Postinfarction Angina Caused by Coronary Arterial Spasm

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SUMMARY Recurrent ST-segment elevations in leads where new Q waves developed were repeatedly recorded in six patients during a recovery phase of acute myocardial infarction. Such ST-segment elevations were transient, occurred with or without chest pain, and returned to control levels. No enzymatic changes signifying recurrent myocardial necrosis were found after each episode. Selective coronary cineangiography in one patient demonstrated a mild segmental stenosis in the coronary artery perfusing the infarcted area; this artery became completely occluded after administration of i.v. ergonovine. Administration of calcium antagonists effectively reduced the frequency of postinfarction angina and ST-segment elevations.

The clinical features suggest that the postinfarction angina in these patients is produced by coronary arterial spasm and that coronary arterial spasm may cause severe life-threatening dysrhythmias.

SPONTANEOUS ANGINA occurs frequently in patients with acute myocardial infarction (AMI). Postinfarction angina is generally considered to be a poor prognostic sign because it may result in an extension of myocardial infarction (MI). However, little is known about the mechanisms of postinfarction angina occurring at rest. In the presence of severe stenosis in a coronary artery, very small increases in heart rate or other determinants of myocardial oxygen consumption, which can occur even at rest, may be enough to alter the myocardial oxygen supply-demand relationship. Schuster and Bullikley recently suggested that an interruption of collateral blood flow caused by acute occlusion of a donor artery may be responsible for postinfarction angina.

Coronary arterial spasm is another possible cause of postinfarction angina. Oliva and Breckinridge indicated that spasm was present in the occluded artery in as many as 40% of patients with AMI. However, there has been no report of patients in whom coronary arterial spasm was responsible for postinfarction angina.

In this report, we describe the clinical features of six patients that strongly suggest that postinfarction angina was produced by coronary arterial spasm.

Materials and Methods

Six patients admitted with AMI to our coronary care unit (CCU) had recurrent ST-segment elevations. The diagnosis of AMI was made on the basis of severe prolonged chest pain and electrocardiographic findings of abnormal Q waves with ST-segment elevations. The diagnosis was confirmed by evolutionary ECG changes and elevations of serum enzymes. There were three males and three females, ages 43-72 years (average 56.8 ± 10.7 years). These patients all had transmural MI. Four patients had inferior and two patients had anteroseptal MI.

All six patients had a history of angina pectoris before AMI. Patients 1, 3, 4 and 5 had both effort and spontaneous angina, patient 2 had spontaneous angina and patient 6 had effort angina. Angina pectoris in patient 3 was diagnosed as variant angina before AMI. Although not confirmed, the clinical picture in patients 1 and 2 was suggestive of variant angina.

After the admission to the CCU, the patients were limited to bed rest. Most patients received sublingual nitroglycerin or morphine HCl for pain on admission and i.v. xylocaine was given to some patients. No other drug was administered. Initial chest pain subsided within 6 hours after admission. No serious complication was observed in these patients before the onset of recurrent angina at rest with ST-segment elevation.

ECG lead CM4 was continuously monitored in every patient after admission. A 12-lead ECG was recorded daily for several days. In all patients, the evolitional ECG changes were completed by the fourth day after admission. The ST segments had returned to an isoelectric level in patients 1, 2, 3 and 6, but remained slightly elevated in patients 4 and 5 at the onset of recurrent angina pectoris at rest with ST-segment elevation. ST-segment elevation was defined as significant when it was elevated from the control level by more than 2 mm or more 0.08 second after the R wave.

Selective coronary cineangiography was performed using the Sones technique in patient 2.

Before discharge, every patient performed a treadmill exercise stress test (Bruce protocol) without any antianginal drug. The interval between the occurrence of AMI and the final exercise test was 31-79 days (average 48.3 ± 18.3 days).

Results

The clinical features are summarized in table 1. The first spontaneous anginal episode occurred by the second day of AMI in all six patients. ST-segment elevation at the time of spontaneous angina was recorded for the first time on the third day of AMI in patient 3,
**TABLE 1. Clinical Features**

