Clin. Cardiol. 13, 49-54 (1990)

Clinical Pathologic Correlations

This section edited by Bruce Waller, M.D.

Coronary Occlusion: Cause or Consequence of Acute Myocardial Infarction?

G. BAROLDI, M.D.,* M. MARZILLI, M.D.,† A. L'ABBATE, M.D.,† E. ARBUSTINI, M.D.

*Institute of Clinical Physiology, CNR, Milan, †Institute of Clinical Physiology, CNR, Pisa, and Institute of Pathology, University of Pavia, Pavia, Italy

Summary: A 45-year-old man with unstable angina developed persistent ECG changes of myocardial ischemia during coronary angiography. Occlusion of the left anterior descending branch (LAD) was documented 20 minutes after these changes. Intracoronary nitrate, Ca antagonist, urokinase, removal by percutaneous transluminal coronary angioplasty (PTCA) of atherosclerotic obstructions, and emergency bypass surgery failed to restore myocardial perfusion. Only short periods of reflow were obtained by urokinase and PTCA. The repeated coronary injections demonstrated a progressive disappearance of the left anterior descending artery (LAD) starting from the distal portion and progressing retrogradely up to the origin of the vessel. The patient developed a transmural anterolateral myocardial infarction and 12 months later underwent cardiac transplantation for untractable failure. His heart was examined and the infarct confirmed. Analysis of this case suggests that coronary occlusion in acute myocardial infarction can be an event secondary to increased intramyocardial resistance rather than the cause of reduced coronary blood flow in subepicardial coronary arteries.

Key words: coronary occlusion, coronary spasm, coronary thrombosis, ischemic heart disease, myocardial infarction

Introduction

Our understanding of the pathogenesis of myocardial infarction is based on observations of the coronary arteries performed after the infarction. The latter is generally attributed to thrombotic occlusion of subepicardial coronary artery or branch.[1,2]

An alternative hypothesis suggests that the coronary occlusion could be the consequence of the infarction rather than the cause. This hypothesis is based on postmortem findings, and is scarcely substantiated by objective clinical data.[3,4]

This dilemma can be resolved only by studies performed not before or after the event, but during its development. Obviously, a study of this type is practically impossible because of the difficulties in identifying the beginning of an infarction or in predicting its occurrence. However, scanty yet precious information can be obtained when an infarction takes place under circumstances that allow the investigator to document the changes occurring in the coronary vessels during diagnostic procedures.

This unique report describes a patient with a myocardial infarction that occurred in the laboratory during a routine coronary angiography. It was possible to follow the changes in the coronary circulation prior to and after therapeutic interventions. Twelve months after the infarction the patient underwent heart transplantation because of progressive failure and the excised heart was examined.

Case Report

A 45-year-old man with a two-week history of unstable angina pectoris was referred to our laboratory for diagnostic coronary angiography. The procedure was performed according to the Judkins technique. Left ventriculography revealed anterolateral and anteroseptal hypokinesis; the right coronary artery (RCA) had presented a proximal near totally occlusive lesion. The left anterior descending coronary branch (LAD) had two severe stenoses, one proximal and one distal to the origin of the

Supported by grants from National Research Council, Rome, Italy (Special Project on Atherosclerosis and Cardiopulmonary Diseases).

Address for reprints:

Giorgio Baroldi, M.D.
Istituto Fisiologia Clinica CNR
Dipartimento Cardiologico De Gasperis
Ospedale Niguarda Ca'Granda
I-20162 - Milan, Italy

Received: June 6, 1989
Accepted with revision: July 14, 1989

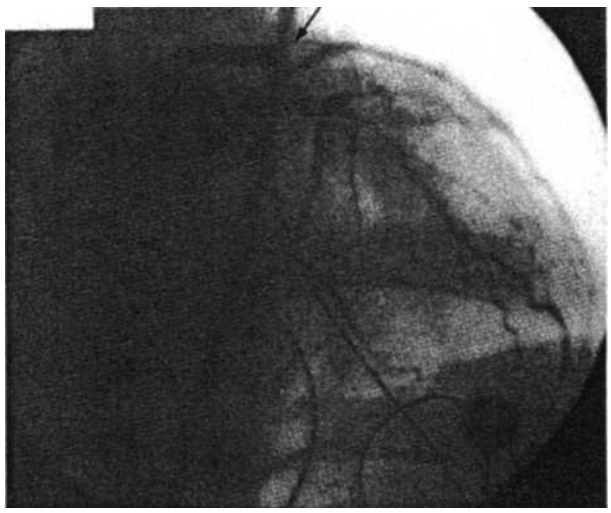

FIG. 7 Angiogram of the left coronary artery in the RAO view: "disappearance" of the LAD artery.

