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Vasospastic Angina in Identical Twins

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 58
Final Diagnosis: Vasospastic angina
Symptoms: Chest pain
Medication: —
Clinical Procedure: Medical treatment
Specialty: Cardiology

Objective: Rare disease

Background: The clinical conditions of various diseases, including coronary artery disease, are determined by genetics and the environment. Previous investigations noted the significance of genetic mutations and polymorphisms in cases of coronary spasm.

Case Report: We report on monozygotic identical twins who almost simultaneously presented with vasospastic angina. The 58-year-old younger twin was admitted to our hospital because of persistent chest pain. An electrocardiogram showed an inverted T wave in the left precordial leads. Coronary angiographies revealed a short left main trunk (LMT) and 50% stenosis at the proximal portion of the left anterior descending artery (LAD). Infusion of acetylcholine to his left coronary artery caused marked vasoconstriction associated with a sensation of chest oppression. Nitroglycerine completely reversed this response. Based on these findings, we diagnosed Twin A with vasospastic angina. At nearly the same time, his identical twin brother was diagnosed with vasospastic angina at another hospital. Comparison of both coronary angiograms indicated similar structure of coronary vessels, including short LMT and mild stenosis at the proximal portion of LAD.

Conclusions: These 2 cases highlight the importance of genetic factors in the pathogenesis of vasospastic angina. It may be important for individuals to receive medical attention if their identical twin presents with vasospastic angina.

MeSH Keywords: Coronary Artery Disease • Coronary Vasospasm • Twins, Monozygotic

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Background

Coronary spasm plays an important role in the pathogenesis of ischemic heart diseases, including vasospastic angina, acute coronary syndrome, and sudden cardiac arrest. The mechanisms underlying its development are still poorly defined and are likely multifactorial, involving disturbance of the autonomic nervous system, endothelial dysfunction, and hypercontractility of smooth muscle cells. In general, the clinical conditions of various diseases, including coronary artery disease, are determined by genetics and the environment. Previous investigations noted the significance of genetic mutations and polymorphisms in cases of coronary spasm. Here, we report a case of monozygotic identical twins presenting nearly simultaneously with vasospastic angina.

Case Report

A 58-year-old man (Twin A) had been suffering from angina for approximately 10 months. It occurred in the early morning and lasted for a few minutes. He was a former smoker and had hypertension and dyslipidemia. One morning he had a feeling of chest oppression associated with diaphoresis at the stool and presented at our emergency department. On admission, the blood pressure was 172/79 mmHg and his pulse rate was regular (66 beats per minute). The jugular vein was not dilated, and heart sound was normal. Laboratory test shows that serum levels of low-density lipoprotein cholesterol and triglycerides were elevated, whereas myogenic enzymes including creatine phosphokinase (CPK), CPK-MB, aspartate aminotransferase, and lactate dehydrogenase were within normal levels. A chest x-ray was normal (Figure 1A), and an electrocardiogram (ECG) showed inverted T waves in the left precordial leads, but showed no abnormal Q waves (Figure 1B). A coronary angiogram revealed a short left main trunk (LMT), and 50% stenosis at the proximal portion of the left anterior descending artery (LAD) (Figure 2A). A provocation test to induce coronary spasm was subsequently performed. An infusion of acetylcholine to the left coronary artery caused marked vasoconstriction (Figure 2B) associated with a sensation of chest oppression, as well as the elevation of the ST segment of the ECG. Nitroglycerine completely reversed it (Figure 2B, 2C). Based on these findings, we diagnosed Twin A with vasospastic angina.

Interestingly, Twin A's older identical twin brother (Twin B) had been diagnosed with vasospastic angina at another hospital 8 months earlier. He had felt chest pain late one winter night and had gone to Obama Hospital in Fukui, Japan. Like his twin, he had hypertension and dyslipidemia. A coronary angiogram revealed a short LMT and 50% stenosis at the proximal portion of the LAD. Thus, the findings of the

