAO) projection. LAD = left anterior descending; LCCA = left circumflex coronary artery. The left main coronary artery is very short. (B) The LAD in the left anterior oblique (LAO) projection. (C) The left circumflex coronary artery in the LAO projection. (D) The right coronary artery (LAO projection) supplies the posterior descending artery (PD) and the artery to the atiioventricular node (AV). At the acute margin of the heart the right coronary artery appears to be less opacified because it overlies the lung. (E) The left ventricle at end-diastole. (F) The left ventricle at end-systole. Its apex and anterior wall contract poorly (arrows).

Although the patient has tired easily since 1965, she has had no pain suggestive of angina pectoris. In May 1970 she was studied at the National Heart and Lung Institute. Her weight (55 kg) was normal for her height (158 cm). Blood pressure was 134/75 mm Hg, and a prominent double impulse was felt at the cardiac apex. A fourth heart sound was heard at the apex and a soft grade 1/6 early systolic murmur was audible along the left sternal border. Physical examination was otherwise normal, and she was menstruating. Plasma cholesterol (180 mg/100 ml)
and triglyceride (89 mg/100 ml) concentrations were normal, as were lipoprotein fractionation by ultracentrifugation and lipoprotein electrophoresis on paper. Fasting and 2-hr postprandial blood sugars also were normal. Hemoglobin, hematocrit, total and differential leukocyte count, platelet count, prothrombin time, partial thromboplastin time, protein-bound iodine, total serum protein, serum protein electrophoresis, hemoglobin electrophoresis, SGOT, uric acid, and serum electrolytes were within normal limits. L.E. cell preparations and a serologic test for syphilis were negative. Chest roentgenogram showed a slightly dilated ascending aorta, but was otherwise normal.

At cardiac catheterization the left ventricular pressure was 108/7 mm Hg. There was no pressure gradient across the aortic valve. Cardiac output was 4.5 liters/min/m². Right atrial pacing to rates of 170 beats/min failed to produce biochemical evidence of myocardial hypoxia;¹¹ ¹² before, during, and after pacing, lactate levels and the lactate/pyruvate ratio in systemic arterial blood were higher than those in simultaneously obtained coronary sinus blood. Left ventricular cineangiography demonstrated hypokinesis of a large segment of the anterior wall and a small area of frankly paradoxical movement at the apex. Selective cinecoronary arteriograms (fig. 4) were normal except for decreased systolic movement of the anterior descending artery. No intercoronary collateral channels were noted.

**Discussion**

The evidence that acute myocardial infarction occurred in the two women described in this report seems indisputable. Both experienced the sudden onset of characteristic chest pain, and in each this was accompanied by ECG changes of acute transmural anterior infarction and by typical serum enzyme changes. In addition, 29 and 57 months later they both have persistent electrocardiographic changes of an old anterior infarct and markedly diminished contractions of a large segment of the anterior wall and apex on left ventriculogram.

Necropsy studies have shown that most patients with myocardial infarcts have occlusive disease of one, and usually several, major coronary arterial branches.¹⁻⁶ Infarcts found in the absence of coronary arterial narrowing of 50% or more are usually small, subendocardial, and clinically unrecognized. Under these circumstances, some other contributing cause for a disparity between myocardial oxygen supply and demand is usually present, such as aortic stenosis, systemic arterial hypertension, severe anemia, pulmonary emboli, or severe...
WITH NORMAL CORONARY ARTERIOGRAMS

Figure 4

Patient M.H.'s cinecoronary arteriograms. (A) Left coronary artery in a shallow RAO projection. The left circumflex coronary artery (LCCA) and its obtuse marginal branch (OM) are large and supply the entire posterior portion of the left ventricle. LAD = left anterior descending; D = diagonal branch. (B) Left coronary artery in a steeper RAO projection. (C) Left coronary artery in the left lateral projection. (D) The right coronary artery (shallow RAO projection) is small and supplies only the right ventricle.

systemic arterial hypotension due to a variety of causes.5, 6, 13, 14 Neither of our patients had any of these conditions, and their infarcts were large, transmural, and readily apparent clinically.

Studies employing selective coronary arteriography also have shown that transmural myocardial infarcts are virtually always associated with occlusive disease of the coronary arteries. Thus, of 176 patients with QRS abnormalities considered by Proudfoot and his associates7 to be characteristic of remote myocardial infarction, 174 had severe (at least 50%) narrowing of one or more major coronary arterial branches. Neither of the two with normal coronary arteriograms had a history of prolonged, severe chest pain, and when the ECG in one of them was reviewed retrospectively, it was recognized that definite evidence of an infarct was not present. The other had a
normal ECG 1 month later. Among 108 men less than 40 years of age who had ECG evidence of old myocardial infarction, Welch et al.\(^8\) found at least 50% narrowing of a major coronary arterial branch in 103. One had a traumatic infarct;\(^15\) three were thought to have primary myocardial disease or myocarditis; and in one the ECG abnormalities could not be explained.

