A Woman with Headache and Chest Pain

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A 34 y/o woman, with a past medical history significant for asthma, newly diagnosed hypertension, and migraines, presented to the emergency department with complaints of sudden onset chest pain. She was an active young woman, who up until the day of admission, had been able to run several miles without chest pain or shortness of breath. Symptoms began the morning of admission, when the patient reported that she developed a migraine heachache, with typical right-sided temporal pain. After administering an injection of Sumatriptan, her headache resolved. Soon thereafter, she noted 5/10 substernal chest pressure occurring suddenly at rest, without radiation to her arms or jaw. It was not associated with nausea, vomiting, diaphoresis or shortness of breath. The patient stated that she had never experienced this type of pain before, which alarmed her enough to come to the hospital. One sublingual nitroglycerin, given in the ED, complete relieved her symptoms.

The patient's medical history included hypertension, asthma, Raynaud's phenomena, and migraine headaches. Hypertension was recently diagnosed, and well controlled off medications with a strict regimen of diet and exercise. Her asthma was stable with very occasional use of an albuterol metered dose inhaler, and she stated that she had never been intubated or required hospitalization for an exacerbation. Her Raynaud's symptoms occured in her fingertips intermittently during the winter months for the past several years. Migraine headaches were diagnosed 2 years prior, and she had been tried on several different abortive therapies without success. The Sumatriptan had just recently been prescribed, and this instance represented her first use.

The patient had no surgical history. She denied alcohol, tobacco, or intravenous drug abuse. She lived at home with her husband and four children. Both parents were still alive, her father with atrial fibrillation and her mother with hypertension. There was no family history of sudden death or coronary artery disease. The patient took no regularly prescribed medications, only prn albuterol MDI and sumatriptan injections. Her allergies included aspirin and shellfish, both of which exacerbate her asthma symptoms. Review of systems was positive only for the chest pain described above, occasional palpitations and migraine headaches.

On physical examination the patient was afebrile with a pulse of 112, respirations of 20, blood pressure of 111/66, and O2 saturation of 100% on 3 liters nasal cannula. She was alert and oriented, in no acute distress. Her oropharynx was clear, and heart regular with a normal S1 and S2, and no audible murmurs, gallops, or rubs. There was no detectable jugular venous distention. Lungs were clear, and her abdomen soft, nondistended, and non-tender. No peripheral edema was appreciated.

Laboratory data is shown in Table 1.

Table 1. **Outpatient Laboratory Values**

WBC	8.0
Hgb	15.9
PLT	228
Sodium	138
Potassium	4.1
Bicarbonate	25
BUN	9
Creatinine	0.8
Glucose	189
Total cholesterol	193
LDL	113
HDL	50
TG	79
CK	321
Troponin	1.9

The admission chest film showed clear lungs. The ECG, however, revealed sinus rhythm with ST elevations in leads II, III, and aVF, as well as ST depressions in the anterior leads. An echo showed normal chamber sizes, with distal lateral and mid to distal posterior wall hypokinesis.

Hospital Course

The patient was admitted to the medical CCU for management of an ST elevation myocardial infarction, presumed to be secondary to coronary artery vasospasm. The vasospasm was attributed to her recent use of Sumatriptan. She was started on intravenous nitroglycerin for relief of ongoing chest pain. A continuous infusion of diltiazem was also started for control of the vasospasm. Given the patient's allergy to aspirin, clopidogrel was initiated. Cardiac enzymes were

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followed and the troponin I peaked at 27 ng/mL. The patient continued to have episodic chest pain during her stay in the CCU and consequently four days after her admission, the patient underwent cardiac catheterization. Catheterization showed luminal irregularities in the left main, left anterior descending, left circumflex and right coronary arteries. The second obtuse marginal, however, showed 99% occlusion. The left ventriculogram revealed posterolateral akinesis. Given the tortuosity of the vessel, the OM2 lesion was not stented. The location of the occlusion, however, did correspond with the area of akinesis. It was thought that the patient had underlying occlusion of the OM2, with superimposed vasospasm secondary to use of Sumatriptan, and this precipitated her acute myocardial infarction. The final decision was to optimize medical management with clopidogrel, diltiazem and a statin.

Coronary Vasospasm

Coronary vasospasm has also been referred to as printzmetal or variant angina. Prinzmetal originally described it in 1959 as a "temporary increased tonus" in areas of high-grade coronary artery occlusion. Vasospasm is a syndrome of cardiac pain secondary to myocardial ischemia. The spasm itself can occur in normal or diseased vessels and usually occurs within one centimeter of an atherosclerotic plaque. The resultant ischemia will appear as ST elevations on ECG, and this can typically be reversed with nitroglycerine or calcium channel blockers.

The patients suffering coronary vasospasm are commonly younger than those who present with other forms of angina. They often lack the cardiovascular risk factors typically associated with heart disease. As in the above case, these patients often have other systemic signs and symptoms of vasospasm, including Raynaud's phenomenon and migraine headaches. Interestingly, there appears to be an increased incidence of symptoms in the hours between midnight and early morning. The most common cause of mortality associated with vasospasm involves arrhythmias, including ventricular tachycardia.

