Noninvasive and Invasive Demonstration of Spontaneous Regression of Coronary Artery Disease

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SUMMARY Spontaneous regression of a left anterior descending coronary artery lesion was diagnosed by noninvasive testing (stress electrocardiography and thallium-201 myocardial imaging) and confirmed on selective coronary angiography in a 46-year-old man. The patient’s clinical improvement, normalization of stress ECG and thallium-201 imaging, together with the loss of collateral filling, confirm that the regression is genuine. This case provides evidence that regression of coronary atherosclerosis can occur in man.

ALTHOUGH Atherosclerotic Lesions in the experimental animal have been documented to undergo regression,1,2 this phenomenon has rarely been demonstrated in man. In treated types II and IV hyperlipoproteinemias, femoral artery atherosclerosis regressed.6 Renal artery atherosclerosis was shown to regress in a treated hyperlipidemic patient with subsequent restoration of a normal blood pressure.7 Likewise, lowering the serum cholesterol level with ileal bypass,8 risk factor modification,8 and exercise and weight reduction10 may influence regression of coronary artery atherosclerosis.

Recently we followed a patient who presented with exertional angina and mild hyperlipidemia and who had a single coronary artery lesion. Six months after his initial assessment, he became asymptomatic, with spontaneous regression of his coronary artery narrowing.

Case Report

A 46-year-old white male lawyer was admitted to the Cardiac Care Unit of University Hospital in July 1977 after an episode of acute dyspnea, chest tightness and presyncope that started while he was playing soccer with his children. In the previous 8 months he had been aware of exertional chest pain that had increased in severity during the few months before his admission. One year earlier he had been told by his family physician that he had a slight increase of his serum triglyceride and cholesterol levels. He had stopped smoking in 1975, but before that had smoked one pack of cigarettes per day for 25 years.

His father had died at age 51 years from a myocardial infarction and a sister had died in her 40s from complications of diabetes mellitus. The functional inquiry was noncontributory.

Physical examination demonstrated a normal 46-year-old male in no distress, with a blood pressure of 120/80 mm Hg and a pulse of 76 beats/min. The only physical findings were the presence of arcus senilis, an S4 gallop and a soft apical systolic murmur. The remainder of the physical examination was unremarkable.

A 12-lead ECG was normal (fig. 1A) and remained unchanged over the next 5 days. The serum enzymes remained normal. The serum electrolytes, BUN and creatinine were normal. The serum uric acid and fasting glucose were 6.4 and 98 mg/dl respectively, and the fasting serum cholesterol and triglycerides were 269 and 205 mg/dl, respectively. A chest x-ray was normal. Several days after admission, an exercise stress test was performed in conjunction with thallium myocardial imaging. The exercise test was discontinued at the end of the second stage (6 minutes), as the patient was experiencing pain that radiated into the left arm and ST depression. His heart rate was 150 beats/min and the 12-lead ECGs showed up to 5.0 mm of downsloping ST-segment depression in the inferolateral leads (figs. 1B and C). The thallium-201 myocardial images showed evidence of an anterior perfusion defect (fig. 2).

The patient was discharged on β blockade in the form of timolol, 5 mg three times daily. He discontinued this medication on his own accord within a few days because of side effects.

One month later coronary angiography was performed to assess the severity of the coronary atherosclerosis. The left ventricle demonstrated normal contractility, with a pressure of 125/12 mm Hg and aortic pressure of 115/70 mm Hg. A nondominant right coronary artery supplied collaterals that filled the left anterior descending coronary artery retrogradely (fig. 3A). The proximal left anterior descending coronary artery had a significant stenosis at the origin of the first septal perforator (figs. 3B–E), which persisted even after the use of sublingual nitroglycerin (fig. 3F). Surgery was advised on the
basis of the patient's age and position of the left anterior descending coronary artery stenosis. However, the patient elected for a nonsurgical approach after the pros and cons of aortocoronary bypass were explained. During the ensuing 6 months the patient became more physically active and made a few changes in diet and lifestyle, eating less meat and dairy products and reducing his law practice. Six months after his initial clinical presentation, his exertional chest pain resolved totally.

In May 1978 the exercise test and thallium myocardial imaging were repeated. This time, the test was terminated at the end of the fourth stage (12 minutes of exercise), when the predicted maximal heart rate was reached without symptoms. Both the 12-lead ECG (fig. 4) and the thallium scan (fig. 5) were normal. A repeat coronary angiogram was obtained a few weeks later. The collateral filling of the left anterior descending coronary artery from the right coronary artery was no longer evident (fig. 6A). The proximal lesion of the left anterior descending coronary artery was smaller (figs. 6B–D). The fasting serum cholesterol and triglyceride values were 201 and 93 mg/dl, respectively.

The patient remains asymptomatic and his exercise ECG and thallium-201 myocardial scans are normal (September 1979).

Discussion

This case provides further evidence that regression of coronary atherosclerosis can occur. That the regression of the coronary lesion seen on selective coronary angiography in this case is genuine is supported by the patient's clinical improvement, the noninvasive stress testing (ECG and thallium-201) and the loss of collateral filling of the left anterior descending coronary artery.

