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# A Rare Case of Vasospasm Presenting with Acute Coronary Syndrome and Leading to Total Occlusion

## Akut Koroner Sendrom ile Başvuran ve Total Oklüzyona Yol Açan Nadir Bir Vazospazm Olgusu

**ABSTRACT**

Coronary vasospasm is characterized by transient and reversible vasoconstriction that can cause myocardial ischemia. Patients with acute coronary syndrome may present to the emergency department with various clinical features, including mortal arrhythmias and cardiac arrest. Coronary angiography was performed in a 61-year-old male patient with the diagnosis of acute coronary syndrome due to recurrent angina attacks and dynamic changes in electrocardiography. In the patient whose critical stenosis was not detected in the first imaging, angina attack developed before the procedure was terminated. On control imaging, we detected total occlusion of the left anterior descending artery due to coronary vasospasm. After the administration of intracoronary nitroglycerin, the total occlusion of the left anterior descending artery due to vasospasm completely resolved and the angina attack relieved. It is uncommon for total stenosis to develop immediately after the coronary angiography observes open coronary arteries. However, if total stenosis is detected in patients with recurrent angina attacks without risk factors, intracoronary nitroglycerin can be administered to appropriate patients before intervention.

**Keywords:** Acute coronary syndrome, angina, coronary vasospasm, vasospastic angina

**ÖZET**

Koroner vazospazm, miyokardiyal iskemiye neden olabilen geçici ve geri dönüşümlü vazokonstriksiyon ile karakterizedir. Akut koroner sendrom (AKS) hastaları acil servise ölümcül aritmiler ve kardiyak arrest gibi çeşitli klinik özelliklerle başvurabilir. Altmış bir yaşında erkek hastaya AKS tanısı ile tekrarlayan anjina atakları ve elektrokardiyografideki dinamik değişiklikler nedeniyle koroner anjiyografi (KAG) yapıldı. İlk görüntülemede kritik darlık saptanmayan hastada işlem sonlandırılmadan önce anjina atağı gelişti. Kontrol görüntülemede sol ön inen arterde (LAD) koroner vazospazm nedeniyle total oklüzyon saptandı. İntrakoroner nitrogliserin uygulaması sonrası LAD arterinde vazospazma bağlı total oklüzyon tamamen düzeldi ve anjina atağı geçti. KAG işlemi esnasında koroner arterlerde bir açıklık gözlemlendikten hemen sonra total oklüzyon gelişmesi nadirdir. Ancak risk faktörü olmayan tekrarlayan anjina atakları olan hastalarda total oklüzyon saptanırsa girişim öncesi uygun intrakoroner nitrogliserin verilebilir.

**Anahtar Kelimeler:** Akut koroner sendrom, anjina, koroner vazospazm, vazospastik anjina

**CASE REPORT**
OLGU SUNUMU

In 1959, Prinzmetal et al[1] first described characteristic clinical features of patients with "variant angina" which could not be explained by significant fixed stenosis of the major epicardial coronary artery resulting in development of classic effort-related angina pectoris.[2] These features include (1) development of chest pain not associated with increased myocardial oxygen requirement such as exercise or emotional excitement, (2) resting chest pain with typical diurnal variation with frequent attack at night or early morning, (3) marked ST segment elevation in the electrocardiogram (ECG), and (4) prompt response to sublingual application of nitroglycerin.[2] The development of chest pain in some patients is associated with alcohol intake. The interesting point is that the angina attack does not occur immediately, but a few hours after alcohol intake. Therefore, many patients may be misdiagnosed as having gastrointestinal problems, including peptic ulcer disease or esophageal reflux disease.[2] One of the important steps in making the diagnosis is the detailed history taking. Treadmill exercise ECG, noninvasive computed tomography,