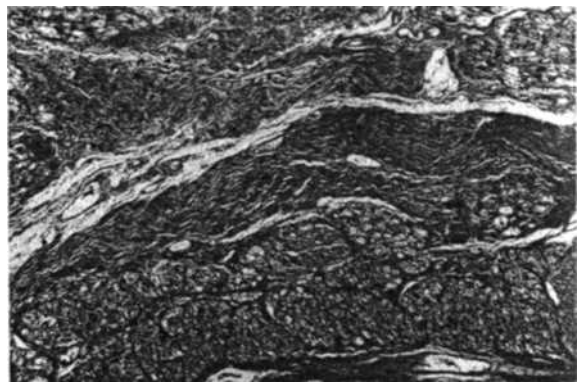

FIG. 8 Extensive dense scar of the anterior wall of the left ventricle with viable hypertrophic myocardium at its margin. The myocardium shows loss of myofibrils.

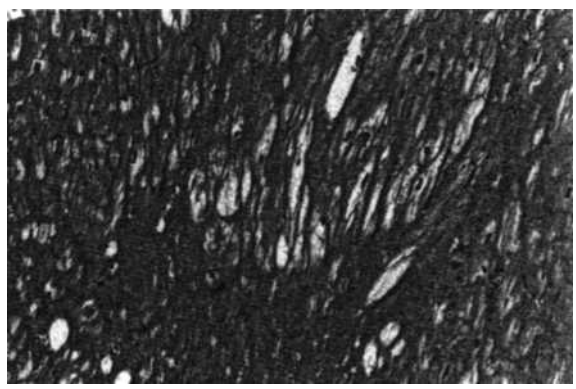

FIG. 9 Diffuse loss of myofibrils in myocardial cells as expression of dilated insufficiency. Chronic or acute changes of any type in the intramural vessel were not detected.

Follow-up

The patient was discharged home 15 days later, having evolved a large anterolateral and septal myocardial infarction. His symptoms progressively increased and he underwent cardiac transplantation for untractable cardiac failure 12 months later. No further episodes of ischemic heart disease were documented. The excised heart has been examined by two of us (GB and EA).

Morphologic Findings in the Excised Heart

Gross Examination

There was marked periepicardial fibrosis of the anterior wall of the left ventricle, mild dilation of the ventricular cavities, and large aneurysm of the anterolateral wall of the left ventricle, massive fibrosis of the anterior intraventricular (IV) septum, anterolateral wall and apex of the left ventricle (approximately 30–40% of the total LV mass). No intracavitary thrombi were found. Cardiac valves were normal. There was endocardial thickening at the IV septum, apex, and anterolateral wall. The coronary arteries and the vein graft were sectioned at 3 mm intervals and each segment processed for histology. Heart weight was 390 g and left wall thickness was 9 mm at the cardiac base and 3 mm at the site of the aneurysm.

Histology of the Myocardium

Massive, transmural, dense fibrosis of the anterior IV septum (normal atrioventricular node and His bundle), and dense laminar fibrosis of the anterolateral left wall with endocardial and epicardial layers of viable myocardium were noted (Fig. 8). Multiple microfoci of fibrosis were present in the remaining portion of the left and right ventricles. The myocardium, particularly in its internal part, showed lysis of myofibrils and vacuolization (Fig. 9).

Histology of the Coronary Arteries

The left main trunk showed only focal fibrosis without significant lumen reduction. The LAD had a severe lumen reduction (90–95%) along its whole course. The unique thrombus found was an occlusive, organized thrombus at the site of the surgical anastomosis (Fig. 10). The circumflex branch of the left coronary artery was mildly stenosed (50%) in its distal tract. The RCA had a severe lumen reduction (90%) in the proximal segment. The residual lumen was occluded by a recanalized thrombus. The vein graft had a thickened, fibrous wall with severe reduction of the lumen (70–80%).