Although the precise mechanisms have not been clearly defined, there are some circulating theories to explain the underlying pathogenesis of coronary vasospasm. One hypothesis involves the autonomic nervous system. It has been shown that both acetylcholine and methacholine can precipitate vasospasm, thus inferring that the parasympathetic nervous system may play a significant role in the pathogenesis. The discovery that atropine and alpha-receptor blockers cay prevent such spasm also supports this theory. In fact, sympathetic denervation (plexectomy) may be therapeutic in refractory patients. Endothelial dysfunction may also play a role in pathogenesis. Decreased levels of the endogenous vasodilator nitric oxide, and increased levels of the vasoconstrictor endothelin have been shown to impair coronary dilatation. These compounds may play an integral role in coronary vasospasm. Finally, patients with areas of diffuse intimal thickening of the coronary vasculature may also be at risk for spasm. With underlying coronary artery disease, episodic vasospasm alters preexisting plaques, leading to intimal disruption and penetration of macrophages or aggregation of platelets. Consequently, vasospasm may contribute to vascular instability in these patients.

Sumatriptan, a serotonin (5-hydroxytryptamine [5-HT]) receptor agonist, causes vasoactive constriction of cerebral vascular beds, making it useful as an abortive therapy for migraine headaches. However, it has also been shown to exhibit vasoactive activity in the systemic, coronary, and pulmonic vascular beds. Three to five percent of patients experience chest tightness, heaviness, pressure, or pain after its administration. Occasionally, the chest pressure or pain radiates to the left arm and hand, imitating angina pectoris. ECG evidence of myocardial ischemia, however, is rare. Recently, Welch reported that while over 3 million migraine attacks have been treated with sumatriptan, there have only been 4 reported patients with myocardial ischemia due to coronary vasospasm, 1 of whom also had cardiac arrhythmia. All four patients had underlying cardiovascular disease. Sumatriptan has a mild constrictive effect on coronary arteries. MacIntyre et al found 10 patients undergoing diagnostic coronary angiography who had a 14 percent reduction in the diameter of the coronary arteries. Based on such evidence and more recent case reports, sumatriptan is contraindicated in patients with coronary artery disease or vasospastic angina.

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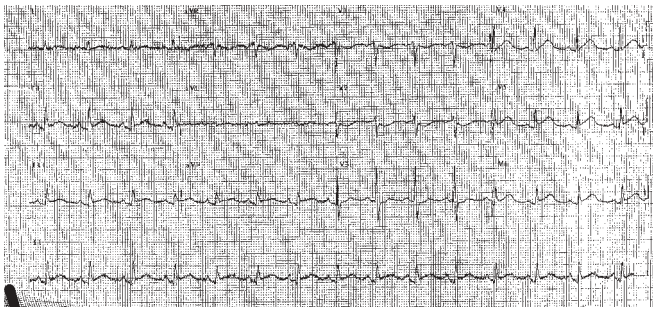
The typical ECG findings in patients with variant angina are transient ST elevations associated with chest pain, that then return to baseline with resolution of symptoms. Cardiac catheterization plays a major role in diagnosis. In patients presenting with the typical signs and symptoms of variant angina, including non-exertional chest pain and ST elevations, angiography may reveal normal vessels or, as in this case, a proximal fixed obstruction in one or more of the coronary arteries. It is in this latter group of patients that vasospasm should be suspected. Two provocative tests can help confirm this condition. The most sensitive and specific test involves injection of intravenous ergonavine, a vasoconstrictor, during catheterization. The test is positive if drug administration replicates symptoms or ECG findings. The effects should be reversed with intracoronary nitroglycerine. Ergonavine can also be used in conjunction with echocardiography. Wall motion abnormalities after injection indicate a positive test. Hyperventilation is a less sensitive test that can also be performed during coronary catheterization. The patient is instructed to hyperventilate for six minutes and if acute ST changes are seen on ECG, coronary vasospasm is inferred.

The image below shows cardiac catheterization with hyperventilation-induced vasospasm of the proximal left circumflex artery that resolved with the administration of intracoronary nitroglycerine and diltiazem.

As with all types of coronary artery disease, risk factor modification is essential. Cessation of smoking must be enforced. Medical management includes lipid-lowering medications, and calcium channel blockers or nitrates to maintain coronary vasodilatory effects. Medical treatment has shown favorable responses in female patients and patients with ST-segment elevation during selective spasm provocation tests. However, patients with either a longer history of episodic chest pain or a history of diffuse spasms do not improve with medical treatment alone. Nonselective beta-blockers should be avoided, as they may exacerbate vasospasm. Angioplasty is helpful if there is a discrete area of occlusion, however its utility is limited by the fact that many patients have multivessel spasms. It has been recommended that calcium channel blockers be continued after percutaneous revascularization for this very reason. In refractory patients, surgical denervation with plexectomy may be an option.



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