ARTERIOGRAPHIC FEATURES OF ANGINA PECTORIS ASSOCIATED WITH ST SEGMENT DEPRESSION DURING CORONARY ARTERIAL SPASM

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To examine the angiographic features of vasospastic angina associated with ST segment depression, we attempted to analyze the coronary arteriograms of 12 patients who exhibited ST segment depression during the ergonovine provocative test. Right and left coronary arteriograms were obtained successively within a short period when the ergonovine administration revealed ST segment depression. Eight out of 12 patients showed non-total spastic obstructions in one of the major coronary arteries. Among them, a collateral augmentation was found only in one patient. Two cases exhibited the well-developed collateral channels during non-anginal periods and in one case a collateral blood supply was reduced by the spasm occurred in the donating artery. In another one, the collateral circulation did not change during anginal period. Three out of 4 patients who showed total spastic obstructions demonstrated transiently augmented collateral circulation which was supplied by the non-spastic artery. These findings may indicate that ST segment depression during coronary artery spasm could attribute to a subendocardial ischemia caused by an incomplete occlusion of large coronary artery and transient reduction or augmentation of collateral blood flow.

CORONARY artery spasm, documented in Prinzmetal's variant angina, has been postulated to have a crucial role in the pathogenesis of various kinds of angina pectoris including rest angina, exertional angina and unstable angina. Such a coronary spasm is usually accompanied by ST segment deviation (elevation or depression) in the electrocardiogram. Maseri et al. reported that the deviation of ST segment might largely depend upon the severity and site of coronary spasm and the presence of collateral circulation. This hypothesis was proved by Yasue et al., who demonstrated that ST segment elevation was seen when a severe vasospastic narrowing occurred in a large coronary artery, while an incomplete obstruction of a major coronary artery or an existence of collateral vessels might result in ST segment depression. We previously found the transiently developed collateral vessel supplied by the non-spastic coronary artery among the patients with ST segment depression during vasospastic attacks, and these collateral circulations could serve to prevent severe myocardial ischemia. It may be indicated that such a dynamic evolution of collateral circulation might play one of the possible mechanisms attribute to subendocardial

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<tr>
<td>1</td>
<td>41 m.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.1</td>
<td>( V_6 - V_6, II, III, aVF ) 0.1-0.2 mV</td>
<td>50% ( S_6 )</td>
<td>99% ( S_6 )</td>
</tr>
<tr>
<td>2</td>
<td>50 m.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.05</td>
<td>( V_6 - V_6 ) 0.1-0.15 mV</td>
<td>50% ( S_6 )</td>
<td>75% ( S_6 )</td>
</tr>
<tr>
<td>3</td>
<td>53 m.</td>
<td>RA</td>
<td>positive</td>
<td>0.2</td>
<td>( V_6 - V_6, II, III, aVF ) 0.1-0.3 mV</td>
<td>normal</td>
<td>90% ( S_4 ), 75% ( S_11 ), 100% ( S_6 )</td>
</tr>
<tr>
<td>4</td>
<td>48 m.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.1</td>
<td>( V_6 - V_6, II, III, aVF ) 0.05-0.1 mV</td>
<td>100% ( S_6 )</td>
<td>100% ( S_6 )</td>
</tr>
<tr>
<td>5</td>
<td>46 m.</td>
<td>RA</td>
<td>negative</td>
<td>0.1</td>
<td>( V_6 - V_6, II, III, aVF ) 0.1-0.2 mV</td>
<td>75% ( S_6 )</td>
<td>100% ( S_6 )</td>
</tr>
<tr>
<td>6</td>
<td>61 m.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.3</td>
<td>( V_6 - V_6 ) 0.05-0.1 mV</td>
<td>normal</td>
<td>90% ( S_{12} )</td>
</tr>
<tr>
<td>7</td>
<td>42 m.</td>
<td>EA &amp; RA</td>
<td>negative</td>
<td>0.2</td>
<td>( V_6 - V_6, II, III, aVF ) 0.05-0.1 mV</td>
<td>90% ( S_1 )</td>
<td>100% ( S_1 )</td>
</tr>
<tr>
<td>8</td>
<td>59 m.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.1</td>
<td>( V_6 - V_6, II, III, aVF ) 0.1-0.2 mV</td>
<td>90% ( S_6 )</td>
<td>99% ( S_6 )</td>
</tr>
<tr>
<td>9</td>
<td>55 m.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.1</td>
<td>( V_6 ) 0.1 mV</td>
<td>90% ( S_6 )</td>
<td>100% ( S_6 )</td>
</tr>
<tr>
<td>10</td>
<td>45 m.</td>
<td>EA &amp; RA</td>
<td>negative</td>
<td>0.1</td>
<td>( V_6 - V_6 ) 0.05-0.1 mV</td>
<td>50% ( S_6 )</td>
<td>90% ( S_6 ), 50% ( S_3 )</td>
</tr>
<tr>
<td>11</td>
<td>48 f.</td>
<td>RA &amp; RA</td>
<td>positive</td>
<td>0.1</td>
<td>( V_6 - V_6 ) 0.1 mV</td>
<td>90% ( S_7 )</td>
<td>99% ( S_7 )</td>
</tr>
<tr>
<td>12</td>
<td>42 f.</td>
<td>EA &amp; RA</td>
<td>positive</td>
<td>0.2</td>
<td>( V_6 - V_6, II, III, aVF ) 0.05-0.1 mV</td>
<td>normal</td>
<td>50% ( S_6 - S_8 )</td>
</tr>
</tbody>
</table>

