The Nature and Clinical Features of Myocardial Infarction with Normal Coronary Arteriogram

Andrew Rosenblatt, M.D., and Arthur Selzer, M.D.

SUMMARY Six new cases of acute myocardial infarction with normal coronary arteriogram are presented and supplemented by 19 collected cases (group I). These are compared with 16 cases of myocardial infarction caused by occlusive coronary artery disease in a comparable population (group II). The following significant differences between the two groups are established: patients in group I were younger (27.5 years vs 33.7 years, P < 0.005); at least one risk factor was present in all patients in group II, but in only 40% of group I (P < 0.0001). Effort angina preceded the attack in ten patients of group II, but in none of group I (P < 0.0001). The attack was unheralded in 24 of the 25 patients in group I, but was preceded by prodromes in 11 of 16 in group II (P < 0.0001). Attacks of pain following myocardial infarction occurred in five patients of group I and 11 of group II (P < 0.001). Results are discussed in the light of the nature of myocardial infarction in group I. No support is found for the coronary spasm theory. The most likely mechanism for development of myocardial infarction in group I is thought to be a thromboembolic "accident." This accident is not necessarily related to atherosclerotic coronary disease and is presumed to be benign in nature.

THE USE OF CORONARY ARTERIOGRAPHY during the past decade and a half has greatly enhanced our understanding of the natural history of coronary artery disease. A good correlation has been established between the presence and location of ischemia and infarction on the one hand and the presence and location of obstructive coronary arterial lesions on the other. Among the few exceptions to this relationship are the occasionally seen myocardial infarcts in patients whose coronary arteriograms fail to reveal evidence of coronary obstructive lesions. Arnett and Roberts estimate that these cases constitute approximately 1% of patients with documented myocardial infarction. This study was undertaken for the purpose of examining the clinical features of myocardial infarction without demonstrable coronary lesions, comparing them with those patients in a similar age group who have coronary disease, and searching for clues regarding the causes of myocardial infarcts of the former variety.

Material and Methods

Among 2507 selective coronary arteriograms performed in our laboratory between 1970 and 1975 there were seven patients in whom the study performed after a documented myocardial infarction unrelated to trauma caused by coronary arteriography did not reveal significant coronary artery disease (i.e., normal coronary arteriogram, or lesions ≤ 40% in one vessel). Criteria for accepting documentation for myocardial infarction included typical evolution of ST-T abnormalities and rise in pertinent enzymes. Abnormal Q waves were present in three of six of the patients in group I, in 14 out of 16 patients in group II, and in all cases collected from the literature. Transmural and nontransmural infarcts were thus included but subendocardial (manifested by ST-segment depression alone) were not. There were six male patients, ages 18-35, and one female patient age 43. Inasmuch as a review of the pertinent literature revealed that myocardial infarction without demonstrable coronary artery disease occurs almost exclusively in young males, it was decided to limit the review to males under the age of 40. In order to increase the number of patients in this category for the analysis, 19 more patients — males under the age of 40 — were collected from the literature.** namely all male patients with transmural myocardial infarction and a normal coronary arteriogram in whom adequate clinical data were made available. Only patients who had no other evidence of cardiac disease were included in the study. Those with myocardial infarction developing after coronary arteriography were also excluded.

Among features recorded for comparison were the following: the presence or absence of risk factors (smoking, hyperlipoproteinemia, hypertension), pattern of the attack, preceding and following effort angina, location of the infarction and late deaths; angiographic features included the presence or absence of minor coronary lesions and of localized abnormalities of left ventricular wall motion. The significance of the differences between the two groups was evaluated by standard statistical methods.

Results

A summary of the findings in the six patients from our department is presented in table 1. Review of risk factors indicate that three patients were moderate smokers, none had hypertension, one had hyperlipoproteinemia. Five patients had typical attacks of pain signifying the onset of myocardial infarction; none of them had prodromal attacks. One patient (BB) had a brief period of atypical chest pain three months prior to the myocardial infarction. In one patient (RC) the electrocardiogram showed typical changes of past myocardial infarction — there was no history of an attack suggesting its date. Ventriculogram revealed a large apical ventricular aneurysm. Five patients had evidence of anterior wall myocardial infarction; one had posterior wall infarction. In all patients the clinical course was uncomplicated and benign. Coronary arteriography, performed four weeks to three months after the infarction, revealed normal coronary arteries in four. In one there was a minor lesion (about 20%) in the left anterior branch; in another a 30% lesion in the same branch. In three patients left ventriculography revealed abnormalities of wall motion. Follow-up revealed
that none of the patients had effort angina or cardiac failure following the attack. In one (PL) another attack of myocardial infarction occurred three months after the original one and after the coronary arteriography. He made an uneventful recovery and remained well for two years thereafter; during the third year he suffered one minor ischemic episode. He was well three years after the study.