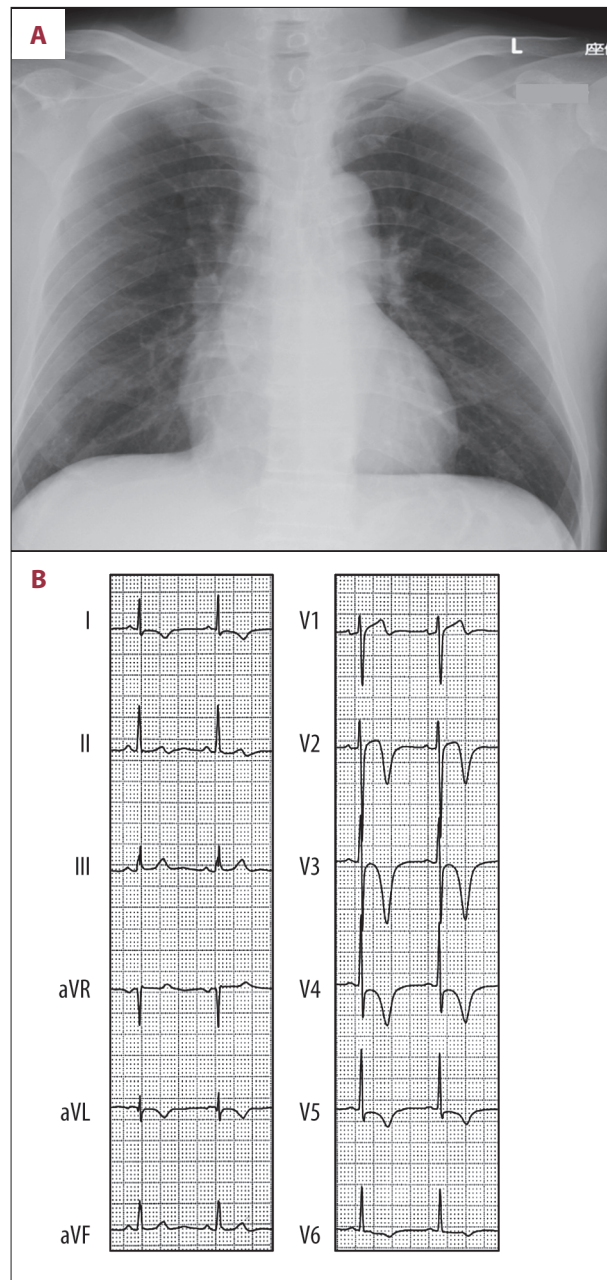


Figure 1. Chest roentgenogram (A) and electrocardiogram (B) at the admission for Twin A. The chest x-ray shows no specific abnormalities. The electrocardiogram shows inverted T waves in the left precordial leads.

coronary angiograms were quite similar in Twin A and Twin B (Figure 3). During his hospital stay, Twin B felt strong chest pain and an ECG showed ST elevation in the precordial leads (Figure 4). This symptom continued for several minutes and subsequently disappeared at the same time as the ST change. Based upon these clinical findings, Twin B was also diagnosed with vasospastic angina.

