CLINICAL VIGNETTE

Suspected Vasospastic Angina with NSTEMI

Michael D. Yashar, MD and William Shyy, MD

Case Presentation

A 40-year-old female presented to urgent care with recent concerns of elevated blood pressure and chest pain. She noted symptoms the night prior, with sudden onset of significant pressure and aching pain in the chest and arms while brushing her teeth around 11 PM. She called paramedics and received an ECG, which she was told was normal, and was found to have an elevated blood pressure of approximately 140/90. Per the patient, the paramedics felt that her symptoms were likely due to anxiety or a musculoskeletal process and she was not transported to the hospital. Early the next morning upon waking, she had recurrent symptoms and contacted her primary care physician and was advised to be evaluated in person.

At the time of her evaluation in urgent care, she reported 3/10 discomfort with occasional palpitations and fatigue. The patient had taken acetaminophen and ibuprofen without significant improvement. She denied any shortness of breath, exertional symptoms, dizziness or syncope She was free of back pain, nausea, vomiting, trauma, abdominal pain, diaphoresis, fever, cough, or neurologic symptoms. She reported recent psychosocial stressors, some prior to symptom onset. She also noted recent travel in the last few weeks, and had a hormonal intrauterine device placed within the last week. Relevant past medical history included intermittent asthma without complication. She also reported prior emergency department evaluation a month prior for left-sided chest pain radiating to the shoulders and abdomen. Chest radiograph raised concern for pneumonia with leukocytosis of 12K and she was treated with oral amoxicillin and azithromycin. Family history was notable for Factor V Leiden in her father, although the patient had been previously tested and found to be negative for the disorder. She also denied any family history of early cardiac disease.

The patient's initial vital signs were unremarkable except for a blood pressure of 138/94. Her physical exam was also unremarkable with a normal cardiopulmonary, extremity, and neurovascular exams. ECG was normal without ischemic changes. Other testing included a high-sensitivity troponin (HS-TnI) of 15,544 (normal <5 ng/L). CBC, CMP, pregnancy test, BNP, TSH, d-dimer, lipase and chest x-ray which were all unremarkable. The patient received 325 mg of aspirin and was transferred to the emergency department for further evaluation and treatment.

En route to the emergency department (ED), paramedics provided 1 spray of nitroglycerin with some relief of symptoms. In the ED, she was noted to have occasional episodes of NSVT. A repeat ECG was stable without ischemic changes. She was started on a heparin drip, was given 180 mg of ticagrelor, and a repeat HS-TnI downtrended to 10,966. A transthoracic echocardiogram showed findings of mildly reduced LV systolic function with hypokinesis of the mid and apical anterior, mid anterolateral segment, and apical lateral walls. Quantified left ventricular ejection fraction was 49%. There was a small pericardial effusion without tamponade. She was admitted for further urgent cardiac evaluation.

Left and right coronary artery angiography performed the next day did not demonstrate any obstructive coronary artery disease. Findings of a myocardial infarction with non-obstructive coronary arteries (MINOCA) with TIMI 2 flow in OM1 as well as tapering of the LAD with TIMI 3 flow were present that improved following intra-coronary nitroglycerin administration. Interventional cardiology noted this was suggestive of coronary vasospasm as a potential etiology for the patient's presentation. A post angiography ECG was positive for T-wave inversions in leads I and aVL. Cardiac MRI with and without contrast was obtained the next day with findings suggestive of an acute or subacute myocardial infarction in the circumflex coronary distribution involving the apical and mid lateral left ventricular wall.

The patient's presentation was consistent with an NSTEMI due to coronary vasospasm. She was started on amlodipine, ranolazine, lisinopril, and atorvastatin, along with aspirin and ticagrelor for an anticipated 3 months followed by indefinite aspirin. Inpatient demonstrated NSVT, and she was started on metoprolol tartrate 25 mg daily.

The patient also experienced significant anxiety and was prescribed a short course of clonazepam, as needed, upon discharge. An ambulatory cardiac monitor was placed on discharge and she was scheduled for follow up with primary care, as well as cardiology.

Discussion

Our patient presented with suspected vasospastic angina, also known as variant angina, or Prinzmetal's angina. This was originally described as a distinct cause of non-exertional angina and ST-segment elevation by Myron Prinzmetal in 1959.[1] The entity is attributed to coronary artery vasospasm,[2] although the

exact pathophysiology and underlying mechanism is not entirely understood. Possible contributing mechanisms include vascular smooth muscle hyperreactivity, autonomic nervous system dysfunction (including increased vagal tone and hyper-reactivity to sympathetic stimulation), endothelial dysfunction, microvascular spasm, allergy mediated reactions, and various causes of smooth muscle dysfunction that can be found in other organ systems, which may co-exist with coronary spasm (such as asthma, Raynaud's phenomenon, and migraines).

