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CLINICAL VIGNETTE

Vasospastic Angina

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A 48-year-old male was referred to cardiology for chest pain. He has no significant past medical history but currently smokes at least 1 pack per day for 30 years. He has no family history of premature coronary artery disease or sudden cardiac death. The patient described daily episodes of burning, sharp chest pressure radiating into both arms and upper back that lasted approximately one minute. Symptoms were rated 10/10 in intensity and were associated with diaphoresis and palpitations but no nausea, vomiting, dyspnea, lightheadedness, or syncope. Symptoms can occur at rest or with exertion, such as getting off the couch too fast or walking up one flight of stairs. The symptoms most often occur in the mornings. He denied paroxysmal nocturnal dyspnea, orthopnea, or lower extremity edema. His physical exam was unremarkable.

Baseline EKG showed normal sinus rhythm with no acute ST changes, no QT prolongation, or delta waves.

He underwent a treadmill stress test with 10 minutes of exercise on a Bruce protocol, achieving 101% of his maximum predicted heart rate (175 bpm). His resting blood pressure was 137/89 and rose to 187/78 at peak exercise. His double product was 32,725. The test was stopped as the patient stated he felt that he was “about to have chest pain” and he also was experiencing shortness of breath, fatigue, and lightheadedness. As the treadmill was stopped, the patient developed 6/10 chest pain with 1-1.5 mm ST segment elevations in V3-V5. He also had multiple episodes of non-sustained ventricular tachycardia and further increase in ST segment elevation to 2.5 mm. He was given sublingual nitroglycerin, and his symptoms resolved completely within 1 minute. Post-stress echocardiogram images showed hypokinesis in the anterior, anteroseptal, and septal walls, concerning for ischemia in the distribution of the left anterior descending artery. He was transported via ambulance to the hospital.

Cardiac catheterization showed a moderate mid-LAD stenosis with no evidence of flow restriction by fractional flow reserve or intravascular ultrasound (Image 1).

The following morning, he had recurrent angina, associated with dramatic ST elevations, which immediately resolved with sublingual nitroglycerin (Image 2).

He was started on isosorbide mononitrate and verapamil. During his hospitalization, he had recurrent angina with ST elevations and non-sustained ventricular tachycardia several

times. Each time, symptoms were promptly relieved with nitroglycerin. His calcium channel blocker and long-acting nitrate medications were uptitrated until he no longer had episodes for 24 hours, after which he was discharged. The importance of smoking cessation was discussed in detail with the patient, and he was provided with nicotine gum and varenicline to assist in quitting.

Coronary vasospasm

Vasospastic angina, previously referred to as Prinzmetal angina, is defined as episodes of angina that are promptly relieved with nitroglycerin, are associated with transient EKG changes, and have angiographic evidence of coronary spasm.¹ Provocative testing can be performed to confirm the diagnosis with ergonovine, acetylcholine, or hyperventilation at the time of cardiac catheterization.²

Vasospastic angina is produced by high-grade obstruction of the coronary artery due to spasm of the smooth muscle layer of the coronary arterial wall.² As a result, the patient may experience angina as a result of transient ischemia or, less commonly, myocardial infarction. Factors contributing to coronary vasospasm include vascular smooth muscle hyper-reactivity, autonomic nervous system dysfunction (with an imbalance in vagal and sympathetic tones), and endothelial dysfunction.³ Microvascular dysfunction has also been demonstrated in some patients with vasospastic angina, where acetylcholine injection produced chest pain, EKG changes, and lactate production in the absence of large epicardial coronary artery spasm.⁴

Smoking is a major risk factor for vasospastic angina.⁵ Other risk factors are poorly defined and may include genetic factors as well as insulin resistance.^{6,7} Interestingly, hypertension and hyperlipidemia, two major risk factors for atherosclerotic coronary artery disease, are not correlated with a higher risk of microvascular disease.³ Possible triggers for a vasospastic episode include changes in autonomic tone,⁸ magnesium deficiency,⁹ food-borne botulism,¹⁰ guide-wire or balloon dilation at the time of angioplasty,¹¹ or multiple drugs, such as ephedrine-based products, cocaine, marijuana, alcohol, sumatriptan, and amphetamines.¹¹⁻¹³

The clinical presentation of vasospastic angina is typically a pattern of recurrent episodes of substernal chest discomfort that is usually gradual in onset and offset, not affected by position,

and may be associated with radiation to the neck, jaw, back, or arm. The chest discomfort may be associated with nausea, diaphoresis, shortness of breath, and palpitations. These symptoms are very similar to classic angina, but the history may be helpful in discerning between these distinct entities. Patients with vasospasm tend to be younger and have fewer traditional cardiovascular risk factors (except smoking)¹⁴ and a history of cocaine abuse may be present. Coronary vasospasm may be associated with other vasospastic disorders, such as Raynaud's phenomenon or migraines.¹⁵ There are no characteristic physical examination findings for vasospastic angina. During an acute episode of angina, the EKG may demonstrate transient ST elevation or depression.

