Clinical Case Report

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Fluctuations in the amplitude of ST-segment elevation in vasospastic angina

Two case reports

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Abstract

Rationale: ST-segment elevation localizes an ischemic lesion to the coronary artery supplying the area of the myocardium reflected by the electrocardiographic leads. Dynamic ST-segment elevation can be due to severe transmural ischemia secondary to a thrombus, vasospasm, or a tightly fixed coronary artery lesion or a combination of these situations.

Patient concerns: In this study, we report on two patients with angina who had fluctuations in ST-segment amplitude on serial electrocardiograms. The amplitude of ST-segment elevation varied between 1-20 mm.

Diagnoses: Vasospastic angina (VSA) was diagnosed based on electrocardiography and coronary angiography.

Interventions: Calcium antagonists were prescribed for both patients.

Outcomes: No recurrent VSA was noted during outpatient follow-up.

Lessons: VSA can be associated with fluctuations in the amplitude of ST-segment elevation, indicating dynamic coronary vasospasm in different locations and extensions in patients with VSA.

Abbreviations: ED = emergency department, VSA = vasospastic angina.

Keywords: angina, case report, electrocardiogram, vasospasm

1. Introduction

Coronary vasospasm causes stable angina, acute coronary syndrome, lethal cardiac arrhythmias, and sudden cardiac death.[1–4] The diagnosis of vasospastic angina (VSA) depends on the history, electrocardiographic follow-up, and coronary angiographic studies. Electrocardiographic changes during VSA include an elevated or depressed ST-segment, peaking T wave, widened R wave due to fusion of the R wave and T wave, disappearing S wave, and negative U wave.[5] The electrocardiographic changes may be the only objective evidence of mild VSA when the coronary vasospasm is not severe enough to totally occlude the coronary artery. Most coronary vasospasms are associated with ST-segment depression rather than ST-segment elevation.[6] Electrocardiographic ST-segment elevation represents transmural myocardial ischemia that often results from totally occluded coronary artery. A reciprocal ST-segment depression in the opposite leads is usually accompanied with ST-segment elevation if we record electrocardiograms with multiple leads. The magnitude of ST-segment elevation increases associated with increases in magnitude and widening of the R wave in the same lead may be noted as the VSA progresses, which may form a "monophasic curve" at the peak of the attack.[5] In general, this "monophasic curve" is not found in obstructive coronary artery disease-induced acute myocardial infarction and is a sign of dynamic extension of coronary vasospasm involving the proximal portion of a major coronary artery.[5]

Variant angina denotes VSA combined with transient ST-segment elevation on electrocardiography and indicates a transient and total spasm of the coronary artery. ST-segment elevation localizes the ischemic lesion to the coronary artery supplying the area of the myocardium reflected by the electrocardiographic leads. Dynamic ST-segment elevation can be due to severe transmural ischemia secondary to a thrombus, vasospasm, or a tightly fixed coronary artery lesion or a combination of these situations. We report 2 cases of frequent VSA associated with fluctuations in the amplitude of ST-segment elevation, indicating a dynamic total coronary vasospasm in different locations and extensions in patients with VSA. This study was granted an exemption from review by the Institutional Review Board of Chang Gung Foundation (application no. 201601524B0 and 201601528B0).

2. Case presentation

2.1. Case 1

A 51-year-old man who smoked presented to the cardiology outpatient clinic with a 1-week duration of intermittent numbness on the lateral sides of both forearms. The numbness often occurred in the afternoon and at night, persisted for less than 10 seconds and then resolved spontaneously. The numbness was associated with palpitations, chest tightness, and cold sweats. He had a history of hypertension that was well-controlled by valsartan 80 mg once daily. He denied having any other chronic