The control group was composed of 16 male patients. In all patients the presence of risk factors was established. Eight had one risk factor, and eight had two risk factors. Ten patients had a history of effort angina ranging from one week to three years prior to the infarction. Ten the attack of myocardial infarction was preceded by prodromal attacks of pain — either as new pain or as accelerating angina. Angiographic studies revealed one-vessel coronary artery disease in three patients, two-vessel disease in nine, and three-vessel disease in four. Abnormalities of left ventricular wall motion were detected in 13 patients. Eleven patients had anginal attacks or nonexertional chest pain following the infarction. One patient died some months later, from an arrhythmia.

Table 2 presents a comparison of the salient features of myocardial infarction in young men with and without demonstrable coronary artery disease. The young age of the patients in group I is apparent, with five patients under the age of 20 (youngest 14), nine in the 20–30 category, and 11 over 30. Patients in group II are older, with a statistically significant difference between the groups. All patients in group II had at least one risk factor present, whereas in group I half had no risk factors at all, and of those who had, one had hyperlipoproteinemia. None of the patients in group I had effort angina; four had atypical, nonexertional episodes of thoracic pain in the past. The onset of acute myocardial infarction was abrupt and without prodromes in 24 patients of group I. On the other hand, ten presented themselves with premonitory attacks of pain in group II.

There was no difference between the groups in the location of the infarction (group I: anterior 12, inferior 13; group II: anterior, seven, inferior, nine). Following the attack, "angina" (details not given) was recorded in three patients in group I; in two others intermittent attacks of chest pain were recorded. Three patients in group II and two patients in group I had more than one myocardial infarction. One patient in each group died.

Table 1.

<table>
<thead>
<tr>
<th>Age</th>
<th>Major Risk Factors</th>
<th>Onset of MI</th>
<th>ECG</th>
<th>Prior Angina</th>
<th>Post infarction Chest Pain</th>
<th>Coronary Arteriogram</th>
<th>Left Ventriculogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>JH</td>
<td>32 S, L</td>
<td>Single attack of pain</td>
<td>AMI with abnormal Q waves, typical evolution</td>
<td>occasional atypical nonexert. pain 1 yr. 4 minor attacks of pain in 8 weeks</td>
<td>none</td>
<td>none</td>
<td>focal lesion 20% LAD</td>
</tr>
<tr>
<td>PL</td>
<td>23 S</td>
<td>Single attack of pain</td>
<td>AMI with typical evolution</td>
<td>none</td>
<td>none</td>
<td>focal lesion 30% LAD</td>
<td>apical skineasia</td>
</tr>
<tr>
<td>HH</td>
<td>32 S</td>
<td>Single attack of pain</td>
<td>AMI with abnormal Q waves, typical evolution</td>
<td>none</td>
<td>none</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>GW</td>
<td>18 —</td>
<td>Single attack of pain</td>
<td>IMI with typical evolution</td>
<td>none</td>
<td>none</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>BB</td>
<td>35 —</td>
<td>Single attack of pain</td>
<td>AMI with typical evolution in 3 mos.</td>
<td>few bouts of atypical chest pain</td>
<td>none</td>
<td>none</td>
<td>normal</td>
</tr>
<tr>
<td>RC</td>
<td>26 H</td>
<td>Not clinically evident</td>
<td>AMI with abnormal Q waves</td>
<td>none</td>
<td>none</td>
<td>normal</td>
<td>large apical aneurysm</td>
</tr>
</tbody>
</table>

Abbreviations: S = smoking; L = hyperlipoproteinemia; H = hypertension; AMI = anterior myocardial infarction; IMI = inferior myocardial infarction; LAD = left anterior descending coronary branch.

Discussion

Myocardial infarction is the result of prolonged, irreversible ischemia of the myocardium and presupposes total or subtotal cessation of coronary blood flow to the infarcted area. As pointed out by Arnett and Roberts, no case was ever reported in which normal coronary arteries were found during the forming stage of myocardial infarction. It can be accepted as axiomatic that some occlusive process operated at the time of development of myocardial infarction but is no longer demonstrable by coronary arteriography when studied after the event. Three possible mechanisms for this discrepancy have to be considered: 1) myocardial infarction

Table 2.