**Abbreviations:** EA = exertional angina; f = female; LAD = left anterior descending artery; m = male; RA = rest angina; RCA = right coronary artery; † = transiently-augmented collateral vessels; †† = transiently-reduced collateral vessels; ††† = previously-existed collateral vessels. Coronary segments were represented by the number of American Heart Association division.}
ischemia associated with ST segment depression\textsuperscript{7,8,9} Feldman et al.\textsuperscript{10} also described a patient with vasospastic angina not associated with ST segment elevation, in whom collateral vessels could be demonstrated transiently. These findings suggest that the ST segment deviation may be modified by the coronary blood flow from the non-spastic artery and that the simultaneous visualization of the left and right coronary arteries during coronary vasospasm would be of necessity to elucidate the precise relationship between vasospasm and ST segment deviation\textsuperscript{8,9} Thus, we attempted to review the angiographic findings of vasospastic angina associated with ST segment depression during ergonovine-induced coronary artery spasm using the method of simultaneous visualization of both left and right coronary arteries.

**SUBJECTS AND METHODS**

**Patient Population**

We analyzed the angiographic findings in 12 patients (10 males and 2 females, average age 49 years, range 41–61 years) who showed ST segment depression during ergonovine-induced vasospastic attacks. These patients were selected from the consecutive 41 patients who exhibited coronary artery spasm associated with significant ST segment deviation (elevation or depression or both) during cardiac catheterization for the diagnosis of chest complaints at rest and/or on exertion, from July, 1979 to June, 1982. The patients' age, sex, clinical features, and a dose of ergonovine are summarized in Table I. All subjects had angina at rest or on exertion or both in a daily activity. Only two patients (case 3 and...
Fig. 2. Case 7. Coronary arteriograms and simultaneously recorded electrocardiograms.

The right and left coronary arteriograms were shown in the upper and lower panels, respectively. (A) During non-anginal period, the right coronary artery (RCA) had 90% narrowing (arrow). The left coronary artery (LCA) was normal. Under these conditions, the peripheral RCA was slightly visualized by collateral channels from the LCA. (B) After provocation with ergonovine (0.1 mg), the patient had angina associated with ST segment depression in leads II, III, aVF, V₅, and V₆. At this time, the RCA was totally occluded by the spasm (arrow) and well-opacified collateral vessels from the LCA were demonstrated in the subsequent left coronary arteriography (arrows). Such collateral vessels completely disappeared after nitroglycerin administration when the angina and ST segment deviation subsided. (Reproduced from Tada M et al, Circulation 67: 693, 1983 with permission of American Heart Association)

5) had pure rest angina. The patients who showed ST segment depression as a reciprocal change of ST segment elevation in the opposing leads were excluded for the patient selection, because it is still controversial whether such ST deviation could actually represent myocardial ischemia.

Exercise Stress Test

A multistage bicycle exercise test in the semi-supine position was performed with an initial work load of 50 watts and subsequent increments of 25 watts every 3 minutes. A standard electrocardiogram of 12 leads was recorded before and at each minute during the exercise and after the terminations. The ST segment deviation was considered to be significant when it exhibited the displacement over 0.1 mV from the base lines. All test were undergone in the afternoon, as a responsiveness to the exercise stress tests was suggested to depend upon the time when it was performed.