The possibility of reversible coronary artery spasm must be excluded. Several factors argue against this. First, we had noninvasive documentation of exercise-induced myocardial ischemia several times before the initial coronary angiogram. Second, the lack of change in the luminal stenosis after sublingual nitroglycerin argues against spasm. Third, the presence of collateral vessels from the right coronary artery, with filling of the left anterior descending coronary artery, has not been described with coronary artery spasm alone. Finally, the patient's clinical course is not in keeping with coronary artery spasm.

Another possible explanation for the reversible obstruction as seen in this case related to recanalization of a thrombus. Recently, Eliot and Edwards\(^\text{1}\) demonstrated that from a pathologic viewpoint, such channels do not appear capable of carrying any significant volume of blood and therefore, a recanalized thrombus is, as a practical matter, an occluded segment. Thus, recanalization of a thrombus is unlikely to provide the explanation for the resolution of obstruction and myocardial ischemia seen in this patient. However, the possibility of lysis of a thrombus that was superimposed upon an atheromatous lesion cannot be excluded. This possibility would be consistent with the relatively short period in which regression of the coronary lesion occurred.

![Figure 1](http://circ.ahajournals.org/)

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Figure 1. (A) (page 889) Normal 12-lead rest ECG. (B) ECG at peak exercise showing ST-segment depression of up to 5.0 mm in V5. (C) ECG at 3 minutes into the recovery phase. Ischemic ST-segment depression is evident in most leads.
FIGURE 2. (left) Postexercise thallium images in the left anterior oblique (LAO), anterior (ANT) and left lateral views (LL) show septal and apical perfusion defects.

FIGURE 3. (A) Left anterior oblique view of normal non-dominant right coronary artery with collateral filling of the left anterior descending coronary artery. (B and C) Coronary angiographic frame of left coronary artery in the right (B) and left anterior oblique (C) projections demonstrate proximal stenosis (> 90%) of the proximal left anterior descending artery. (D and E) An enlarged view of the stenotic area. (F) The stenosis was unchanged after 0.6 mg of sublingual nitroglycerin.

FIGURE 3. (Continued on next page)
Another feature of this case is to the disappearance of collateral flow when the need for such flow was corrected. Levin showed that collateral vessels in humans were seen only when the degree of arterial narrowing exceeded 90%. This degree of luminal narrowing was present in the initial left coronary angiogram of our patient. Khouri et al. demonstrated in dogs that collateral channels become nonfunctional when the need for them is removed, but reopen when coronary artery obstruction is induced. Postoperative angiographic studies have shown that successful aortocoronary bypass grafting usually leads to loss of previously well developed collaterals.

In man, few angiographic data support the concept of regressing coronary atherosclerotic lesions. In a recent study of qualitative coronary arteriography in patients with unstable angina, Rafflenbeul and his colleagues showed that five of 25 patients exhibited regression of a coronary artery stenosis over a 1-year period. In one such patient collateral vessels were visualized in the initial study but not in the follow-up study. The present case report provides further evidence in a natural setting that collateral channels do close when they are no longer needed.

Although experimental evidence in animals has shown that regression of atherosclerosis is possible,
FIGURE 4. (Continued on next page)
Figure 4. (A) (top, page 893) The normal resting ECG at 1 year. (B) (bottom, page 893) Twelve-lead ECG at peak exercise. Note both the increased heart rate (180 beats/min) and the normal ST-segment response. The latter persists during the recovery tracing taken at 2 minutes (C).

Figure 5. (left) Postexercise thallium images showing normal perfusion. LAO = left anterior oblique; ANT = anterior; LL = left lateral.
the evidence for regression of disease in human coronary arteries is not as definite. In animals, the reduction in the size of an atherosclerotic lesion has been felt to be due to reduction only of the intracellular content of cholesterol. However, the generalization of this concept to humans is difficult to establish pathologically. Using angiographic comparisons over a 7-year period, Kuo et al. showed stabilization of coronary atherosclerotic lesions in 21 of 25 type II hyperlipoproteinemia patients, suggesting a satisfactory hypolipidemic response. In their study they noted no examples of regression. The primary and secondary clinical drug trials to reduce serum cholesterol were disappointing in their results, and failed to provide evidence of clinical benefit of such therapy. Although the degree of lipid lowering observed (without medication or stringent diet) was approximately twice that seen in any large-scale

Figure 6. (A) (left) Left anterior oblique view of right coronary artery. Note the lack of collaterals. (B and C) Left coronary artery in right and left anterior oblique positions, respectively. (D and E) Enlarged views of the proximal vessels. Regression of stenosis is evident on comparison with figure 3.
clinical trial, we are not certain that this had any effect on the coronary lesion in this single case. The natural history of this patient suggests that previous attitudes regarding this irreversibility of coronary artery atherosclerosis must be reevaluated.

References

2. Wissler DW, Vesselinovitch D, Borenstain J, Hughes R: Regression of severe atherosclerosis in cholesteryamine-treated rhesus monkeys with or without a low-fat, low cholesterol diet. (abstr) Circulation 52 (suppl II): 11-16, 1975
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