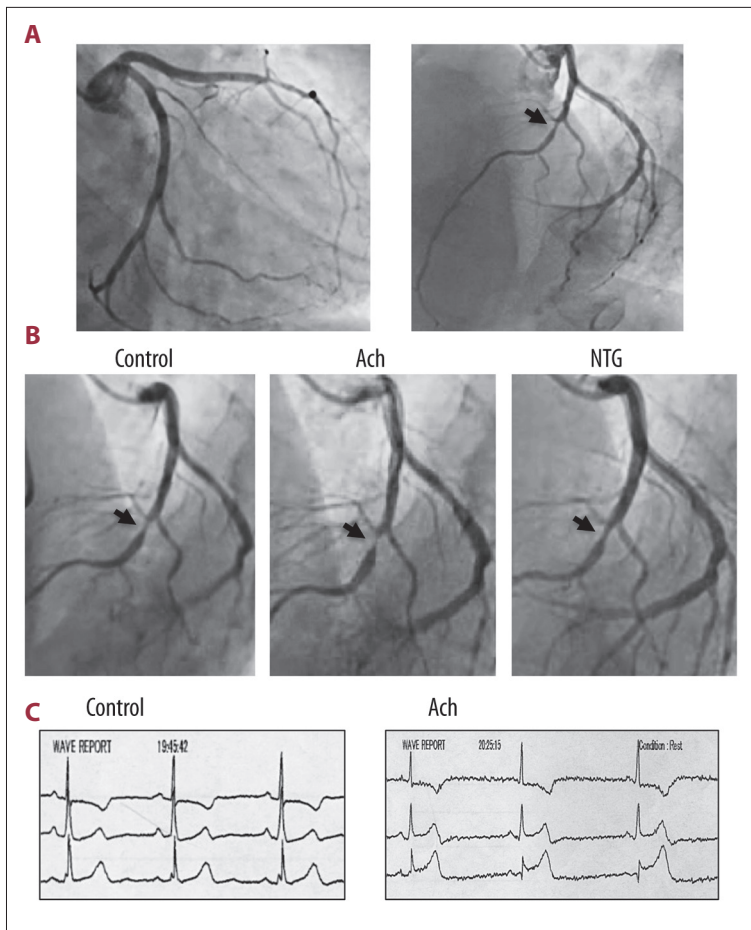


Figure 2. (A) Right anterior oblique view (left panel) and left anterior oblique view (right panel) of the coronary angiogram for Twin A showing a short left main trunk and 50% stenosis at the proximal portion of the left anterior descending artery in left anterior oblique view, as indicated by an arrow. (B) Provocation test to induce a coronary spasm via the intracoronary infusion of acetylcholine (Ach) into the left coronary artery. Left panel: left anterior oblique view (right panel) of the coronary angiogram indicating mild coronary stenosis (arrow). Middle panel: Marked vasoconstriction induced by the infusion of Ach (100 μ g) to the left coronary artery. Right panel: Reversal of the coronary spasm induced via the intracoronary infusion of nitroglycerin. (C) Changes of the ECG during the provocation test for coronary spasm. During the induction of the coronary spasm, the ST segment was elevated.

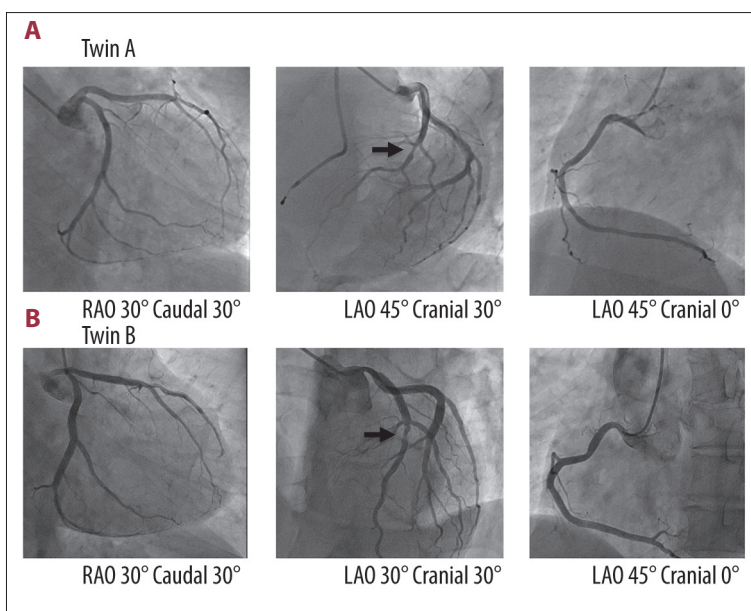


Figure 3. Comparison of the structure of the left (left and middle panels) and right (right panel) coronary arteries between Twin A (A) and Twin B (B). The right upper (Twin A) and lower (Twin B) panels show left coronary arteries from the right anterior oblique (RAO) 30°/caudal 30° views. The middle upper (Twin A) and lower (Twin B) panels show left coronary arteries from left anterior oblique (LAO) 45° and LAO 30°/cranial 30° views, respectively. The left upper (Twin A) and lower (Twin B) panels show right coronary arteries from LAO 45° views. Comparison of coronary angiograms indicated similar structure of coronary vessels, including short left main trunk. Referring to the middle panels, coronary angiograms revealed there was 50% stenosis at the proximal portion of the left anterior descending coronary artery (indicated by an arrow), although the angles of LAO view were different.