Although patients with unequivocal evidence of myocardial infarction almost always have demonstrable coronary artery disease, there have been occasional exceptions. For example, Ross and Friesinger\(^9\) found normal coronary arteries in three patients with good historical and enzymatic evidence of myocardial infarction but no permanent electrocardiographic changes or subsequent angina pectoris. To explain these findings they proposed that a coronary arterial “twig” had thrombosed and could not be visualized arteriographically. In addition, Campeau et al.\(^16\) have described unobstructed coronary arteries in six of 71 patients with clinical and electrocardiographic evidence of previous myocardial infarction. In three of the six the infarct was related to mitral valve replacement or cardiac catheterization. The other three, however, experienced no such precipitating event and were similar to our patients in that each was young (ages 27–32 years), had normal blood-lipid concentrations, and never developed angina pectoris. In contrast to our patients, all were men. In two of the three patients the arteriographic appearance of one major coronary branch was unusual, but neither artery was obstructed.

Like our patients, those of Ross and Friesinger\(^9\) and Campeau et al.\(^16\) had no apparent history of angina either before or after infarction. In contrast, Hale and associates\(^17\) described a 39-year-old man in whom angina pectoris preceded an anterior myocardial infarct. Subsequent coronary arteriograms were normal. The patient died suddenly 6 months after the study; necropsy was not performed. Similarly, Sidd et al.\(^18\) described a 19-year-old boy whose coronary arteriograms were found to be normal 3 months after acute inferolateral myocardial infarction. He had chest pain interpreted as angina pectoris both before and after infarction. Perhaps related to these latter two cases are patients reported to have normal coronary angiograms, but who have recurrent chest pain considered by their physicians to be angina pectoris.\(^11, 12, 19–22\) Most of these patients are women. In some the pain is not characteristic of angina pectoris, but in others it appears to be typical. Four such patients have died.\(^20, 21\) At necropsy all had unobstructed coronary arteries, and three of the four had areas of subendocardial necrosis. Our patients had infarcts without prior angina, and at least clinically appear to differ from those patients with recurrent chest pain in whom transmural infarction is uncommon.

The pathogenesis of myocardial infarction in our patients is unknown. Although “excluding” coronary disease by arteriography admittedly is associated with numerous pitfalls,\(^23\) we believe that we have avoided these as much as is possible. In both patients the selective coronary cineangiograms were of good quality. Films were taken in numerous projections and all major coronary arterial branches were identified. It should be pointed out that complete occlusion at the origin of a diagonal branch of the anterior descending coronary artery can be impossible to detect by arteriography when there are no collateral channels. However, such an occlusion would be most unusual in young, premenopausal women without a lipoprotein abnormality, diabetes, hypertension, obesity, or a family history of premature coronary disease\(^24–28\) and without any abnormality of other coronary arteries. Also, occlusion of a single diagonal branch would not be expected to result in such extensive damage to both the anterior wall and apex of the left ventricle. Likewise, disease of small coronary arteries\(^29\) or a generalized defect in oxygen transport or release\(^20\) would not be expected to cause a transmural infarct in the distribution of a single major coronary artery.

Because neither patient had any preceding history of ischemic myocardial pain, we believe the most likely cause of the infarcts
was sudden occlusion of an essentially normal anterior descending coronary artery. Either embolization or in situ thrombosis could have been responsible for such an event, and subsequent lysis of the clot could account for the absence of angina after infarction. Re- 
canalization of an organized clot might also occur but probably would not fully restore the arterial lumen. Neither of our patients had evidence of embolization of other organs, nor do they have mitral stenosis or other condi-
tions which might predispose to systemic emboli. One of our patients was taking an oral contraceptive, and the other was 11-days post- 
partum. Although oral contraceptives have been implicated in thromboembolic disease, thus far thrombophlebitis, pulmonary embo-
lism, and cerebral thrombosis are the only thromboembolic disorders that have been documented to occur with increased frequency in women taking these agents. Moreover, the patients of Campeau et al. were men.

Whether our patients' prognosis is like that of other patients with myocardial infarction or like that of persons with normal coronary arteries will only be determined by further follow-up. If they are not subject to recurrent myocardial infarction, the outlook may well be influenced by the extent of the original infarct. In both patients large hypokinetic areas were seen on left ventriculogram, and in one the left ventricular end-diastolic pressure was markedly elevated.

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