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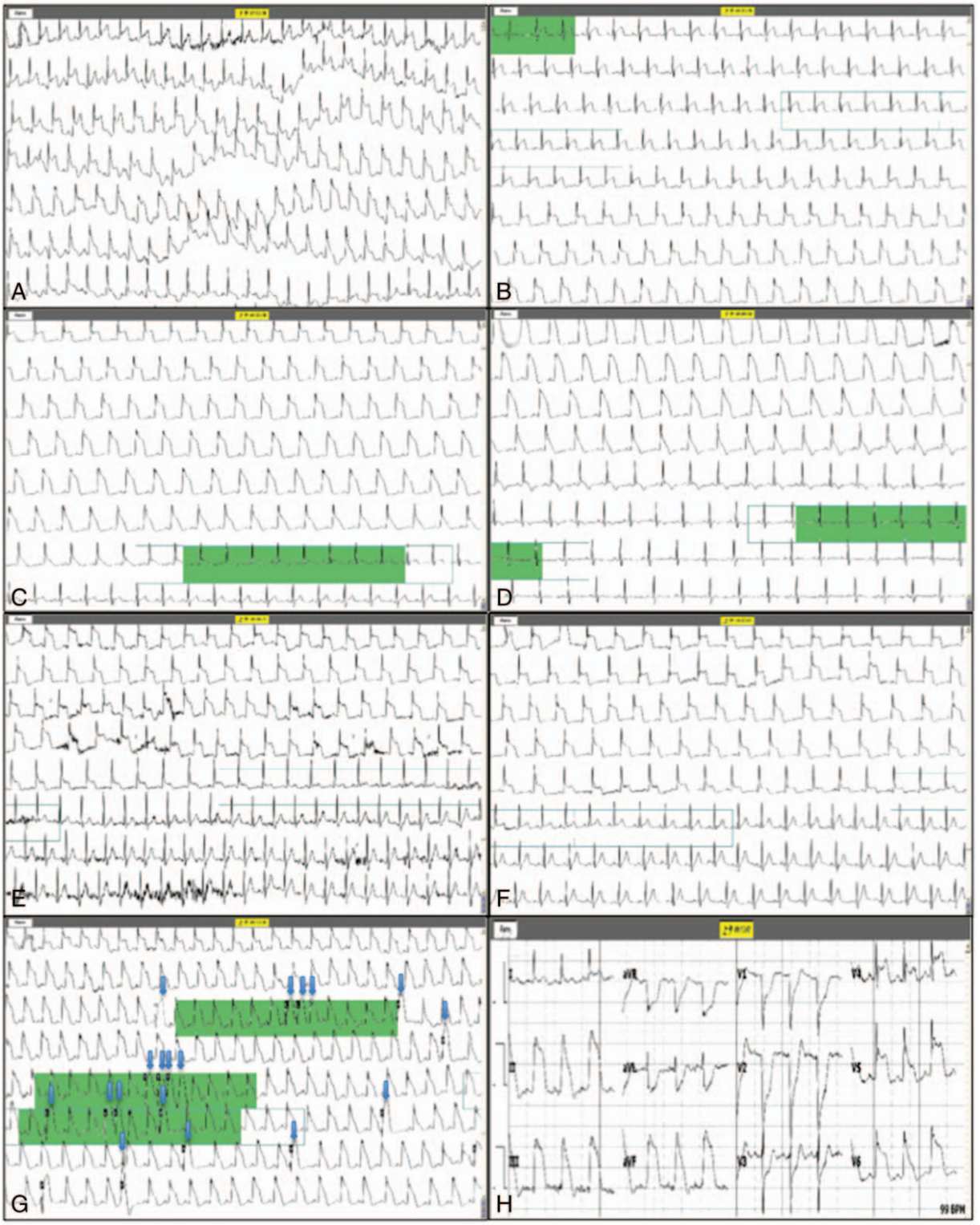

Figure 1. Twenty-four Holter electrocardiography in case 1. Transient ST-segment elevation is seen at 2:53 PM (A), 4:33 (B) to 4:35 PM (C), 6:09 PM (D), 10:10 PM (E), 10:37 PM (F), and 9:13 AM (G). Multiform premature ventricular contractions, including isolated beats, couplets, triplets, and quadruplets, were also noted at 9:13 AM (G, blue arrows). The transformed 12-lead electrocardiogram at 9:13 AM shows ST-segment elevation in the inferior and $V_{4–6}$ leads (H).