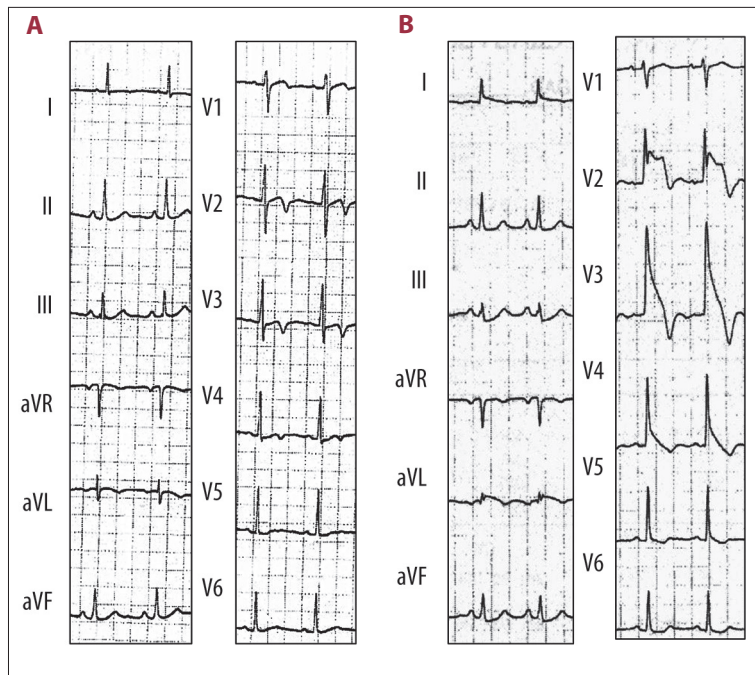


Figure 4. ECG changes during chest pain attack for Twin B. Compared with ECG at the admission (A), the ST segment at V2–V4 was elevated during the chest pain attack (B). This ST elevation disappeared along with remission of symptoms.

Discussion

It is well established that smoking, hyperlipidemia, and mental stress are potent modifiable environmental risk factors for vasospastic angina. Polymorphisms of some genes such as those encoding endothelial nitric oxide synthase (eNOS) [1,2] and phospholipase C- δ 1 [3–5] are also associated with vasospastic angina. In a Japanese cohort study, the NADH/NADPH oxidase *p22 phox* gene was a susceptibility locus for coronary spasm in men, while the genes encoding stromelysin-1 and interleukin-6 genes were susceptibility *loci* in women [6]. Thus, there is a possibility that genetic factors are involved in the pathogenesis of vasospastic angina. Although gene polymorphisms were not analyzed, our cases highlight the importance of the genetic factors in the pathogenesis of vasospastic angina.

Several cases of coronary artery disease in identical twins have been reported [7–11], showing the similarities in the coronary anatomy and atherosclerotic lesions in identical twins, as in the present case report. Interestingly, Turley et al. described a pair of identical twins presenting almost simultaneously with coronary artery disease and identical atherosclerotic lesions despite significant differences in their environmental risk factors and geographic location (12 000 miles apart) [9]. Only 1 case of vasospastic angina in identical twin has been published in a Japanese journal, although cases of vasospastic angina in brothers and sisters have been reported [12–14].

Both twins had a short left main trunk and the atherosclerotic stenosis lesions at the proximal lesion of LAD, and the timing of the onset of angina was nearly simultaneous. These findings suggest that the development of the coronary vessel tree has a genetic basis. Cohort studies have shown a high concordance of coronary artery disease in monozygotic twins. For example Zdravkovic et al. showed moderate-to-high heritability of CHD mortality [15, 16], and a recent large genome-wide association study (GWAS) identified 46 *loci* that are significantly related to coronary artery disease [17]. In addition to genetic factors, environmental risk factors, such as diet or those encountered in daily life, may also be shared by identical twins. Therefore, a gene-environment interaction should be considered.

Conclusions

Coronary angiography revealed similarities in the coronary artery anatomy of identical twin brothers. Their concomitant onset of vasospastic angina suggests that genetic factors contribute significantly to the pathogenesis of vasospastic angina. Therefore, it may be important for individuals to receive medical attention if their identical twin presents with vasospastic angina.

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