Coronary Arteriography

Coronary arteriography was performed by the Judkins technique. In the present study, it is of
necessity to obtain simultaneously both left and right coronary arteriograms during the same vasospastic attack. Thus, we attempted to change the left and right coronary catheters quickly (within 30 seconds) using the arterial percutaneous catheter introducer (HEMAQUET, USCI) or also attempted to insert both left and right coronary catheters via bilateral femoral arteries. These techniques enabled us to obtain the left and right coronary arteriograms without a time delay during a vasospastic attack. Coronary arteriograms were initially obtained in the spasm-related vessels and subsequently in the non-spastic vessels before, during and after the vasospasm. A spastic narrowing of coronary artery was evaluated according to the definition of Curry et al.\textsuperscript{13} in which a coronary diameter reduction over 50\% with a chest symptoms and ST depression suggesting transient myocardial ischemia, was considered indicative of a coronary artery spasm. The fixed coronary stenosis over 50\% was also considered indicative of a significant organic lesion. Coronary arteries were divided into 15 segments according to American Heart Association Report\textsuperscript{14} and the narrowed coronary arteries were shown by the number of such division. The electrocardiogram was continuously monitored and recorded every 30 seconds in the standard 12 leads using X-ray transparent carbon fiber electrodes. The magnitude of ST segment depression was determined by measuring the difference between the position of the ST segment during non-anginal periods and ergonovine-induced vasospastic attacks. The ST segment depression over 0.05 mV was considered a significant change. As described before, ST segment depression which was observed as a reciprocal change of ST segment elevation in the opposing leads was not included for the patients selection in this study.

Administration of all anti-anginal agents such as long acting nitrates and calcium antagonists except nitroglycerin were avoided at least 24 hours before the coronary arteriography.

**Protocol of Ergonovine Provocative Test**

After control electrocardiograms and coronary arteriograms in the right anterior oblique view, ergonovine maleate was administered intravenously in a dose of 0.05 to 0.1 mg every 3 to 4 minutes until angina or ST segment depression was induced. When angina and/or ST segment depression was provoked, the electrocardiogram and the left and right coronary arteriograms were recorded. Immediately after these procedures, nitroglycerin (0.3 to 0.6 mg) was sublingually administered to relieve the angina and ST segment depression. Under these conditions, the coronary arteriography was again performed to reveal a release of the vasospasm. Any serious complications of the ergonovine provocative test have not been experienced in our laboratory.

**RESULTS**

**Clinical Features of Angina Pectoris**

All 12 patients had typical rest angina. Ten out of these patients also had exertional angina. Eight out of the 10 patients complicated the exertional angina exhibited a significant ST segment depression in the exercise stress test. However, none of these patients demonstrated ST segment elevation in the exercise electrocardiogram.

In Case 3 who had rest angina, the exercise stress test could provoke the angina. Three patients (Case 5, 7 and 10) did not exhibit angina and ST segment deviation during the exercise stress test.

**Ergonovine Provocative Test and Coronary Arteriograms**

Nine patients exhibited significant vasospastic narrowings in the left coronary system and 2 patients in the right coronary system. Vasospasm in both left and right coronary arteries were seen in one patient (Case 10).

Significant spastic narrowing without total obstruction was noticed in 8 patients, in whom coronary artery spasm occurred at the segment where the fixed organic stenosis was present (Case 1, 2, 8, 10 and 11) or not (Case 4, 6 and 12). Diffusely narrowed coronary artery was observed in Case 12. In Case 6, spasm was found at the proximal obtuse marginal branch of the left circumflex artery (LCx). The remaining 7 patients exhibited the spasm in the left anterior descending artery (LAD) and/or right coronary artery (RCA). Case 2 showed ST segment depression when the spastic narrowing of the LAD was 75%. Although the angina and ST segment depression temporarily resolved after nitroglycerin administration, the patient again had chest pain associated with ST segment elevation without additional dose of ergonovine. Under these conditions, the LAD was subtotally occluded by the spasm at the site of previous 75% spastic narrowing (Fig. 1). In the patients not showing total spastic obstructions, collateral vessels were visualized only in one patient (Case 1).

In contrast, a total spastic obstruction of the large coronary artery was found in 4 patients. Three out of these patients showed the spasm in the left coronary artery (Case 3, 5 and 9) and another one in the RCA (Case 7). As reported previously, it is important to define the possible existence of collateral vessels in such patients exhibiting ST segment depression despite the total coronary obstruction. Case 9 had the patent collateral circulation before ergonovine administration and the collateral flow did not change during coronary artery spasm. In Case 3, 5 and 7, no collateral vessels were found before ergonovine administration. However, a significant evolution of collateral circulation, which was supplied by the non-spastic arteries, was demonstrated in these patients during the angina associated with ST segment depression (Fig. 2). When the angina and ST segment depression resolved after nitroglycerin administration, these collateral vessels were no longer visualized.

It may be possible that the reduction of collateral flow could result in provoking myocardial ischemia. During the non-anginal period, Case 4 exhibited the well-developed collateral vessels from the RCA to the LAD with total occlusion in its proximal portion. After provocation with ergonovine, a spastic narrowing of the mid portion of RCA provoked reduction of the collateral flow, thus resulting in the occurrence of angina associated with ST segment depression in the anterior and inferior leads (Fig. 3).