<table>
<thead>
<tr>
<th>Group I (N = 26)</th>
<th>Group II (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>27.5</td>
</tr>
<tr>
<td>Range</td>
<td>14–37</td>
</tr>
<tr>
<td>No Risk Factor (S,L,H)</td>
<td>15</td>
</tr>
<tr>
<td>History of Effort Angina</td>
<td>0</td>
</tr>
<tr>
<td>Un heralded Onset of MI</td>
<td>24</td>
</tr>
<tr>
<td>Post MI Pain</td>
<td>5</td>
</tr>
<tr>
<td>Late Deaths (to 1 yr.)</td>
<td>1</td>
</tr>
<tr>
<td>Multiple Documented MIs</td>
<td>2</td>
</tr>
</tbody>
</table>

For abbreviations see table 1.
is produced by coronary arterial spasm; 2) the usual coronary lesions cause myocardial infarction, but their presence is missed by the subsequent coronary arteriogram; 3) occlusive lesions, present at the time of the infarction, actually disappear (e.g., recanalization or lysis of a thrombus).

Since the demonstration that spasm of a coronary artery that appears normal can produce variant angina, life-threatening arrhythmias and death, it has been widely assumed that coronary artery spasm is a cause — perhaps the principal cause — of myocardial infarction without demonstrable coronary artery disease. We agree with Arnett and Roberts that myocardial infarction seldom, perhaps never, is caused by coronary arterial spasm. Not only has a case of transmural myocardial infarction associated with coronary artery spasm never been authenticated, but a study from our laboratory showed that patients with variant angina due to spasm of normal coronary arteries follow a distinctive clinical pattern characterized by recurrent, usually nocturnal, attacks of chest pain — a feature never found in conjunction with myocardial infarction in our group I.

The reliability of coronary arteriography as demonstrating obstructive lesions in the coronary arteries depends upon many technical factors such as the equipment, clarity of the films, number of views, etc., as well as experience of the readers. However, it has been recognized and repeatedly pointed out by pathologists that significant coronary disease may be present and missed by the best coronary arteriography. The two commonest causes for this are a slit-like crescentic lumen caused by eccentric plaques and occlusion of an artery at its origin from the parent vessel with collateral arteries enlarging to a point of being mistaken for the occluded branch. The latter mechanism may be responsible for some cases in group I.

Perhaps the most attractive hypothesis is one assuming thromboembolism as a cause of the infarction, with lysis or recanalization of the occluding thrombus. Although its source may not be known, coronary embolism may be commoner than generally assumed; furthermore, thrombosis in situ initiated by trivial vessel wall irregularities may also occasionally occur.

Results of this study bring out several important points that shed some light upon the origin of myocardial infarction with normal coronary arteriogram. The unusually young age of some patients and the common absence of risk factors suggest a different population than that in group II, the latter representing accelerated atherosclerotic coronary artery disease. The most important yield of the study is the observation regarding the onset of the myocardial infarction. The abrupt onset in all cases of group I (except one where clinical manifestations were altogether absent) as contrasted with the presence of angina and pre-infarction prodrumes in the second group supports the hypothesis that myocardial infarction in group I represents an "accident" of the coronary circulation, rather than chronic disease.

One could not be justified in claiming that all patients in group I represent a homogenous population; it is highly probable that some may have had atherosclerotic single-vessel disease with complete occlusion, missed on the coronary arteriogram. Nevertheless, the highly significant difference between the two groups suggests that thromboembolism with lysis or recanalization may be the commonest cause of myocardial infarction with normal coronary arteriogram.

The material at hand does not supply sufficient information to survey the diagnostic differences between the two groups. Inasmuch as survival of the acute attack is the prerequisite for the performance of the coronary arteriogram, mortality from the attack is known in either group. Follow-up studies did not sufficiently extend in time to obtain meaningful figures for late mortality. Thus one can only surmise that a patient suffering from a single episode of pain, representing myocardial infarction, has a better prospect than one suffering from postinfarctional effort angina (68% of group II). Furthermore, well known actuarial figures of survival of patients with one, two and three vessel involvement by coronary atherosclerotic disease suggest a guarded prognosis for patients in group II, not only because 81% of them have at least two-vessel disease, but also because of their youth, suggesting an accelerated atherosclerotic process. A benign course is expected for patients with a normal coronary tree and a thrombotic "accident," although in a few, such accidents may well be repetitive.

As a final comment one should point out that the difference between our two groups could be used in the diagnostic evaluation of myocardial infarction in young subjects. An un heralded attack of myocardial infarction with a prompt and complete recovery offers a high probability that it is caused by a relatively benign coronary "accident." Myocardial infarction preceded by accelerating angina, and/or followed by persistent angina is virtually certain to represent serious and premature coronary artery disease, probably with multivessel involvement.

References

The nature and clinical features of myocardial infarction with normal coronary arteriogram.
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