Immediate Relief of Spontaneous Coronary Artery Spasm by Intracoronary Infusion of an Endothelium-dependent Vasodilator, Substance P

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SUMMARY

This report describes a 45-year-old Japanese man who had episodes of anginal chest pain on effort. Coronary arteriography in the baseline state revealed subtotal occlusion in the mid-portion of the left anterior descending coronary artery. After intracoronary infusion of an endothelium-dependent vasodilator, substance P, the subtotal occlusion was immediately abolished. We concluded that endothelium-dependent vasodilation evoked with substance P was present at the site where coronary vasospasm occurred spontaneously in our case. (Jpn Heart J 36: 111-114, 1995)

Key words: coronary artery spasm endothelium-dependent relaxation substance P

It has been postulated that defective endothelium-dependent vasodilation evoked with vasoactive substances may contribute to the occurrence of coronary artery spasm.1) This assumption is based on the fact that intracoronary administration of an endothelium-dependent vasodilator, acetylcholine, provokes coronary spasm in patients with variant angina.2) However, the provocation of coronary spasm by acetylcholine may result from augmented vasoconstriction of vascular smooth muscle, because acetylcholine has a direct vasoconstricting action on vascular smooth muscle.

We recently demonstrated that coronary vasodilation evoked with another endothelium-dependent vasodilator, substance P, was preserved at the site where spasm was provoked by acetylcholine in patients with variant angina,3) suggesting that acetylcholine-induced coronary spasm was caused by augmented constric-
tion of vascular smooth muscle evoked with acetylcholine but did not result from endothelial dysfunction.

In this report, we describe a case in which spontaneously-occurring coronary spasm was relieved immediately after intracoronary administration of substance P.

**CASE REPORT**

A 45-year-old man was admitted to our institution on 26th November, 1990 for evaluation of chest pain. He had episodes of anginal chest pain on effort with cold sweating 3 months before the admission. Physical examination revealed no abnormality. Electrocardiograms on admission revealed a small q wave in lead V4, poor R progression in leads V1 to V5, and T-wave inversion in aVL and V1. Chest X-ray revealed normal heart size and pulmonary vasculature. Ultrasound cardiography revealed hypokinesis at the antero-apical wall with preserved global left ventricular function. Treadmill exercise test revealed pseudonormalization of T waves in V2 to V5 without symptoms. 201Tl-exercise scintigram showed a persistent perfusion defect in the apical wall and an exercise-induced perfusion defect suggesting the presence of viable myocardium, in the anterolateral wall. Cardiac catheterization was performed in the fasting state.

![Before and After substance P](image)

**Figure 1.** Serial angiograms of the left coronary artery (a right anterior oblique view) at baseline and after substance P (100 pmol/min). At baseline (before substance P), subtotal occlusion of the mid-portion of the left anterior descending coronary artery was noted (arrow). Although the distal segment of the left anterior descending coronary artery was still spastic, there was no significant stenosis after substance P. This suggests that substance P relieved spontaneously occurring coronary artery spasm.
after premedication with 5 mg of diazepam, orally. All drugs such as diltiazem were discontinued 48 hours before catheterization. Coronary arteriography at baseline revealed subtotal occlusion in the mid-portion of the left anterior descending coronary artery. The patient had neither symptoms nor ischemic electrocardiographic ST-T changes during the coronary arteriography. After intracoronary infusion of substance P (100 pmol/min) for a minute as described previously, the subtotal occlusion was immediately abolished (Figure 1) and only luminal irregularities were seen at the same site. Intracoronary infusion of 2 mg isosorbide dinitrate did not further dilate the lesion or other branches of the coronary arteries (data not shown). The patient had no significant stenosis in the left circumflex and right coronary arteries.

**DISCUSSION**

Clinical and angiographic findings in our patient indicate that coronary spasm might have contributed to the occurrence of ischemic events. The most interesting finding in our patient was that spontaneously-occurring coronary spasm resolved immediately after intracoronary infusion of an endothelium-dependent vasodilator, substance P (Figure 1).

It has been shown that substance P produces endothelium-dependent vasodilation, but has no direct action on the vascular smooth muscle of human coronary arteries in vitro.\(^4\) Vasodilating actions of substance P were abolished after the removal of endothelium or inhibited in the presence of L-arginine analogue.\(^4\) Crossman et al\(^5\) showed that substance P dilated the large epicardial coronary arteries of humans. These previous studies strongly suggest that we may assess endothelium-dependent dilation of the large epicardial coronary arteries by evaluating the vasodilating responses evoked with intracoronary infusion of substance P. Thus, our results indicate that, in our case, endothelium-dependent vasodilation evoked with substance P was present at the site where coronary vasospasm occurred spontaneously.

It is unlikely that the dilation evoked with substance P was specific to the spastic site, because first, substance P also produced dilation of a nonspastic site (the left circumflex coronary artery) and second, the magnitude of coronary vasodilation evoked with substance P was comparable to that evoked with isosorbide dinitrate.

Egashira et al\(^3\) and Okumura et al\(^6\) demonstrated that the vasodilating response to substance P at the site of acetylcholine-induced coronary spasm did not differ from that at the nonspastic site. Our present results agree with our previous observation and further suggest that endothelium-dependent vasodilation evoked with substance P was present at the spontaneously occurring coro-
nary vasospastic site.

In conclusion, we have described a case in which an endothelium-dependent vasodilator, substance P, relieved coronary artery spasm that had occurred spontaneously.

REFERENCES