Myocardial Infarction Without Obstructive Disease at Coronary Arteriography

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MYOCARDIAL infarction as diagnosed post mortem is almost regularly associated with severe and widespread obstructive coronary disease. The following report concerns six cases of myocardial infarction proved on clinical grounds without evidence of significant obstructive disease at coronary arteriography obtained several months later.

MATERIALS AND TECHNIQUES

These cases were selected from a series of 350 patients subjected to coronary cinearteriography, of whom 71 had an abnormal electrocardiographic pattern indicative of myocardial infarction in the past or at the time of the study, together with an adequately documented clinical history and angiograms of good quality. Six cases without significant arteriographic evidence of obstructive coronary disease were thought from the clinical evidence to have had a myocardial infarction.

The technique of selective coronary arteriography of Sones was used. The arteriograms were obtained with a 35 mm. arriflex cine-camera at 60 frames per second with a 6″ Picker image intensifier. Each coronary artery was studied in the right and left 30° to 60° oblique planes; the left coronary was also visualized in the left lateral, and the right coronary in the frontal plane in most cases. The coronary cinearteriograms were reviewed by at least two radiologists.

CASE REPORTS

CASE 1.—H.M., a 53-year-old white man, had a mitral Starr-Edward valve insertion on May 3, 1965. He had moderately severe diabetes which was relatively well controlled. Ten days later, he experienced transient aphasia and on August 30, 1965, he had a severe substernal pain lasting three hours and associated with diaphoresis and vomiting. An electrocardiogram taken the following day was compatible with an anterior myocardial infarction and the SGOT was 166 units. The ECG did not show a transmural infarction, but the R waves in V1 to V3 decreased in amplitude (Fig. 1). The coronary arteriograms obtained on January 23, 1967 were entirely normal. Although he had no subsequent angina pectoris, he remained markedly incapacitated thereafter.

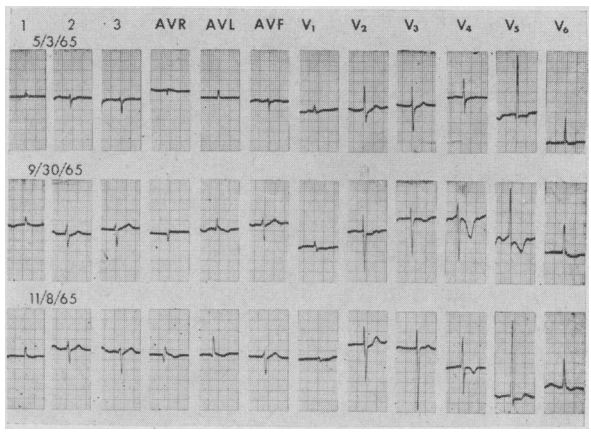

Fig. 1.—Serial electrocardiograms showing changes compatible with a subendocardial anterior myocardial infarction on September 30, 1965 (Case 1).

CASE 2.—J.R., a 37-year-old white woman, was admitted on March 16, 1964, for evaluation of aortic valve disease. She complained of chest pain and dyspnea of moderate intensity on exertion. The aortic valve was not calcified. During combined right and retrograde left heart catheterization, she experienced prolonged and severe retrosternal pain.

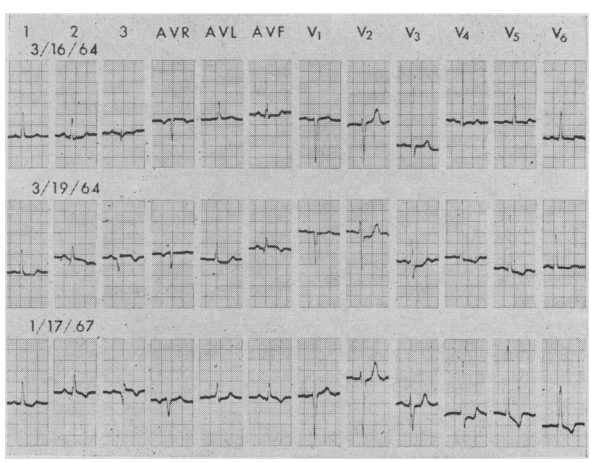

Fig. 2.—Serial electrocardiograms illustrating the appearance of an acute inferior myocardial infarction pattern on March 19, 1964 (Case 2).

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The following day the electrocardiogram showed evidence of an acute inferior myocardial infarction (Fig. 2). The SGOT was elevated at 341 units and the lactic dehydrogenase at 1806 units.