medical diseases. His physical examination showed no abnormalities. Hemograms and biochemical test results were within normal limits with total cholesterol and low-density lipoprotein levels of 156 and 89 mg/dL, respectively. Subsequently he underwent 24-hour Holter electrocardiographic monitoring to evaluate the possible causes of palpitations and chest tightness. During the electrocardiographic recording, he reported intermittent numbness on the lateral side of both forearms in association with palpitations, chest tightness, and cold sweats. The 24-hour Holter electrocardiography showed many episodes of transient

ST-segment elevation with spontaneous resolution (Fig. 1A–G). During the 24-hour recording, the amplitude of the elevated ST-segment varied between 1 and 17 mm and was complicated by multiform premature ventricular contractions with isolated beats to quadruplets. The transformed 12-lead electrocardiogram showed ST-segment elevation in the inferior and $V_{4–6}$ leads (Fig. 1H), indicating multivessel coronary vasospasms. The patient underwent coronary angiography during which triple-vessel spontaneous coronary vasospasm was documented after intracoronary nitroglycerin administration. A diagnosis of VSA was made and a calcium antagonist, verapamil 120 mg once daily, was prescribed instead of valsartan. The patient has been doing well without any evidence of VSA during a follow-up of 1.5 years.

2.2. Case 2

A 67-year-old man with a history of cigarette smoking, chronic hepatitis B virus infection, and well-controlled hypertension presented to the emergency department (ED) at midnight with sudden severe chest pain associated with cold sweats. The angina was relieved after sublingual administration of 0.6 mg nitroglycerin. The patient reported that he had experienced many 5- to 10-minute episodes of chest pain over at least 15 years. He also noted that the angina occurred at night or in the early morning and was relieved soon after taking sublingual nitroglycerin. However, the patient reported that the frequency and severity of the chest pain had increased within the last 12 months. During the previous 15 years he had undergone coronary angiography 5 times and each examination revealed a patent coronary artery. His physical examination results showed no abnormalities. Upon arrival in the ED, 12-lead electrocardiography revealed atrial fibrillation with a ventricular rate of 64 beats per min (Fig. 2A). No ST-segment changes were found. The initial blood tests showed no evidence of acute myocardial injury. Approximately 2 hours after arriving in the ED, he experienced chest pain again. Electrocardiography revealed ST-segment elevations in leads $V_{1–4}$ (Fig. 2B). The chest pain was again relieved after sublingual administration of 0.6 mg nitroglycerin (Fig. 2C). Approximately 80 minutes later, there was recurrence of the angina (Fig. 2D) which was more intense than the previous 2 episodes and was not relieved after sublingual administration of 1.2 mg nitroglycerin (Fig. 2E). We noted ST-segment elevation in both inferior and precordial leads. Therefore, intravenous nitroglycerin was administered and the chest pain and ST-segment elevation gradually resolved (Fig. 2F and G). The troponin-I level measured 6 hours after arriving in the ED was normal. The total cholesterol and low-density lipoprotein was 104 and 62 mg/dL, respectively. Coronary vasospasm complicated by VSA was suspected. On day 2, he underwent coronary angiography and intracoronary methylergonovine provocation testing confirmed coronary vasospasm in the left anterior descending and circumflex coronary arteries (Fig. 3). A patent right coronary artery with aneurysm formation was also noted. Based on the coronary angiographic findings and the serial changes in ST-segment elevation on electrocardiography, VSA due to triple-vessel coronary vasospasm was diagnosed. The patient was treated with 2 calcium antagonists, verapamil 120 mg twice daily and amlodipine 5 mg once daily at night, and isosorbide mononitrate 60 mg once daily. He had no evidence of VSA recurrence on cardiology outpatient follow-up (Fig. 2H). However, the patient died 4 years later due to rupture of hepatocellular carcinoma complicated by septic shock.