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Type of angina before AMI</th>
<th>Location of abnormal Q waves</th>
<th>Interval between AMI and post-infarction angina (days)*</th>
<th>ECG during postinfarction angina</th>
<th>Calcium antagonist</th>
<th>Drug (dosage/24 hrs)</th>
<th>Other drugs† (dosage/24 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43</td>
<td>M</td>
<td>Effort and spont.</td>
<td>II, III, aV_f</td>
<td>1 (4)</td>
<td>II, III, aV_f, V_1-6</td>
<td>PAC, PVC, VT</td>
<td>Diltiazem (150 mg)</td>
<td>+ None</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>M</td>
<td>Spont.</td>
<td>V_1-3</td>
<td>2 (4)</td>
<td>V_1-4</td>
<td>PVC</td>
<td>Diltiazem (150 mg)</td>
<td>+ Molsidomine (6 mg)</td>
</tr>
<tr>
<td>3</td>
<td>48</td>
<td>F</td>
<td>Effort and spont.</td>
<td>II, III, aV_f</td>
<td>1 (3)</td>
<td>II, III, aV_f, V_1-6</td>
<td>PAC, PVC, VT</td>
<td>Diltiazem (240 mg)</td>
<td>+ ISDN (40 mg)</td>
</tr>
<tr>
<td>4</td>
<td>62</td>
<td>M</td>
<td>Effort and spont.</td>
<td>V_1-3</td>
<td>2 (7)</td>
<td>V_1-4</td>
<td>PAC, PVC, VT</td>
<td>Diltiazem (120 mg)</td>
<td>+ ISDN (20 mg)</td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td>F</td>
<td>Effort and spont.</td>
<td>II, III, aV_f</td>
<td>2 (32)</td>
<td>II, III, aV_f, V_1-5</td>
<td>PVC, AVB</td>
<td>Diltiazem (120 mg)</td>
<td>+ None</td>
</tr>
<tr>
<td>6</td>
<td>63</td>
<td>F</td>
<td>Effort</td>
<td>II, III, aV_f</td>
<td>2 (5)</td>
<td>II, III, aV_f, V_1-6</td>
<td>PAC, PVC, CAVB, VT</td>
<td>ISDN (40 mg)</td>
<td></td>
</tr>
</tbody>
</table>

*Number in parentheses indicates interval between onset of AMI and occurrence of postinfarction angina with ST-segment elevation first confirmed by 12-lead ECG.
†Diltiazem was replaced with nifedipine because systemic skin eruptions developed.
§Not administered.

Abbreviations: spont. = spontaneous; AMI = acute myocardial infarction; ST † = ST-segment elevation; ST ‡ = ST-segment depression; PAC = premature atrial complexes; PVC = premature ventricular complexes; VT = ventricular tachycardia; AVB = first-degree atrioventricular block; CAVB = complete atrioventricular block; ++ = complete suppression of postinfarction angina; + = marked reduction in frequency of postinfarction angina; ISDN = isosorbide dinitrate.

on the fourth day in patients 1 and 2, on the fifth day in patient 6, on the seventh day in patient 4 and on the thirty-second day in patient 5. Spontaneous angina occurred frequently in every patient, as frequently as nine times per day in patient 3. Spontaneous angina usually subsided spontaneously or was relieved within 5 minutes by 0.3–0.9 mg of sublingual nitroglycerin. Recording of a 12-lead ECG was attempted during each episode of angina in every patient, and ST-segment elevation during spontaneous angina was confirmed at least six times in each patient. With relief of angina, ST segments returned to the level before angina and serum enzymes subsequently did not show any elevation. We attempted to record heart rate and blood pressure during each episode of angina. Usually, both heart rate and blood pressure increased during angina and decreased after it subsided. When severe dysrhythmia occurred, the blood pressure decreased.

In every patient, the location of ST-segment elevation in the 12-lead ECG during spontaneous angina always coincided with the area where new Q waves developed (table 1, fig. 1). During angina, three patients had ventricular tachycardia and one patient had complete atrioventricular block (table 1).

Twenty-four-hour Holter monitor recordings using an Avionics recorder were done several times on each patient, and frequently demonstrated recurrent ST-segment elevation that was not always associated with chest pain. Figure 2 shows an example of recurrent ST-segment elevations in patient 1. Eleven occurrences of spontaneous ST-segment elevation were recorded during 24 hours, but the patient had chest pain only four times.

Left ventriculography and selective coronary cineangiography were performed in patient 2 on the fifty-fourth day after AMI. The ventriculogram revealed an area of akinesis in the anteroseptal portion of the left ventricle. The angiogram demonstrated only 50% segmental stenosis at the proximal left anterior descending coronary artery (LAD) (fig. 3A). After i.v. ergonovine maleate, 0.05 mg, the LAD was completely occluded at the stenotic portion and the distal portion was opacified by retrograde flow from the left circumflex coronary artery (fig. 3B). After administration of ergonovine maleate, the patient developed chest pain, and ST segments were elevated in leads V_1-4, as in a spontaneous anginal attack. The occlusion of the LAD induced by ergonovine maleate was promptly relieved by sublingual nitroglycerin and the electrocardiographic changes returned to the original level.

Several drugs were administered to treat recurrent spontaneous angina (table 1). One and one-half to 2 inches of nitroglycerin ointment given every 6 hours in patients 1 and 5 did not completely control angina or ST-segment elevation. Calcium antagonists, diltiazem‡–13 or nifedipine‡–14 were administered to five patients (table 1). In patients 1 and 5, spontaneous angina was completely eliminated by diltiazem or nifedipine. In three other patients, the frequency of angina was markedly reduced by diltiazem and completely suppressed after an addition of nitrate, either molsidomine‡–17, 18 or isosorbide dinitrate. In patient 6,
administration of isosorbide dinitrate resulted in a complete relief of spontaneous angina.