The patient was readmitted on January 20, 1967. She had continued to have angina pectoris, but her functional capacity had not changed appreciably. The fasting blood sugar was normal; cholesterol was 162 mg. per 100 ml.; triglycerides were 183 mg. per 100 ml. (normal: < 134 mg.), and total lipids were 795 mg. per 100 ml. (normal: < 675 mg.). Selective coronary arteriography showed a markedly dominant right artery and a left circumflex with no terminal branch, but no definite evidence of obstructive disease. The aortic valve was slightly stenotic and moderately regurgitant.

It was considered that a coronary embolism had occurred during catheterization. The absent or unrecognized small terminal branch of the left circumflex artery associated with a dominant right artery may have been either a normal variant or due to an occlusion at the origin of this branch with compensatory development of the right artery.

CASE 3.—J.D., a 44-year-old white woman, had a Starr-Edward mitral valve insertion on January 12, 1966. The ascending aorta was clamped for 36 minutes because of an aortic valve regurgitation which had not been clinically evident. The coronary arteries were not cannulated. Atrial fibrillation persisted after the operation, and the postoperative course was uncomplicated. On December 15, 1966, a routine postoperative ECG revealed an anterior myocardial infarction (Fig. 3). The patient was

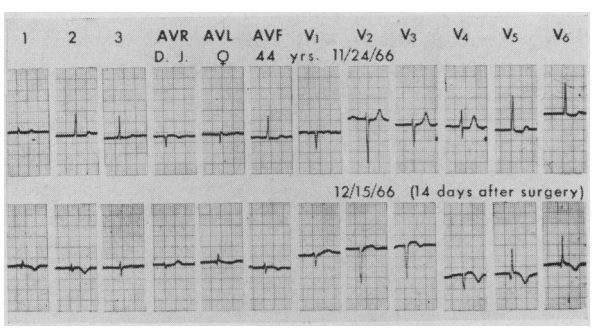

Fig. 3.—Serial electrocardiograms showing the appearance of an anterior myocardial infarction pattern on December 15, 1966 (Case 3).

readmitted in September 1967, because of congestive heart failure without angina pectoris. The fasting blood sugar was normal; the cholesterol was 160 mg. and total lipids 697 mg. per 100 ml. Selective coronary arteriograms were entirely normal. There was no evidence of significant mitral regurgitation at left ventriculography, but the left ventricle appeared dilated and showed markedly decreased contractility. An akinetic area in the projection of the anterior wall was compatible with a previous myocardial infarction. The left ventricular end-diastolic pressure was 20 to 24 mm. Hg and the mean pulmonary capillary venous pressure 22 mm. Hg.

CASE 4.—J.M., a 27-year-old white man without previous illness and with no family history of coronary disease, presented on the morning of April 10, 1966, with severe substernal pain associated with vomiting and diaphoresis; the pain had been present throughout the night and on admission he appeared severely ill. The blood pressure was 90/80 mm. Hg, the jugular veins were slightly distended, there was a sinus tachycardia at 140 per minute, with a gallop rhythm, and rales were heard over the lung bases. An ECG showed a complete right bundle branch block and an acute anterior myocardial infarction pattern (Fig. 4). In spite of ade-

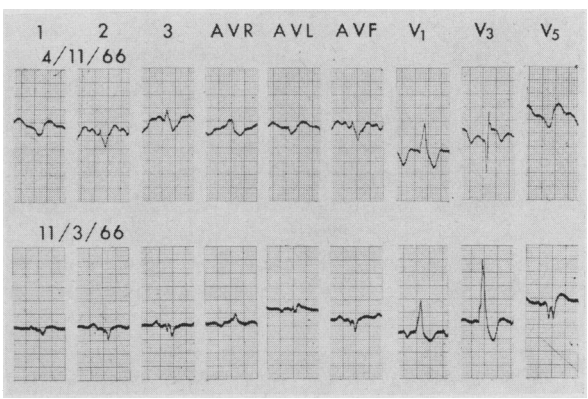

Fig. 4.—Serial electrocardiograms showing a complete right bundle branch block and an acute anterior myocardial infarction pattern on April 11, 1966, which subsequently disappeared (Case 4).