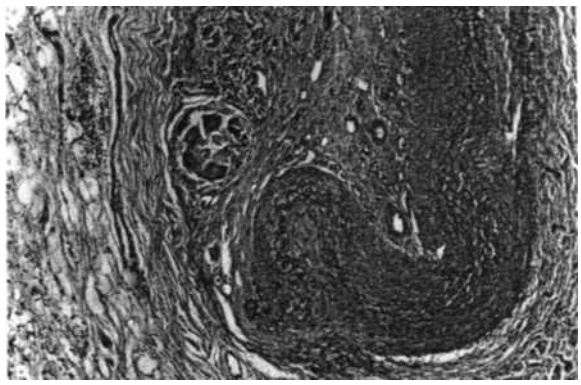

FIG. 10 Occlusion by organized thrombus at the site of vein graft anastomosis in the distal tract of LAD.

The atherosclerotic plaques in all coronary arteries revealed severe atheroma, calcification, and lymphoplasmacellular inflammation.

No alterations of any type in the intramyocardial vessels were observed.

Discussion

We do not know how representative this case is of the whole population of patients with acute myocardial infarction. However, to our knowledge, a similar case illustrating events before and after the infarction has never been reported. Consequently it seems appropriate to discuss the pathogenesis of myocardial infarction in humans based on the following points:

1. The first ischemic ECG change began and persisted for 20 minutes without angiographic evidence of coronary occlusion and chest pain.

2. At 20 minutes, angiographic occlusion occurred without worsening of the ECG and chest pain. The two preceding coronary injections did not show any appreciable modification of the pre-existing LAD stenoses. Only a progressive faintness of the whole vessel was observed.

3. Intracoronary vasodilator and calcium antagonist failed to restore flow. After 20 minutes of intracoronary fibrinolytic agent, a short period of recanalization with ECG improvement was obtained. Reocclusion and recurrence of the ischemic ECG happened during the urokinase infusion. At the end of this infusion (approximately 90 min after the first ischemic ECG) chest pain started.

4. Despite successful angioplasty only short periods of recanalization were visualized with parallel and progressive worsening of ECG and chest pain.

5. The LAD coronary branch disappeared and reappeared several times before its final closure, which started from the distal LAD and progressed retrogradely up to its origin from the left main trunk.

6. Evidence at surgery of patent LAD filled with a fresh coagulum which was easily aspirated.

7. Pathologic examination of the excised heart confirmed a large infarction confined to the territory of the LAD. Only two organized occlusive thrombi were found: one in the LAD at the level of surgical anastomosis and one in the proximal part of the RCA. There was no evidence of myocardial infarction in the corresponding territory.

Nature of the Occlusion Observed at Angiography and Its Relation to Infarction

According to the sequence of events, one must conclude that in this patient the first ischemic ECG occurred in the absence of coronary occlusion. It seems obvious that these ischemic changes signaled the beginning of the infarct. Thus the infarction began without obvious coronary artery occlusion and perhaps the occlusion 20 minutes later was a secondary event. The second possibility is that the real initiation of the infarct started after the first occlusion observed during angiography. One cannot exclude the possibility that the occlusion was due to a thrombus. However, it seems unlikely for the following reasons: (a) no ECG, hemodynamic deteriorations, or subjective symptoms were observed after occlusion—worsening of ECG pattern and chest pain occurred approximately 70 minutes later; (b) temporary recanalization by urokinase showed no angiographic evidence of plaque rupture, thrombosis, or distal embolization; (c) the progressive disappearance of LAD with the two injections preceding occlusion occurred without appreciable changes of the LAD/"fixed" stenoses.

Spontaneous permanent or intermittent coronary occlusion in acute myocardial infarction had been attributed to a combination of thrombosis and/or vasoconstriction.[5] In this case coronary vasoconstriction was never demonstrated. In addition, repeated coronary angiography failed to demonstrate or suggest coronary artery dissection. In contrast, the angiographic observations are all compatible with increased peripheral resistance to intramural flow in the LAD territory resulting in reduced and abolished forward coronary blood flow. Occlusion started distally and progressed retrogradely to the LAD near the left main coronary artery. The left circumflex branch had unrestricted flow. This hindrance to flow in the LAD resulted in clot formation (not thrombosis) in the whole vessel. This was documented at angioplasty and at the time of coronary artery bypass surgery.

Intramural Flow Impairment

The mechanism that initiated these observations which suggested increased peripheral coronary artery resistance remains obscure. One can speculate on several hypotheses:

1. Spasm of the intramural arterial vessels. This hypothesis has never been substantiated in human acute my-

ocardial infarction. Moreover, in this case, no increase in flow was noted after intracoronary administration of vasodilating agents.