Without antianginal medication, all six patients achieved at least stage II of exercise (Bruce protocol) before discharge. Patients 1, 2, 3, 4 and 6 achieved more than stage III without experiencing angina.

**Discussion**

Coronary arterial spasm occurs spontaneously or can be induced by drugs such as methacholine and ergonovine maleate, by manipulations of autonomic nervous system by alkalosis and even by exercise. Coronary arterial spasm is considered to be responsible for clinical features known as variant angina, which is characterized by recurrent angina at rest associated with ST-segment elevation. Several studies have shown that cyclic ST-segment elevations without chest pain are often recorded on 24-hour Holter recordings in patients with spasm-induced angina. Cyclic ST-segment elevations in patients with angina are characteristic of spasm-induced angina, because coronary arterial spasm can almost always be documented in such patients. Calcium antagonists are specifically effective in preventing spasm-induced angina.

The clinical features of postinfarction angina in these six patients suggest that angina is probably caused by coronary arterial spasm. This conclusion is based on the following observations: postinfarction angina in these patients occurred at rest and was always associated with ST-segment elevation; calcium antagonists (diltiazem or nifedipine) effectively controlled angina in five of these six patients (a calcium antagonist was not given to one patient, because angina in this patient was effectively controlled with isosorbide dinitrate); 24-hour Holter recordings revealed cyclic ST-segment elevations, only some of which were associated with chest pain.

Coronary arterial spasm was induced by i.v. ergonovine maleate in one patient, and the ECG changes during this ergonovine-induced coronary arterial spasm were similar to those during spontaneous angina.

Extremely severe, fixed coronary arterial stenosis might have been responsible for postinfarction angina in these patients. However, this seems to be unlikely. Beside clinical features that strongly suggested spasm-induced angina, most of these patients achieved stage III of the Bruce exercise protocol without any antianginal drug before their discharge. Exercise studies were done a few weeks after the time of recurrent angina so that one could argue that good exercise tolerance was due to the development of collaterals. However, a recent study suggests that improved exercise tolerance after relief of unstable angina is not caused by the development of collaterals.

ST-segment elevation occurred in the area of AMI. This implies that coronary arterial spasm occurred at the occluded artery or at the artery that supplied collateral blood flow to the infarcted area. These findings are in agreement with observations by Oliva and Breckinridge, who reported that coronary arterial spasm in patients with AMI was always in the occluded artery.

We do not know why coronary arterial spasm occurred only in the area of MI. It might be because the coronary artery in the infarcted area tends to develop spasm, as suggested experimentally ("injury spasm"). However, it is more likely that coronary arterial spasm was the cause of MI in these patients and continued to occur in the same artery even after MI. Three of six patients had a history of angina.

**Figure 1.** Twelve-lead ECGs of patient 1 before and during chest pain and after nitroglycerin recorded on the fourth day after inferior myocardial infarction. During pain at rest, ST segments were elevated in leads II, III and aVF and reciprocal depression of ST segments was noted in leads I, aVL and V6. After sublingual nitroglycerin, the pain was terminated in 3 minutes with a return of ST-segment elevations.
before AMI, which was compatible with variant angina. In patient 2, the coronary arterial obstruction responsible for MI reduced the lumen by only 50%; the artery became completely occluded after administration of ergonovine maleate. These findings suggest that coronary arterial spasm was a likely cause of MI.

The findings of ST-segment elevation during angina over the infarcted area suggests that there were remaining viable tissue as well. In fact, several studies...
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have shown that the electrocardiographic term transmural infarction does not mean histologically transmural infarction, and that the area occupied by AMI included some part of the normal myocardium.47,48

Previous studies have indicated that serious dysrhythmias, such as ventricular tachycardia or complete atrioventricular block, may frequently develop during coronary arterial spasm.45,46 In our six patients, ventricular tachycardia occurred in three patients and complete atrioventricular block in one patient during ST-segment elevation. These findings indicate that coronary arterial spasm occurring during a recovery phase of AMI may be a cause not only of postinfarction angina but also of serious dysrhythmias in some patients. Coronary arterial spasm could also result in an extension of MI.

The incidence of coronary arterial spasm in AMI is not known. However, from December 1979 through July 1980, 18 patients with AMI were admitted to our CCU, including the six patients described in this study. This suggests that coronary arterial spasm during AMI is not rare and should be considered as an etiology of postinfarction angina. Recent studies suggest that coronary arterial spasm may show ST-segment depression rather than elevation.49-53 Postinfarction angina with ST-segment depression on ECGs could also be caused by coronary arterial spasm.

Addendum

From August 1980 through March 1981, we had 25 patients with AMI. In four, recurrent ST-segment elevation in the leads where new Q waves developed were confirmed at least four times on a 12-lead ECG in each patient. The clinical features in these four patients during the recovery phase were similar to those in the six patients presented above.

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