quate digitalization and diuretic therapy, he developed severe pulmonary edema with hemoptysis on April 13, 1966, and subsequently remained in right heart failure. The SGOT rose to 78 units, the SGPT to 114 units and the lactic dehydrogenase to 1275 units; these enzymes remained at abnormally high levels until April 18, 1966. The cholesterol was 152 mg., the triglycerides 141 mg. and the total lipids 421 mg. per 100 ml. He again suffered prolonged chest pain on April 24, and the following day a pericardial friction rub was heard which persisted for at least six days. The enzyme levels increased again and were highest on April 26, the SGOT rising to 150, the SGPT to 216 and the LDH to 975 units. The results of tests for antibodies to influenza A and B, parainfluenza I, II and III and adenovirus were normal on May 5 and May 11. Before discharge on May 21, a chest radiograph revealed a slightly enlarged heart with a cardiothoracic ratio of 16/31 and a left ventricular prominence. The coronary arteriograms obtained on November 30, 1966, were normal except for a rigid and slowly emptying diagonal branch of the left coronary artery (Fig. 5). A left ventriculogram showed a slightly dilated left ventricle with a dif-

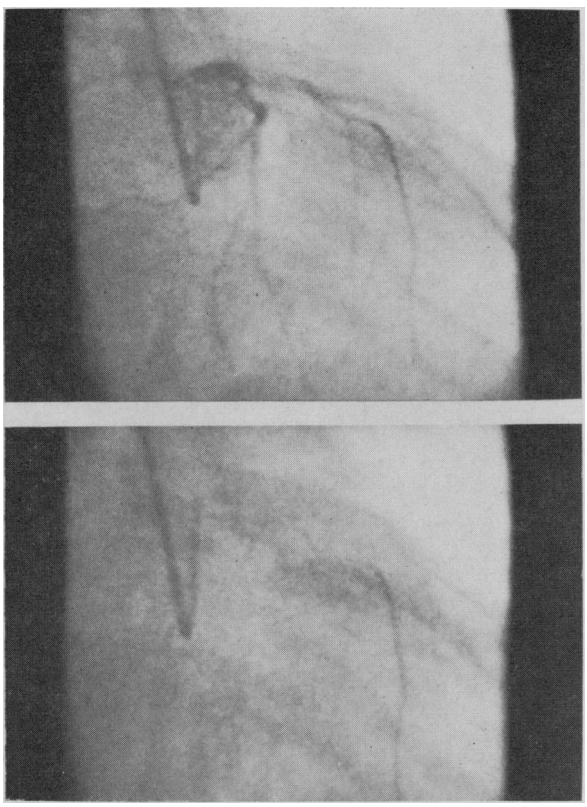

Fig. 5.—Single frames from the cine-coronarograms showing the left coronary artery in the right anterior oblique view (Case 4). Top: all branches of the left coronary artery are visualized. Bottom: a diagonal branch remains opacified.

fuesly poor contraction. The patient remains moderately incapacitated by chronic heart failure but has had no angina pectoris. The last ECG, taken on November 21, 1967, was similar to that of March 11, 1966.

The history of two episodes of chest pain associated with enzyme abnormalities and the electrocardiographic changes were believed to be compatible with a myocardial infarction. The slowly emptying diagonal branch may be the only evidence of a recanalized thrombosis. An acute myocarditis could not be excluded in spite of the electrocardiographic evidence of transmural necrosis. In fact, the electrocardiogram is quite similar to that which Friedberg[1] presents as illustrative of acute myocarditis.

CASE 5.—R.C., a 29-year-old white man, previously treated for ulcerative colitis, with no family history of coronary disease, complained of severe epigastric and lower substernal pain of several hours' duration on November 1, 1965. The pain radiated to the left arm and was associated with vomiting. An electrocardiogram taken 10 days later showed an anterior myocardial ischemia (Fig. 6). He was well until December 25, when he presented with similar pain at St. Joseph's General Hospital,

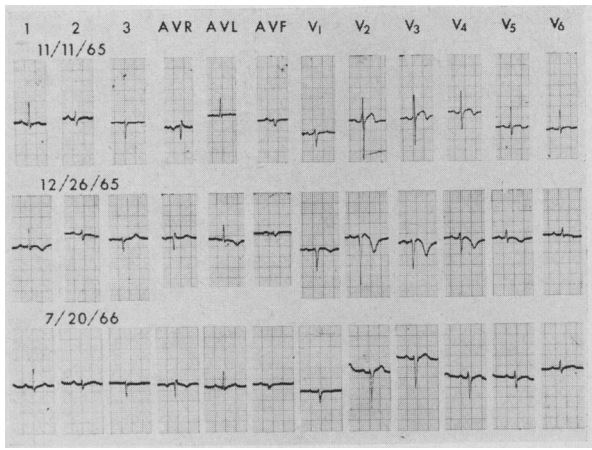

Fig. 6.—Serial electrocardiograms showing changes compatible with an acute anterior myocardial infarction on December 26, 1965.

