Case Reports

Vasospastic Angina in Two Sisters

Kazunobu Tachibana, M.D., Yukio Kazatani, M.D., Koji Kodama, M.D., Keisuke Matsuzaki, M.D., Eiki Murakami, M.D.
and Tatsuo Kokubo, M.D.

SUMMARY

Vasospastic angina was observed in two sisters. The 52-year-old younger sister presented with rest angina at midnight and in the early morning. The coronary arteriogram showed no significant organic stenosis. Vasospasm to the left anterior descending and right coronary arteries was induced by the intracoronary administration of acetylcholine. The 57-year-old elder sister complained of rest and effort angina. Her coronary arteriogram was also normal. Vasospasm to the left circumflex and right coronary arteries was provoked by acetylcholine. In both cases, human leukocyte antigen DQw3 was negative. In the present cases, genetic factors may partly contribute to the mechanism of vasospastic angina. (Jpn Heart J 36: 669–673, 1995)

Key words: Vasospastic angina Sisters Acetylcholine Genetic factors

More than thirty years have passed since Prinzmetal et al.1) described a variant form of angina pectoris, now known as vasospastic or variant angina. However, little information is available on familial occurrences of the disease. We describe two sisters who had vasospastic angina.

CASE REPORT

A 52-year-old woman, having two brothers and two sisters, presented with a two-month history of rest angina at midnight and in the morning, lasting for a few minutes to several hours. She had an 11-year history of hypertension. She was a nonsmoker and had neither hypercholesterolemia nor diabetes mellitus.

On admission, the blood pressure was 150/92 mmHg and the pulse rate 72/min and regular. The electrocardiogram (ECG) at rest showed negative T waves in leads I, II, III, aVR and V2-6, but showed no abnormal Q waves. A
Figure 1. A: right coronary arteriogram after intracoronary acetylcholine administration in left anterior oblique projection; B: after intracoronary administration of isosorbide dinitrate; C: left coronary arteriogram after intracoronary acetylcholine administration in right anterior oblique projection; D: after intracoronary administration of isosorbide dinitrate.

The treadmill exercise test was negative. The chest x-ray was normal. The left ventriculogram showed akinesis in the anterior wall and severe hypokinesis in the septal and inferior walls; the ejection fraction was 48%. The coronary arteriogram demonstrated no organic stenosis in any major artery or branches. Therefore, according to the method described by Okumura et al, a provocative test for coronary artery spasm was performed with the administration of 50 μg of acetylcholine into the right and left coronary arteries. Segment 4 of the right coronary artery (Figure 1A) and segment 7 of the left anterior descending artery demonstrated severe vasoconstriction (Figure 1C), accompanied by chest pain. No ECG change was observed during the provocative test. The spasm subsided after intracoronary administration of isosorbide dinitrate (Figure 1B, D).

Her 57-year-old elder sister presented with a six-month history of effort angina, followed by the recent onset of rest angina. She was a nonsmoker also. She had hypercholesterolemia (serum total cholesterol 249 mg/dl, serum HDL-
cholesterol 64 mg/dl) and no diabetes mellitus.

Physical examination on admission was normal. The blood pressure was 148/88 mmHg and the pulse rate 72/min, regular. The ECG at rest was normal and a treadmill exercise test resulted in ST segment depression in leads V5,6. The chest x-ray was normal and the coronary arteriogram showed no significant stenosis. The left ventriculogram was normal and the ejection fraction was 64%. A provocative test for coronary arterial spasm\(^2\) was performed with the administration of 50 μg of acetylcholine into the right and left coronary arteries. Segment 4 of the right coronary artery (Figure 2A) and segment 11 of the left circumflex artery demonstrated severe vasoconstriction (Figure 2C), along with the usual angina and ST-segment depression in leads V5,6. The spasm subsided after intracoronary administration of isosorbide dinitrate (Figure 2B, D).

In both cases, no vasodilators, including calcium antagonists and nitrites, were used before the exercise tolerance tests and cardiac catheterizations.
DISCUSSION

Since vasospastic angina appears to occur more frequently in certain geographic locations, such as Japan, Italy and Canada, its underlying pathophysiologic abnormality is assumed to be transmitted genetically. Numano et al investigated the relationship between vasospastic angina and human leukocyte antigen (HLA), and showed that the HLA type DQw3 was significantly less frequent among Japanese patients with vasospastic angina. In both our cases, HLA type DQw3 was not observed, although it is not adequate to demonstrate the importance of genetic factors. Some authors have described cases of vasospastic angina in families, mainly in Japanese, including, those of brothers, sisters, a father and his son, and a mother and her daughter. These findings reinforce the theory that vasospastic angina has a genetic factor, especially in Japan.

On the other hand, Mauritson et al investigated 32 family members of eleven patients with vasospastic angina, but none had a history of angina. Furthermore, 24 of them underwent ergonovine provocative tests, but in no individual was spasm provoked. The authors concluded that coronary spasm was acquired rather than inherited. Therefore, familial occurrences of vasospastic angina may be related to specific races and environments.

Although several authors have reported cases of vasospastic angina in families, most of them were diagnosed on the basis of spontaneous attacks and of spasm provoked by hyperventilation, exercise or the administration of ergonovine or isoproterenol. We used acetylcholine to induce coronary artery spasm. Acetylcholine is supposed to induce vasospasm by means of muscarinic receptors on the smooth muscles of the coronary artery and is inactivated in a short time. Therefore, the provocation test using acetylcholine is more sensitive, reliable and safer than any other test.

In conclusion, vasospastic angina was seen in two sisters. Genetic factors may partly contribute to familial cases of vasospastic angina. Much more effort should be focused on the detection of genetic factors involved in the mechanism of vasospasm.

REFERENCES