2. Embolization and/or platelet aggregates in the intramural vessels. There was not cineangiographic evidence of thrombosis or emboli in the large vessel, which would serve as a possible source of distal embolization. Furthermore, in the many myocardial sections of the excised heart we were unable to observe histologically atheromatous or any other type of organized emboli in the still viable myocardium.
3. "No reflow phenomenon." This pattern has been described in the temporary arterial occlusion in kidney, brain, and heart as a consequence of vascular damage, interstitial exudation and/or hemorrhage, and swelling of the parenchymal cells.[6-9] In canine heart these changes were observed after temporary occlusion (20–60 min) followed by a relatively longlasting continuous reflow (20 min or more), frequently associated with malignant arrhythmias.[9,10] In this patient, reperfusion was intermittent for short periods of time without evidence of arrhythmias. However, we cannot exclude the possibility that this mechanism may have played a pathogenic role.
4. Extravascular compression of the intramural vessels. In this patient, the infarct developed in a pre-existing dyskinetic area (?"stunned" myocardium?).[11] Aggravation and/or expansion of the ischemia-related dyskinesia may have contributed to the impairment of the intramural perfusion by extravascular compression.

Conclusion

This case (a) does not support the current concept that myocardial infarction is *always* caused by an acute and sustained coronary occlusion due to thrombosis superimposed on the rupture of an atherosclerotic plaque; (b) emphasizes the need for direct and early investigation of the sequence of events to discriminate causes and consequences; (c) outlines how rapidly (approximately from 20 to 70 min) a large transmural infarction may fully develop despite appropriate and well-timed therapy (chest pain is an unreliable signal to time the event); (d) demonstrates that occlusive coronary artery thrombosis is not necessarily followed by an infarction, since infarction was not detected in the vascular territory of the right coronary artery occluded by an old, organized thrombus; (e) shows how myocardial dysfunction due to a large infarct may determine, in a relatively short period of time (12 months), a severe stenosis along the whole course of the coronary artery—an indication that myocardial dysfunction aggravates coronary atherosclerosis.

One obviously should always consider the possibility of multiple causes and pathogenesis of the same clinical result, namely ischemic necrosis of the myocardium. This single case asks the following scientific question: How many of the 87% of acute myocardial infarctions with angiographic evidence of total occlusion observed within four hours may have the same pathogenesis as that proposed in this case?[1]

References

1. De Wood MA, Spores J, Notske RN, Mouser LT, Burroughs R, Golden MS, Lang HT: Prevalence of total coronary occlusion during the early hours of transluminal myocardial infarction. *N Engl J Med* 303, 897 (1980)
2. Davies MJ, Thomas A: Thrombosis and acute coronary lesions in sudden cardiac ischemic death. *N Engl J Med* 310, 1137 (1984)
3. Baroldi G: Acute coronary occlusion as a cause of myocardial infarct and sudden coronary heart death. *Am J Cardol* 16, 859 (1965)
4. Baroldi G: Diseases of the coronary arteries. In *Cardiovascular Pathology* (MD Silver Ed). Churchill Livingston, New York (1983) 317
5. Hackett D, Davies G, Chierchia S, Maseri A: Intermittent coronary occlusion in acute myocardial infarction: Value of combined thrombolytic and vasodilator therapy. *N Engl J Med* 317, 1055 (1987)
6. Summers WK, Jamison RL: The no-reflow phenomenon in renal ischemia. *Lab Invest* 25, 635 (1971)
7. Flores J, Di Bona DR, Beck CH, Leaf A: The role of cell swelling in ischemic renal damage and the protective effect of hypertonic solute. *J Clin Invest* 51, 118 (1972)
8. Majno G, Ames A, Chaing J, Wright RL: No-reflow after cerebral ischemia. *Lancet* 2, 569 (1967)
9. Kloner RA, Ganote CE, Jennings RB: The "no-reflow" phenomenon after temporary coronary occlusion in the dog. *J Clin Invest* 54, 1496 (1974)
10. Gavin JB: The no-reflow phenomenon in ischemic myocardium. *Int Rev Exp Pathol* 25, 361 (1983)
11. Przyklenk K, Kloner RA: Superoxide dismutase plus catalase improve contractile function in the canine model of the "stunned myocardium." *Circ Res* 58, 148 (1986)