North Bay, Ontario. On admission he was in a state of peripheral collapse with a blood pressure of 90/70 mm. Hg. The electrocardiogram showed a decreased R wave in the precordial leads V1 to V4 (Fig. 6). The SGOT shortly after admission and again on January 4, 1966, was normal. No

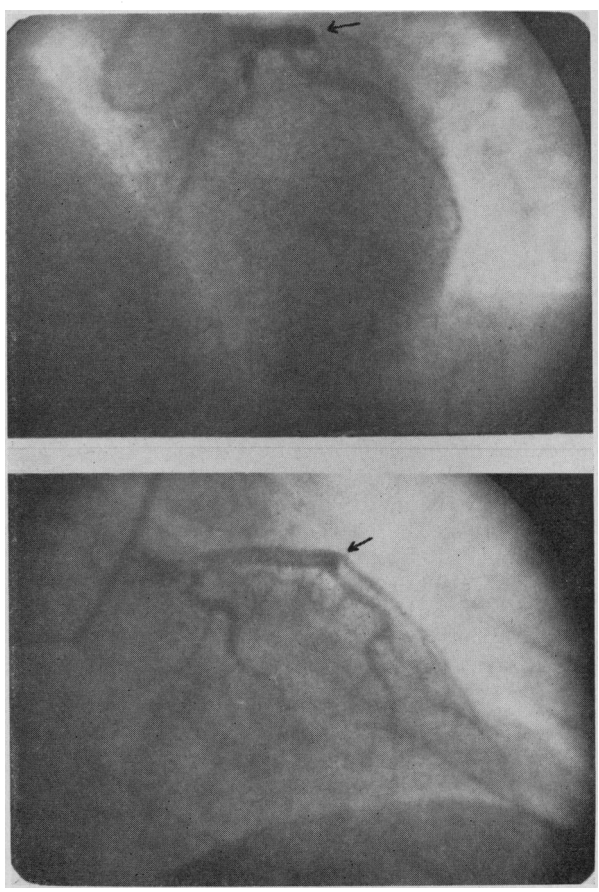

Fig. 7.—Single frames from the cine-coronarogram showing the left coronary artery. (Case 5) Top: left anterior oblique view showing a dilated and kinked left anterior descending coronary artery. Bottom: right anterior oblique view showing an unusual bifurcation of the left anterior descending artery.

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pericardial friction rub was described. The chest radiograph was normal and showed a normal-sized heart. Several months later, in July 1966, the total lipids were 852 mg. and the cholesterol 265 mg. per 100 ml. Upper gastrointestinal and gallbladder radiographic studies were normal. The coronary arteriogram on July 22 showed normal right and left circumflex arteries, but the left anterior descending had an unusual appearance (Fig. 7). In the left anterior oblique view it appeared dilated and kinked. In the right anterior oblique view, the anterior descending artery divided in an unusual way, leaving both branches widely separated at their origin. However, no obstruction was observed. The patient had no angina during the following two years.

The history and serial ECG's are compatible with a myocardial infarction, and the incomplete enzyme study does not rule out this possibility. This patient may have had a congenital anomaly of the anterior descending artery which made him more susceptible to coronary thrombosis. Moore[2] theorizes that bad angle branching may lead to intimal trauma and eventual thrombosis. The peculiar appearance of this anterior descending vessel suggests a recanalized thrombosed artery with thickening of the walls of its branches at their origin.

CASE 6.—J.H., a 32-year-old white man, presented on August 19, 1966, with a severe substernal pain of several hours' duration associated with diaphoresis and extreme fatigue. The pain reappeared during the following few days; it was transmitted to the left shoulder and arm and accentuated by deep inspiration. He had no family history of coronary disease and had had no previous angina. He was admitted the same day to LeMoyne Hospital, St. Lambert, Quebec. No pericardial friction rub was described. The blood pressure was normally maintained and he showed no signs of heart failure. The electrocardiograms showed an extensive inferior and lateral myocardial infarction (Fig. 8). The SGOT was 132 units on the day after admission but was not repeated. The chest radiograph showed a heart of normal size. The fasting blood sugar was normal; the blood cholesterol was 188 mg., the triglycerides 181 mg., and the total lipids 634 mg. per 100 ml. The coronary arteriograms obtained on March 6, 1967, were entirely normal. An ECG obtained on February 19, 1968, was similar to that of February 28, 1967. A Master two-step test was negative except for the appearance of numerous ventricular premature beats.

The diffuse ECG changes, particularly when seen in all three peripheral leads, did suggest a pericarditis, but the appearance of the Q waves in the leads exploring the inferior and lateral walls was considered more compatible with a myocardial infarction. An acute myocarditis with necrosis appears unlikely in the presence of a normal-sized heart but cannot be entirely excluded.