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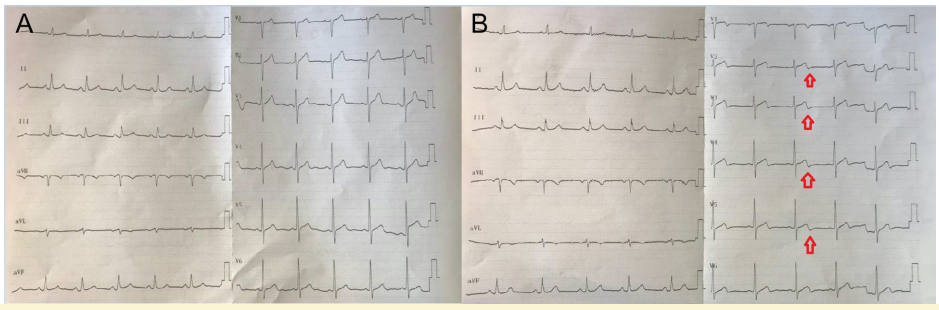


**Figure 1. (A) Emergency room admission ECG. (B) ECG during angina attack in the emergency room. ECG, electrocardiogram.**

and coronary angiography (CAG) are required to rule out severe stenosis in major epicardial coronary arteries.[3,4] The next step is Holter monitoring to detect ECG changes. Especially with a slight increase in heart rate during sleep and in the early morning, changes in the ECG or ST segment elevation can be diagnostic.[2] Coronary vasospasm (CVS) plays an important role in the pathogenesis of resting angina, effort angina, and acute coronary syndrome (ACS). Although the main cause of ACS is plaque rupture, vasospasm can also be a potential cause of ACS. Besides ACS, it can cause severe ventricular arrhythmias, syncope, and sudden cardiac death. However, it is very rare and sometimes difficult to make an accurate diagnosis. Here, we wanted to present an ACS case with recurrent angina attacks resulting in total occlusion of the left anterior descending (LAD) artery due to CVS.

## Case Report

A 61-year-old male patient presented to the emergency department with recurrent angina attacks for 3 days. Angina attacks were unrelated to effort and lasted about 2-3 minutes and resolved spontaneously. He did not have any chronic disease in his past medical history. He didn't smoke. The most recent angina attack was about 2 hours before the emergency room admission. No significant pathology was detected in the ECG at the time of admission to the emergency department (Figure 1A). No wall motion defect was detected in the echocardiography (ECHO). Troponin I was within the normal reference range. Dynamic changes were detected in the anterior leads in the ECG, which was re-examined after an angina attack was observed in the follow-up (Figure 1B). The patient was taken to the catheter laboratory for emergency CAG. CAG revealed non-critical atherosclerotic plaques in LAD, circumflex (Cx) and right coronary arteries (RCA) (Figure 2). Before the termination of the procedure, the patient developed angina attack and ventricular tachycardia (VT) that did not cause deterioration in hemodynamics. In the control CAG imaging, within 2 minutes after the first angiography, total occlusion was observed in the LAD artery after crossing the diagonal branch line without any provocation (Figure 3A). After intracoronary nitroglycerin administration, coronary flow completely recovered, vessel diameter expanded, and angina resolved (Figure 3B). In addition, VT rhythm spontaneously returned to normal sinus rhythm, and ST segment changes returned to normal (Figure 4). Diltiazem, isosorbide dinitrate, clopidogrel, and atorvastatin were recommended for severe spontaneous vasospasm with mild atherosclerosis. In addition, the patient was educated about the importance of regular drug use. The patient was discharged 2 days later and his symptoms did not recur for 1 month.