3. Discussion

A diagnosis of VSA can be difficult to establish because symptoms and electrocardiographic changes are not always present during the investigation period. VSA may be asymptomatic but can be lethal because of life-threatening cardiac arrhythmias.[4,7,8] Although VSA is more commonly associated with ST-segment depression,[6,9] ST elevation on an electrocardiogram can indicate transmural myocardial ischemia. The diagnostic criteria for VSA proposed by the Coronary Vasomotion Disorders International Study Group include nitrate-responsive angina, transient ischemic electrocardiographic changes during spontaneous episodes and angiographic coronary vasospasm.[10] If angina spontaneously occurs at rest and is associated with transient ischemic electrocardiographic changes, and there is no other identifiable cause for the electrocardiographic changes, coronary vasospasm is most likely responsible, and a definite diagnosis of VSA can be made without documented angiographic evidence of coronary vasospasm. However, documenting ischemic electrocardiographic changes during VSA is not always possible because the incidence of silent ischemia caused by coronary vasospasm is more than 2 times higher than that of symptomatic ischemia.[11] In addition, VSA occurs most often at rest between midnight and early morning, making it difficult to record ischemic ST-T changes. Therefore, 24-hour Holter electrocardiographic recording is useful for recording myocardial ischemic changes.[12]

In patient 1, ambulatory Holter electrocardiographic monitoring recorded frequent episodes of transient and symptomatic ST-segment elevation, allowing a definitive diagnosis of VSA. Interestingly, the transformed 12-lead electrocardiogram showed ST-segment elevation in both inferior and $V_{4–6}$ leads, indicating multivessel coronary vasospasm. In patient 2, serial 12-lead electrocardiograms also recorded frequent episodes of symptomatic ST-segment elevation in the precordial leads initially and later in the inferior and precordial leads. In both patients, the amplitudes of ST-segment elevation varied, both in the same and in different leads, indicating occlusion of a major coronary artery in the proximal, middle, or distal segment. This fluctuation in amplitude shows that VSA is not always localized to a segment. In other words, VSA is a generalized coronary vasomotor disorder.[13] Recently, Ong et al[14] found that VSA was as common in Western countries as in Asian countries such as Japan,[12] Korea,[2] and Taiwan.[3] Therefore, VSA should not be overlooked in the differential diagnosis in patients with angina pectoris.

Prevention is the best treatment option for VSA. Intravascular imaging has demonstrated that arteries involved in coronary vasospasm are not normal.[15,16] Therefore, control of cardiovascular risk factors is highly suggested to avoid vascular damage. This includes smoking cessation, blood pressure control, maintenance of ideal body weight, glucose control, correction of lipid abnormalities, avoidance of excessive fatigue and mental stress, and reduction of alcohol consumption.[12] In addition, drugs that can induce coronary vasospasm should be avoided, for example catecholamines, ergot alkaloids, prostaglandins, and propranolol.[5] Nitrate is effective in the acute treatment of VSA by either the sublingual or intravenous route. However, there is no evidence that chronic nitrate therapy reduces the incidence of