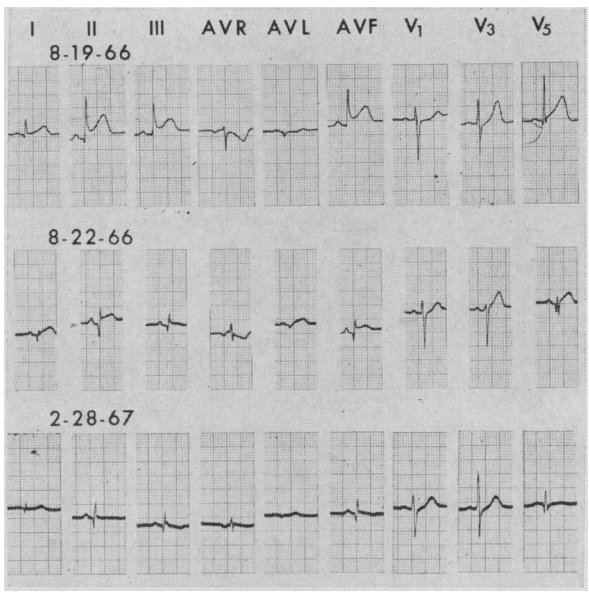

Fig. 8.—Serial electrocardiograms showing changes compatible with an acute inferior and lateral myocardial infarction (Case 6).

DISCUSSION

Few cases of myocardial infarction with normal coronary arteriograms have been reported and there has been postmortem confirmation in none. Ross and Friesinger[3] observed three "individuals with a good history of myocardial infarction with accompanying enzymatic alterations but without permanent electrocardiographic changes or development of angina pectoris". They presumed that a "twig" thrombosis had occurred or that a larger vessel had become occluded and subsequently recanalized. Proudfit, Shirey and Sones[4] found only two cases in a group of 176 cases of myocardial infarction, and in one of these the QRS changes of anteroseptal and posterior infarction had disappeared one month later. Hale *et al.*[5] have also described one case and state that some sites of narrowing may be overlooked, particularly after recanalization of a thrombosed artery. Angina pectoris with normal arteriograms, however, appears to be much more frequent.[2, 6-8]

The infarction in the first two cases was most likely secondary to coronary artery emboli which were subsequently lysed. Penther *et al.*[9] and Cordeiro *et al.*[10] have described cases of myocardial infarction probably due to coronary emboli with no evidence of coronary occlusion post mortem. The cause of the myocardial infarction in Case 3 is less certain. Myocardial necrosis has been described following open-heart surgery.[11]

Calcific emboli, air embolism and clogging of small arteries with platelet thrombi or antifoam material have been suggested as possible causes.

The diagnosis of a genuine myocardial infarction in the last three cases is not absolutely certain, particularly in the third case. Although all three patients may have had an acute myocarditis, the clinical picture and the electrocardiographic changes were thought to be more compatible with a myocardial infarction of the classical variety. It is of interest, however, to note that none had a family history of coronary disease, none had abnormal lipid patterns, and none had angina pectoris before or after the acute episode. It is also noteworthy that all three were very active young males in excellent physical condition before the acute attack.

The mechanisms possibly involved in the production of such myocardial infarction without arteriographic obstruction are summarized in Table I. If the classic concept of pathogenesis, whereby the myocardial infarction is secondary to an occlusion of a coronary artery, is correct, one must assume that the occlusion in these cases was not evident on the arteriograms for one of the following reasons: erroneous interpretation, recanalization, functional constriction, or pathology of the microcirculation not detected by cine-coronarography.

The obstructive disease may have been overlooked, underestimated, or considered as a normal variant. In fact, diffuse thickening of the arterial wall which does not encroach on the arterial lumen cannot be recognized as obstructive disease, and the involved artery may be described as unusually small. Similarly, occlusion at the origin of relatively large coronary branches may be overlooked and considered as an anatomic variation. Although studies[12, 13] have shown that myocardial infarction is associated with significant obstructive lesions of two to three main coronary arteries, Proudfit, Shirey and Sones[14] report a high incidence of obstruction in only one vessel at selective coronary cinearteriography in patients who had myocardial infarction without angina pectoris. Myocardial infarction may therefore result from an occlusion of a single artery which may leave no definite arteriographic evidence of obstructive disease except possibly an abnormal distribution, at times difficult to distinguish from normal anatomical variants.

A functional arterial constriction or coronary spasm of long duration has been postulated as a primary cause of myocardial infarction.[15] Although coronary spasm has been observed frequently during selective coronary arteriography, particularly at the origin of the right coronary artery, it is generally not accepted that such unusual vasomotor activity is responsible for myocardial infarctions.