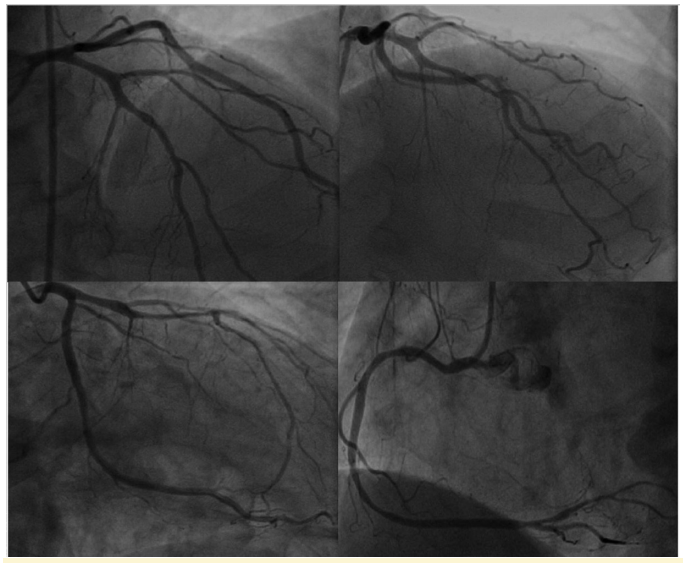

**Figure 2. First coronary angiography images of the patient. Anterior–posterior cranial, right cranial, right caudal, and left caudal poses were given, respectively. Here, noncritical atherosclerotic lesions are observed in the LAD, Cc, and RCA arteries, respectively. Cx, circumflex; LAD, left anterior descending; RCA, right coronary artery.**

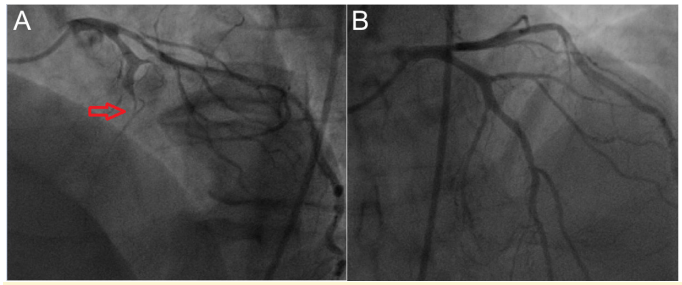


**Figure 3. (A) Development of LAD total occlusion due to vasospasm during angina attack. (B) Complete disappearance of vasospasm in the LAD artery after intracoronary nitroglycerin administration. LAD, left anterior descending.**