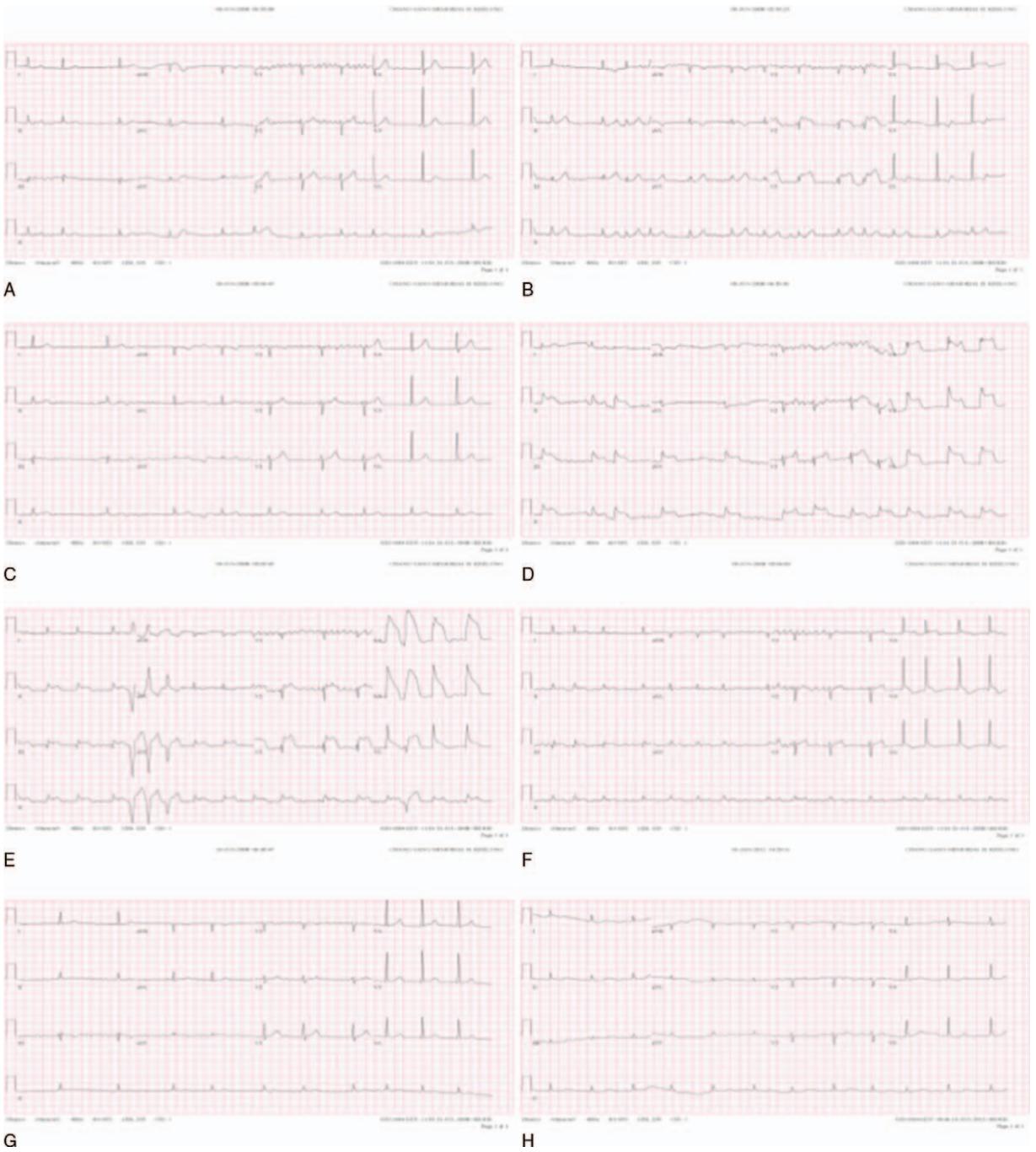

Figure 2. Electrocardiography in case 2. Atrial fibrillation without ST elevation on arrival in the emergency department (A). ST-segment elevation in leads V_{1-4} 2 hours later (B). Resolution of ST-segment elevation after sublingual 0.6 mg nitroglycerin (C). Recurrent ST-segment elevation in the inferior and precordial leads 80 minutes later (D). More intense chest pain 3 minutes later (E) with isolated and triplet premature ventricular contractions, which resolved after intravenous nitroglycerin administration (F). Resolution of ST-segment elevation at discharge (G). No recordable ST-segment elevation 4 years later (H).

major cardiovascular events.[17] Long-acting calcium antagonists are the first-line therapy because they are very effective in reducing symptomatic VSA episodes.[18] Most importantly, a calcium antagonist is an independent determinant in preventing future major cardiovascular events for VSA patients.[19] Other pharmacological therapies which have been shown to relieve VSA and therefore might be considered include nicorandil, fasudil, and statins.[12] Percutaneous coronary intervention is generally not useful in patients with VSA who have no obstructive coronary artery disease.[18] However, it may be considered in those with concomitant obstructive coronary artery disease. Nevertheless, these patients should have maintenance calcium antagonists and/or nitrate therapy after percutaneous intervention to prevent spasms in other sites in the coronary arteries. For refractory VSA unresponsive to 2 coronary vasodilator medications at conventional doses, larger doses (verapamil or diltiazem 960 mg/day and/or nifedipine 100 mg/day) and a combination of different classes of calcium antagonists may be necessary. Other additional pharmacological therapies as mentioned earlier are possibly helpful in such situations. However, some refractory VSA episodes cannot be completely controlled by these medications.