TABLE I.—POSSIBLE MECHANISMS OF MYOCARDIAL INFARCTION WITHOUT EVIDENCE OF "ARTERIOGRAPHIC" OBSTRUCTION

A. Infarction caused by a coronary occlusion not evident on coronary cinearteriograms
   1. Occlusion overlooked
   2. Pathology of the microcirculation
   3. Temporary occlusion by a functional constriction (spasm)
   4. Lysis of thrombus or emboli (recanalization)

B. "Infarction" not caused by a coronary occlusion.
   1. Markedly decreased coronary blood flow
   2. Oxygen diffusion and/or utilization impairment
   3. Coronary arteriovenous shunting
   4. Non-ischemic necrosis

Pathology of the microcirculation (intramural arteries of less than 200 μ. in calibre) is not usually recognized by the available cinearteriographic techniques. Focal necrosis of the myocardium has been observed in systemic arteritis and thrombotic thrombocytopenic purpura.[16, 17] Although occlusions of small arteries may cause rhythm disturbances, cardiac enlargement and insufficiency and possibly angina pectoris, it does not seemingly lead to the classical syndrome of myocardial infarction.[16]

Minor anomalies, such as wall irregularities, rigidity, small size, reduced flow and abnormal branching, difficult to distinguish from normal variants, may well be the only evidence of previous thrombotic occlusion followed by recanalization. Cases 4 and 5 may be examples of such a phenomenon. If such an occlusion does occur, one may theorize that it is primarily of a thrombotic nature, occurring with or without arteriosclerotic changes not easily recognized at cinecoronarography.

On the other hand, myocardial necrosis may not have been produced by a coronary artery occlusion at all. The high incidence of myocardial necrosis without thrombotic occlusion of coronary arteries observed post mortem suggests that the thrombosis is secondary to the necrosis and that such "lesions of the myocardium have possibly resulted from as yet obscure mechanisms."[18] Prioreschi,[19] in a study of a collected series of 4020 cases of recent and old myocardial infarction, found that 28.6% did not have coronary occlusion. Most of these patients, however, did have moderate to severe obstructive coronary disease. We have found that 10.8% of a collected series of 500 cases of myocardial infarction did not have significant coronary obstruction, although slight to moderate arteriosclerotic coronary disease was noted in many cases (Table II). Nevertheless, 4.8% of these cases had minimal to non-existent coronary dis-

TABLE II.—AUTOPSY STUDIES OF MYOCARDIAL INFARCTION WITHOUT SIGNIFICANT OBSTRUCTION AND WITH MINIMAL TO ABSENT CORONARY DISEASE

Authors	*No. of cases with infarction*	*Cases without significant obstruction*	*Cases with minimal to no coronary disease*
Ehrlich and Shinohara[18]	38	9	1
Lisa and Ring[2]	90	8	7
Friedberg and Horn[22]	153	18	11
Mitchell and Schwartz[23]	79	4	4
Allison *et al*[24]	140	15	1
Total	500	54 (10.8%)	24 (4.8%)

ease. The distinction between recent and fresh infarction was not always clearly indicated. The cases of Ehrlich and Shinohara as well as those of Friedberg and Horn were all of fresh infarction. Rona[21] reports coronary artery occlusion in 22 out of 23 cases of fresh infarction as compared to an incidence of 71.8% in cases of old infarction. He believes that the absence of coronary artery occlusion in the latter group can be explained by recanalization and reopening of the occluded coronary segment during the healing of the infarct.

Friedberg and Horn[22] concluded that "the myocardial lesions were interpreted as being due to an intensive myocardial ischemia caused by an inadequate coronary blood flow supply". All their patients with absent or only a slight degree of coronary narrowing had associated conditions such as aortic valve disease, severe hypertension, pulmonary emboli, shock or acute anemia. The lesions were more often "smaller isolated or disseminated foci of myomalacia recognizable grossly". Of Mitchell and Schwartz's[23] four cases without coronary obstruction, two had mitral stenosis but no other associated conditions which could have affected coronary blood flow were noted in the other cases. Allison *et al.*[24] also mention that in "all 15 cases with mild to moderate coronary artery disease", without occlusion, "there were factors that may have contributed to the infarction", such as anemia, valvular disease, hypertension and severe pulmonary disease. Only one case had no coronary disease, but it was associated with diabetes and chronic anemia. Gross and Sternberg[25] reported 14 cases of extensive healed myocardial infarction and one of fresh infarction in which the intimal changes in the coronary arteries were insignificant and the lumen remained patent. Five of these patients had an anginal syndrome. A definite history of hypertension was present in nine cases. Polycythemia vera was noted in two and diabetes in one case. Atrial fibrillation and evidence of emboli in other organs were observed in four cases. To sum up, there were only five cases without evidence of associated disease possibly related to the infarction.