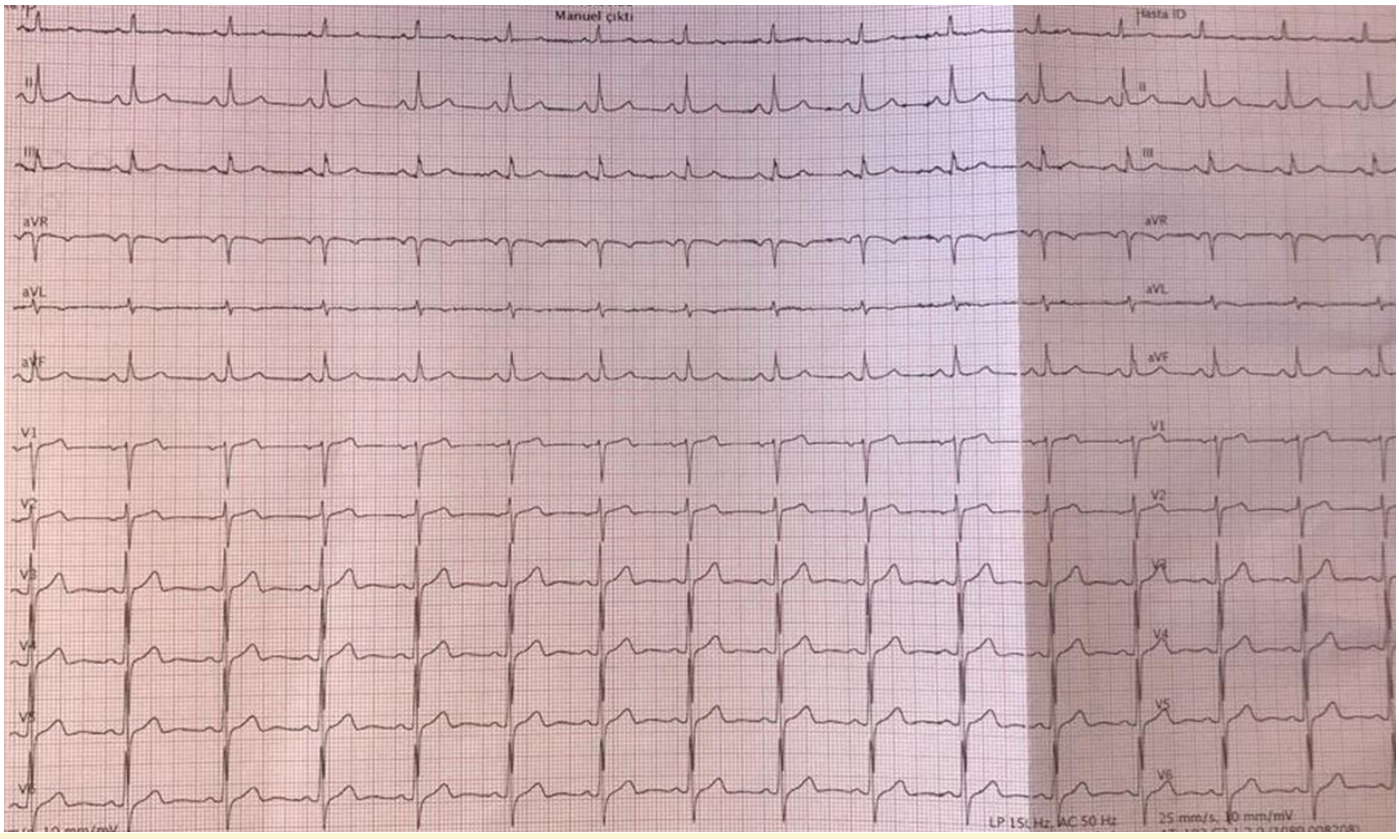


**Figure 4. Electrocardiogram after coronary angiography.**

## Discussion

Vasospastic angina (VSA) usually occurs at night or early in the morning. It is a temporary occlusion of the epicardial coronary arteries that is mostly not associated with increased myocardial oxygen demand.[5] In our case, the patient's angina attacks occurred at night. The spontaneous occurrence of CVS during CAG is well documented in single vessels.[6] However, multivessel spasm is much less common. The pathophysiological mechanisms are not yet fully understood. It is defined that lack of endogenous nitric oxide activity, increased phospholipase C activity, increased oxidative stress and inflammation markers, some behavioral features (e.g., type A personality, panic disorder, and severe anxiety), and smoking are associated with coronary artery vasospasm.[6,7] If VSA is clinically suspected, a provocation test is required for definitive diagnosis.[3] For spasm provocation test, physiologic stimulation including hyperventilation or cold exposure once has been suggested, but the diagnostic sensitivity of these maneuvers is reported to be low and pharmacologic stimulation is usually preferred.[2] The two most commonly used pharmacological agents for the spasm provocation test are ergonovine and acetylcholine. For spasm provocation of ergonovine, intravenous or intracoronary administration is possible. Ergonovine is contraindicated in uncontrolled systemic hypertension, as it may cause progressive increase in blood pressure by vasoconstriction of peripheral vessels.

Acetylcholine was introduced clinically by Japanese researchers for the spasm provocation test. Since this drug is rapidly metabolized by cholinesterase, which is abundant in human plasma, systemic administration is not possible and only intracoronary administration is used. Due to its very rapid metabolism, the use of intracoronary acetylcholine is expected to be beneficial in selective and sequential intracoronary administration, allowing separate provocation of the right and left coronary arteries. Adverse effects such as bronchospasm, hypotension, bradycardia, dyspnea, VT, and shock may develop.