**DISCUSSION**

The present report indicated that the ex-
ertional and/or rest angina pectoris with ST segment depression due to coronary vasospasm was associated with the non-total obstruction of the large coronary artery, the total occlusion with patent collateral circulation or the reduction of collateral flow during ergonovine-induced coronary artery spasm.

Coronary vasospasm had been postulated to have a pivotal role in provoking myocardial ischemia in rest angina, exertional angina, and myocardial infarction. A disintegrated coronary tonicity (spasm) usually accompanies ST segment displacement in the electrocardiogram. Several workers indicated that the ST segment deviation may be largely dependent upon the severity or location of the spasm and patent collateral circulation. The ST segment elevation was suggested to represent the transmural myocardial ischemia due to total occlusion of major coronary artery, while ST segment depression to reflect the subendocardial ischemia. Yasue et al. angiographically demonstrated that ST segment depression might represent a lesser degree of myocardial ischemia than ST segment elevation. However, arteriographic features of angina exhibiting ST segment depression during coronary spasm have not been well elucidated. We previously reported that the transiently evolved collateral vessels supplied by the non-spastic artery could serve to prevent severe transmural myocardial ischemia and resulted in subendocardial ischemia associated with ST segment depression, suggesting a significance of the role of non-spastic artery in determining the severity of myocardial ischemia. These observations suggest the necessity of the simultaneous visualization of the spastic and non-spastic coronary arteries during angina to define the precise relationship between angiographic findings and ST segment deviation.

On the present study, non-total spastic obstruction of a large coronary artery was found in 8 out of 12 patients and the finding seemed to be in a good agreement with the report by Yasue et al. who showed that 17 out of 26 patients exhibiting ST segment depression had non-total vasospasm during anginal periods. It may be postulated that an incomplete occlusion of a major coronary artery might produce modest myocardial ischemia which is expressed as ST segment depression.

Total occlusion of the major coronary artery was demonstrated in 4 out of 12 patients in the present study. Under these conditions, in 3 patients, collateral blood supply was temporarily augmented during coronary artery spasm. Yasue et al. indicated that the patent collateral vessels were accompanied more frequently by ST segment depression than by ST segment elevation during coronary vasospasm. Our findings may point to the possibility that the dynamic collateral blood supply was enough to prevent the total ischemia, resulting in a lesser degree of myocardial ischemia. However, Takeshita et al. reported two cases with vasospastic angina associated with ST segment elevation in whom immediate appearance of collateral vessels were observed, suggesting that these collateral supplementation could not effectively salvage otherwise jeopardized ischemic areas. One might speculate that the severity of myocardial ischemia could be determined by regional blood supply which depends upon the reduction of blood flow due to vasospasm and the supplementation of collateral blood flow.

These forms of collateral supplementation in vasospastic angina had been described by Gensini, who suggested that abruptly occurred pressure gradients between spastic and non-spastic arteries might induce collateral flow. If such a mechanism is functional, the observed ST segment depression could be interpreted by the transiently salvaged myocardial ischemia due to spasm-induced collateral flow from non-spastic coronary artery. Although we did not confirm whether our patients had the angina associated with ST segment elevation, the elevation of ST segment which is commonly observed during attacks of variant angina may possibly be replaced by the depression with a development of such a collateral circulation.

As seen in Case 4, whether the patent collateral circulation could be reduced during anginal periods is also of interest. Biagini et al. reported that the spontaneous reduction of collateral supply, which had maintained a good perfusion during non-anginal period, was found in unstable angina, suggesting that this mechanism may play one of the possible roles in provoking myocardial ischemia. A reduction of collateral flow during exercise was described by Nobuyoshi et al. who suggested such mechanism also could serve to provoke myocardial ischemia in exertional angina. One might speculate that the transient reduction of collateral flow to the ischemic areas would be capable of provoking myocardial ischemia in such patients.

It is important to define the possible clinical
implications of these mechanism in the pathogenesis of spontaneous episodes of exertional and/or rest angina associated with ST segment depression. In 9 patients, the exercise stress test was positive. Five out of these did not show a critical organic stenosis (≥75%) during non-anginal periods. In these patients, exercise-induced coronary artery spasm may cause myocardial ischemia associated with ST segment depression, as reported by several authors. As the ergonovine-induced coronary spasm has been suggested not to be necessarily similar to the spontaneously-occurred vasospasm, the present observations may not directly indicate the possible mechanism by which ST segment depression was evoked during the spontaneous anginal attacks on exertion or at rest. However, it may be postulated that the vasospastic angina associated with ST segment depression could be derived from incomplete occlusion of large coronary artery, reduction of collateral flow and patent collateral circulation; also considered is the functional development of collateral vessels which could be supplied by the non-spastic coronary arteries. Further studies are in progress to examine whether the dynamic augmentation or reduction of collateral flow may be critical in determining the severity of myocardial ischemia during coronary artery spasm.

REFERENCES


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