It appears from this review that myocardial infarction without moderate to severe arteriosclerotic coronary disease occurs rarely, except when caused by coronary emboli. It is almost always accompanied by conditions leading to decreased coronary blood supply. It is also postulated that recanalization of an occluded coronary artery may explain certain cases of old infarction without coronary artery occlusion.

Metabolic, electrolytic and chemical abnormalities have been shown to produce idiopathic myocardial coagulation necrosis and infarctoid cardiopathy in experimental animals.[26-28] Likewise, coronary arteriovenous shunting, observed in animal studies, has also been suggested.[29] More recently, Eliot and Bratt[30] have described patients with myocardial necrosis in whom anomalous hemoglobin - oxygen dissociation curves were found and suggested that "abnormal binding of oxygen by hemoglobin may account for anomalous release of oxygen in the myocardium with resultant ischemia, necrosis or both". These cases were of pre-menopausal women under age 40 in whom cessation of cigarette smoking brought about restoration of abnormal hemoglobin-oxygen dissociation curves. Carbon monoxide poisoning has also been reported to produce myocardial ischemia and infarction through failure of the oxygen transport mechanism.[31] Other rare causes of myocardial necrosis are myocardial contusion[32] and cardiac vein thrombosis.[33]

If the lack of definite arteriographic evidence of obstructive coronary disease does not necessarily exclude ischemic heart disease and myocardial infarction, a satisfactory explanation of these rare cases is not easily obtained at the present time. It is postulated that our last three patients had coronary thrombosis with subsequent recanalization. One can speculate that the incidence of such a syndrome may be higher than presently suspected, since these cases may be overlooked because of the absence of angina, the disappearance of the ECG pattern of infarction,[3, 4] and the normal arteriogram. Such diagnostic problems which might not have been suspected before the availability of coronarography will undoubtedly become more frequent with a more objective study of patients with myocardial and coronary disease during life. On the other hand, some of these problem cases most likely have coronary obstructive disease which is reflected on the angiogram by anomalies of size and distribution frequently not distinguishable from normal variants and which are therefore overlooked. Finally, these rare

cases highlight intriguing aspects of the pathogenesis of ischemic heart disease, and of related and possibly other conditions simulating coronary heart diseases.

Summary In a series of 350 patients who were examined by cineangiocardiography, no obstructive disease was found in six patients in whom myocardial infarction had been diagnosed clinically. It is suggested that the symptoms of infarction in three patients were produced by coronary emboli which had subsequently undergone lysis—two with a Starr-Edwards' mitral prosthesis, and one with aortic stenosis in whom the infarction occurred during retrograde left heart catheterization. On the basis of the unusual aspects of the left coronary artery noted in two patients, it is postulated that in the three remaining patients the coronary thrombosis had been followed by recanalization. Erroneous interpretation of the arteriograms, pathology of the microcirculation undetected by this technique, and coronary spasm are unlikely explanations for the findings. Other mechanisms, based on metabolic, electrolytic and chemical abnormalities, have been suggested as causative factors in myocardial infarction without evidence of obstructive disease both in man and in experimental animals.

It is concluded that myocardial infarction without evidence of obstructive coronary disease does occur, although rarely, and that a normal coronary arteriogram does not eliminate the possibility of a previous myocardial infarction.

Résumé L'infarctus du myocarde s'accompagne le plus souvent de lésions artérioscléreux obstructives diffuses et sévères des artères coronaires. Nous avons observé parmi 350 patients soumis à la coronarographie sélective, six patients atteints d'infarctus du myocarde dont la coronarographie n'a pas démontré de lésions obstructives. Nous croyons que l'infarctus chez trois de ces patients a été provoqué par une embolie coronarienne. En effet, deux de ces sujets étaient porteurs d'une prosthèse mitrale Starr-Edwards et le troisième, une patiente atteinte d'une maladie aortique, a fait l'infarctus au cours d'un cathétérisme gauche par voie rétrograde aortique. Chez les trois autres patients, l'infarctus est possiblement secondaire à une thrombose d'une artère coronarienne qui s'est par la suite recanalisée. En effet, des anomalies légères au niveau de la coronaire gauche chez deux de ces sujets nous ont semblé représenter possiblement les seuls vestiges d'un tel phénomène.