Medications that have the potential to affect coronary vascular tone should be discontinued before the spasm provocation test is performed. Calcium channel blockers, beta receptor blockers, and nitrates are typical examples that should be discontinued. These drugs should be discontinued for at least 3 or 4 days. Angiotensin converting enzyme inhibitors or angiotensin receptor blockers are usually used for adequate control of systemic hypertension.

A positive provocative test for CVS must include all of the following in response to the provocative stimulus: (1) reproduction of the usual chest pain, (2) ischemic ECG changes (ST elevation, ST depression, and U wave changes), and (3) >90% vasoconstriction on angiography.[4,8] The test considered equivocal if the provocative stimulus does not induce all 3 components.

Although there are no evidences supporting that the incidence of CVS is declining these days, provocative tests for CVS are now done much less frequently in the United States and Europe than in former years and reliable spasm provocation agents (both ergonovine and acetylcholine) are not U.S. Food and Drug Administration approved for the indication of CVS diagnosis;

moreover, spasm provocation test is not included or addressed in the recently published American College of Cardiology/American Heart Association clinical guidelines.[9,10]

In our case, we were able to detect a reversible and transient CVS episode without provocation during CAG. This episode also occurred spontaneously. In this respect, it was a demonstrative case. As a result of stable, insignificant atherosclerotic lesions and vasospastic activity, total stenosis developed in the proximal part of the LAD. Atherosclerotic lesions of the LAD, observed even after nitroglycerin injection, may be a cause for CVS. β-receptor blockers are generally contraindicated in patients with vasospasm, as they may adversely increase vascular tone. Calcium channel blockers (CCBs) and nitrates are generally recommended. But in rare cases, chest pain can become persistent. In this case adding CCBs with different classes is effective. Antiaggregants and statins are not routinely recommended. There may be attacks of chest pain in the early morning, as there may be a decrease in the effective blood levels of the drugs at night. For this reason, it is recommended to take the drug not immediately after a meal, but before going to sleep. In addition, it is highly recommended to prepare sublingual nitroglycerin at the bedside to effectively and quickly relieve an attack of chest pain during sleep or in the early morning. Clopidogrel and statin were also prescribed in our patient because of stable atherosclerotic lesions and diagnosed gastritis. Depending on the extent and localization of CVS, VSA may present with a variety of clinical manifestations, including variant angina, effort-induced angina, ACS, mortal arrhythmias, and sudden cardiac death. Initially, it was rarely thought that CVS could lead to life-threatening complications such as mortal arrhythmias or sudden cardiac arrest. However, recent studies show that CVS is responsible for 7% of out-of-hospital cardiac arrest cases.[11] Lee et al[12] reported that some cases experienced recurrent attacks within 4 years after the first episode of CVS despite medical treatment. According to the JCS/JHRS 2019 Non-Pharmacotherapy of Cardiac Arrhythmia guidelines, the recommendation for an implantable cardioverter defibrillator (ICD) for ventricular fibrillation due to CVS is considered class IIa when medical therapy is ineffective.[13] It is considered class IIb when medical treatment is effective.[13] However, the time of implantation is a matter of debate. In addition, patients with severe hypoxic ischemic encephalopathy are considered class III.[13] Implantable cardioverter defibrillator was not considered because the patient did not have recurrent mortal arrhythmias during the follow-up period.

## Conclusion

Vasospastic angina causing ACS is a rare but important condition that should be investigated carefully. It is not easy to decide with CAG that the cause of coronary stenosis is vasospasm in patients presenting with ACS. In our case, it is rare to develop total stenosis immediately after the observation of the open coronary arteries during the CAG procedure. However, if total stenosis is detected in patients with recurrent angina attacks without risk factors, intracoronary nitroglycerin can be administered to appropriate patients before intervention.

**Informed Consent:** Written and verbal consent was obtained from the patient at the time of reporting the study.

**Peer-review:** Externally peer-reviewed.

**Declaration of Interests:** The author declare that they have no competing interest.

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