Ambulatory EKG monitoring can detect ST segment deviations and can be considered in the work-up of a patient with chest pain in whom vasospasm is being considered. Stress testing is recommended in patients with chest pain to evaluate for fixed coronary stenosis. While most patients with vasospastic angina have normal stress tests, approximately 10-30% may have exercise-induced spasm.¹⁶ Cardiac catheterization is recommended for patients with abnormal stress tests as well as those who have normal stress tests when vasospasm is suspected in order to definitively rule out a severe fixed coronary obstruction. In our patient, coronary spasm was not seen on cardiac catheterization, but there was clearly evidence of non-obstructive coronary disease. When the presentation is classic and no stenosis is seen on catheterization, it is reasonable not to pursue pharmacologic provocation.³

First line treatment for vasospastic angina is calcium channel blockers to prevent vasoconstriction and promote coronary vasodilation.¹⁷ Long-acting nitrates are also effective at alleviating symptoms, but use is limited by the occurrence of nitrate tolerance.¹⁸ Short-acting sublingual nitroglycerin should be prescribed for break-through episodes. Statins have been shown to aid in preventing spasm, possibly through effects on endothelial nitric oxide or directly on the vascular smooth muscle. Non-selective beta-blockers (e.g., propranolol) should be avoided as they can exacerbate coronary spasm. In patients without evidence of atherosclerotic coronary disease, aspirin should be used with caution as it inhibits prostacyclin at high doses. In patients with migraine and coronary spasm, the triptan class of medications should be avoided.³ Percutaneous coronary intervention (PCI) is not routinely recommended for vasospasm treatment however, can be considered in select patients with continuing vasospasm despite adequate medical therapy. In these patients, the coronary segment with the vasospasm needs to be clearly defined and they should be continued on medical therapy after the PCI.¹⁹

Complications of coronary vasospasm include myocardial infarction and heart arrhythmias, such as heart block and ventricular arrhythmias. Defibrillator placement should be considered for patients with high-risk features or with history of aborted cardiac arrest.²⁰

Fortunately, the prognosis for patients with coronary vasospasm is good on medical therapy with survival at 5 years as high as 94%.²¹

Images

Image 1: A moderate mid-LAD stenosis with no evidence of flow restriction by fractional flow reserve or intravascular ultrasound.

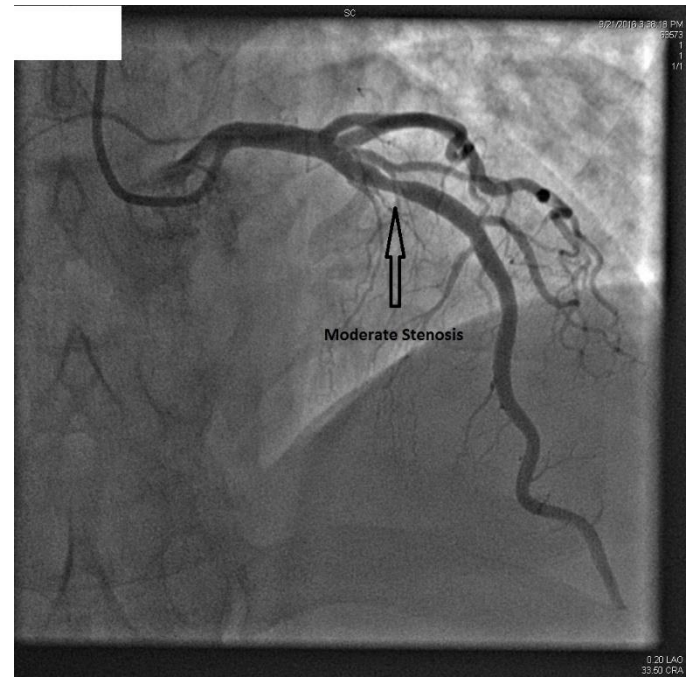
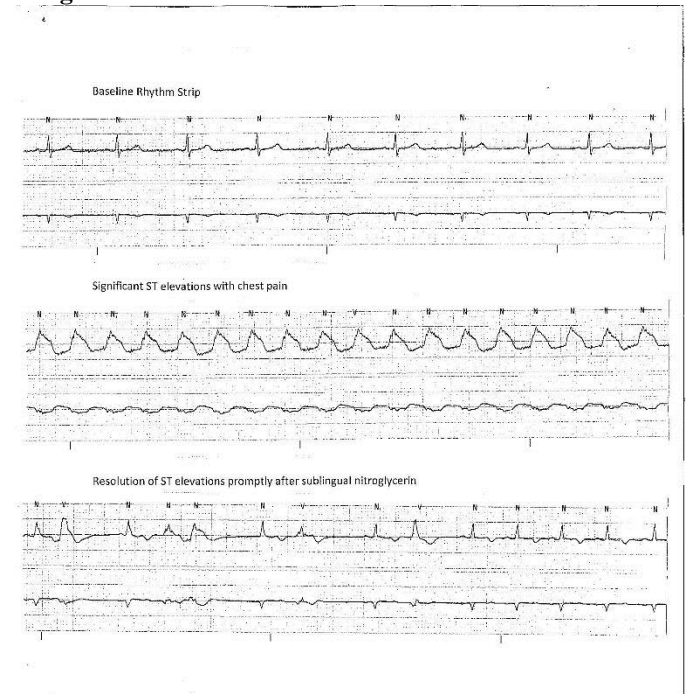


Image 2: ST elevations.



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