Les divers mécanismes susceptibles d'expliquer ces observations inhabituelles sont discutés. Il n'est pas impossible que le diagnostic d'infarctus ait été erroné en particulier chez un des trois derniers patients dont la coronarographie était absolument normale et chez qui une myocardite aigüe sévère a pu simuler l'infarctus du myocarde.

Ces cas illustrent qu'une coronarographie presque normale n'exclut pas nécessairement un accident coronarien dans le passé. Il n'est pas impossible que des embolies et des thromboses coronariennes disparaissent après avoir provoqué un infarctus du myocarde.

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REFERENCES

1. FRIEDBERG, C. K.: Diseases of the heart, 3rd ed., W. B. Saunders Company, Philadelphia, 1966, p. 991.
2. MOORE, C. B.: *Med. Clin. N. Amer.*, **51**: 941, 1967.
3. ROSS, R. S. AND FRIESINGER, G. C.: *Amer. Heart J.*, **72**: 437, 1966.
4. PROUDFIT, W. L., SHIREY, E. K. AND SONES, M. F., JR.: *Circulation*, **33**: 901, 1966.
5. HALE, G. *et al.*: *Brit. Heart J.*, **28**: 40, 1966.
6. LIKOFF, W., SEGAL, B. L. AND KASPARIAN, H.: *New Eng. J. Med.*, **276**: 1063, 1967.
7. Medical News; *J. A. M. A.*, **201**: 27, August 28, 1967.
8. ELIOT, R. S. AND MIZUKAMI, H.: *Circulation*, **34**: 331, 1966.
9. PENTHER, P. *et al.*: *Acta Cardiol. (Brux.)*, **22**: 309, 1967.
10. CORDEIRO, A. *et al.*: *Brit. Heart J.*, **29**: 91, 1967.
11. MORALES, A. R., FINE, G. AND TABER, R. E.: *Arch. Path. (Chicago)*, **83**: 71, 1967.
12. FRENCH, A. J. AND DOCK, W.: *J. A. M. A.*, **124**: 1233, 1944.
13. SEGAL, B. L.: The distribution and relation of atherosclerosis to coronary heart disease. *In*: Coronary heart disease; the seventh Hahnemann symposium held April 16-18, 1962 in Philadelphia, edited by W. Likoff and J. H. Moyer, with the assistance of S. R. Bender and others, Grune & Stratton Inc., New York, 1963, p. 140.
14. PROUDFIT, W. L., SHIREY, E. K. AND SONES, F. M., JR.: *Circulation*, **36**: 54, 1967.
15. SEWELL, W. H.: *Angiology*, **17**: 1, 1966.
16. JAMES, T. N.: *Amer. J. Cardiol.*, **20**: 679, 1967.
17. BAROLDI, G. AND MANION, W. C.: *Amer. Heart J.*, **74**: 173, 1967.
18. EHRLICH, J. C. AND SHINOHARA, Y.: *Arch. Path., (Chicago)*, **78**: 432, 1964.
19. PRIORESCHI, P.: *Canad. Med. Ass. J.*, **97**: 1339, 1967.
20. LISA, J. R. AND RING, A.: *Arch. Intern. Med. (Chicago)*, **50**: 131, 1932.
21. RONA, G.: *Canad. Med. Ass. J.*, **95**: 1012, 1966.
22. FRIEDBERG, C. K. AND HORN, H.: *J. A. M. A.*, **112**: 1675, 1939.
23. MITCHELL, J. R. A. AND SCHWARTZ, C. J.: *Brit. Heart J.*, **25**: 1, 1963.
24. ALLISON, R. B. *et al.*: *Circulation*, **27**: 170, 1963.
25. GROSS, H. AND STERNBERG, W. H.: *Arch. Intern. Med. (Chicago)*, **64**: 249, 1939.
26. RONA, G. *et al.*: *Arch. Path. (Chicago)*, **67**: 443, 1959.
27. THOMAS, W. A. AND HARTROFT, W. S.: *Circulation*, **19**: 65, 1959.
28. RAAB, W.: *Amer. J. Cardiol.*, **5**: 571, 1960.
29. HIRSCH, S.: *Acta Med. Scand.*, **138**: 449, 1950.
30. ELIOT, R. S. AND BRATT, G. T.: *Amer. J. Cardiol.*, **21**: 98, 1968 (abstract).
31. COSBY, R. S. AND BERGERON, M.: *Ibid.*, **11**: 93, 1963.
32. DEMUTH, W. E., JR. AND ZINSSER, H. F., JR.: *Arch. Intern. Med. (Chicago)*, **115**: 434, 1965.
33. RYWLIN, A. M. *et al.*: *Amer. J. Cardiol.*, **21**: 269, 1968.