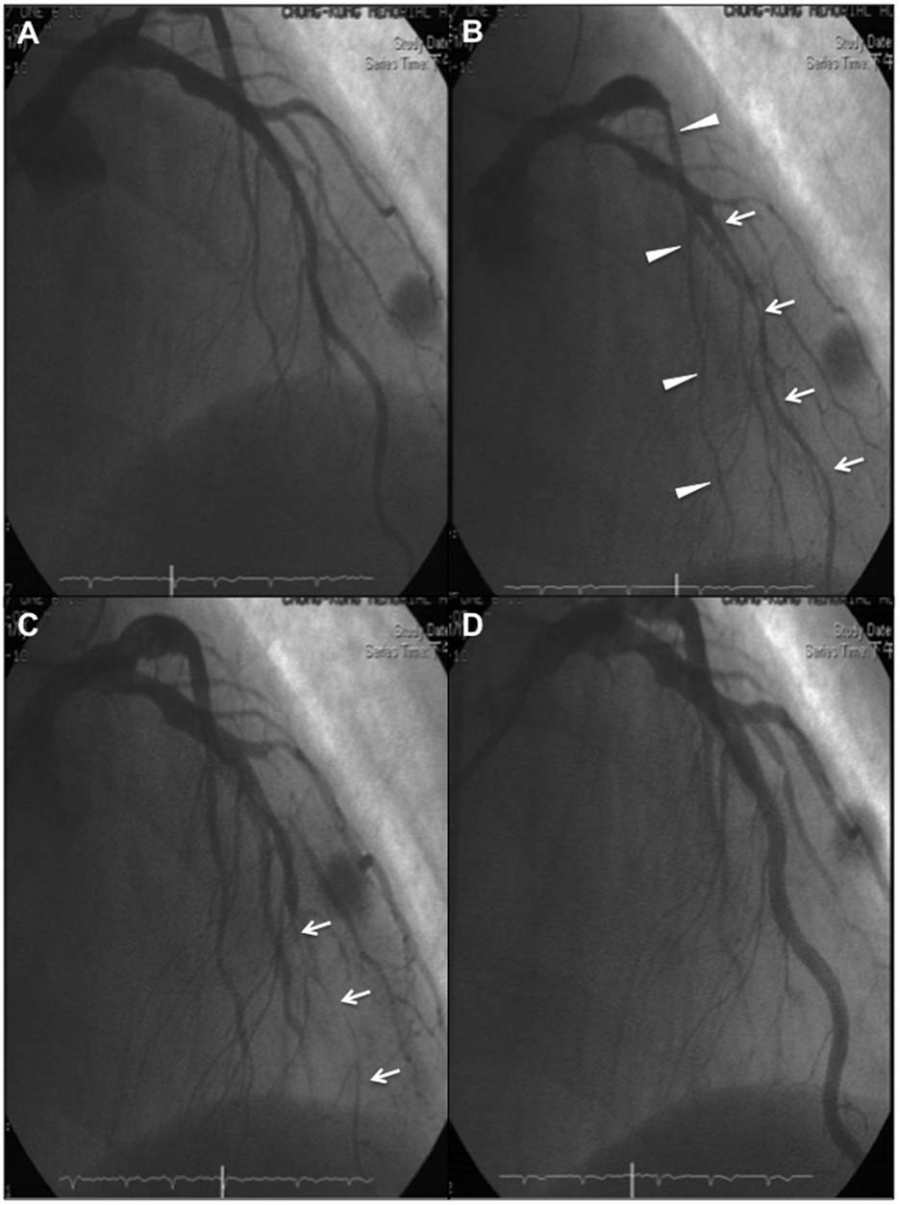

Figure 3. Coronary angiograms in case 2. Left anterior oblique view shows nonobstructed coronary arteries (A), and diffuse coronary vasospasms beginning in the middle portion of the left anterior descending (arrows) and left circumflex (arrowheads) coronary arteries after intracoronary methylergonovine 15 μg administration (B). Partial relief with persistent coronary vasospasm in the distal portion of the left anterior descending coronary after intracoronary nitroglycerin 100 μg administration (C). Total relief of spasm in the left coronary arteries after further intracoronary nitroglycerin 100 μg administration (D).

4. Conclusion

Continuous electrocardiogram monitoring, either with an ambulatory electrocardiographic device or repeated 12-lead recordings, is very helpful in establishing the diagnosis of VSA. Fluctuation in the amplitude of electrocardiographic ST-segment elevation is indicative of dynamic coronary vasospasm at different locations and extensions in patients with VSA.

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