The prevalence is similar in males and females, though in some populations, there may be a male predominance. Risk factors include cigarette smoking and migraines and triggers may include the use of sympathomimetic and parasympathomimetic agents, mental stress, increased vagal tone, smoking, alcohol consumption, beta-blocker use, hyperventilation, and migraine therapies (including triptan and ergot alkaloid use).[3]

Historical features which are distinct for vasospastic angina, as compared to classical angina include a more rapid response to short-acting nitrates, symptoms occurring at rest, history of chronic symptoms occurring more often from midnight to early morning, marked diurnal variation in exercise tolerance, and episodes predominantly lasting for 5 to 15 minutes.[4] The physical examination otherwise may be nonspecific and the presence of ischemic abnormalities on the ECG may be variable depending on whether an active episode is occurring.[2]

The Coronary Vasomotion Disorders International Study (COVADIS) group has established a set of diagnostic criteria elements to assist with the identification of vasospastic angina.[5] Diagnosis of the condition requires (i) the presence of nitrate-responsive angina during a spontaneous episode, (ii) transient ischemic electrocardiogram changes during a spontaneous episode (including the presence of ST-segment elevation, ST-segment depression, and/or new negative U-waves in at least two contiguous leads), and (iii) documented coronary artery spasm, with at least 90% constriction, whether spontaneously or physiologically induced (often via the use of acetylcholine, ergonovine, or hyperventilation). Meeting all of the criteria definitively establishes a diagnosis of vasospastic angina. In cases where only some of the criteria are met, such as with our patient, the diagnosis may still be suspected based on history, clinical findings, and response to empiric therapies without the use of provocative testing. At present, pharmacologic provocative testing during coronary arteriography is not frequently performed.[2]

In the acute setting, the evaluation of the patient with suspected vasospastic angina should continue to prioritize ruling out obstructive coronary artery disease, especially in those with intermediate to high risk of atherosclerotic cardiovascular disease (ASCVD) who may be at risk for a combined clinical picture. ECG testing (ideally during an active chest pain episode), evaluation of troponin levels, stress testing, coronary CT angiography, and coronary arteriography are each relevant and important in evaluation of vasospastic angina, as they are in fixed coronary lesions. Additionally, in patients whose diagnosis is equivocal, ambulatory ECG monitoring may be helpful in detecting more infrequent episodes and any associated ST-segment changes and arrhythmias. It can also be helpful in determining the efficacy of therapeutic measures, especially given that asymptomatic episodes can occur and can be associated with high-risk rhythm abnormalities.[6]

Mainstays of initial treatment focused around use of calcium channel blockers and sublingual nitroglycerin. For those with persistent symptoms, long-acting nitrates, such as isosorbide mononitrate can be considered. Certain medications which can precipitate episodes should be avoided. These include non-selective beta blockers, triptans, and fluorouracil, which can precipitate coronary artery vasospasm. It has also been suggested that high dose aspirin should also be avoided due to the inhibition of prostacyclin production.[7]

The survival and prognosis of patients diagnosed with and appropriately treated for vasospastic angina is excellent at approximately 97% at 5 years.[8] This underscores the importance of correct diagnosis, especially due to frequent underdiagnosis of the condition.[9] While reassuring, there is still potential in for dangerous arrhythmias with an increased risk for cardiac death, making early identification important.[10] In those with MINOCA, all-cause mortality at 2 years is approximately 5%.[11]

As with our patient, psychological stress, anxiety, and depression can be associated in patients with vasospastic angina — both as a potential cause and effect of the disease.[9,12] Ensuring access to mental health resources and counseling are also vital for comprehensive, holistic patient care.

REFERENCES

1. **Prinzmetal M, Kennamer R, Merliss R, Wada T, Bor N**. Angina pectoris. I. A variant form of angina pectoris; preliminary report. *Am J Med*. 1959 Sep;27:375-88. doi: 10.1016/0002-9343(59)90003-8. PMID: 14434946.
2. **Rodriguez Ziccardi M, Hatcher JD**. Prinzmetal Angina. 2023 Jul 25. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 28613527.
3. **Picard F, Sayah N, Spagnoli V, Adjedj J, Varenne O**. Vasospastic angina: A literature review of current evidence. *Arch Cardiovasc Dis*. 2019 Jan;112(1):44-55. doi: 10.1016/j.acvd.2018.08.002. Epub 2018 Sep 7. PMID: 30197243.
4. **Sinha A, Rahman H, Perera D**. Vasospastic Angina: A Contemporary Review of its Pathophysiology, Diagnosis and Management. *Heart Int*. 2022 Jul 26;16(2):99-104. doi: 10.17925/HI.2022.16.2.99. PMID: 36741101; PMCID: PMC9872780.
5. **Beltrame JF, Crea F, Kaski JC, Ogawa H, Ong P, Sechtem U, Shimokawa H, Bairey Merz CN; Coronary Vasomotion Disorders International Study Group (COVADIS)**. International standardization of diagnostic criteria for vasospastic angina. *Eur Heart J*. 2017 Sep 1;38(33):2565-2568. doi: 10.1093/eurheartj/ehv351. PMID: 26245334.

6. **Enseleit F, Duru F**. Long-term continuous external electrocardiographic recording: a review. *Europace*. 2006 Apr;8(4):255-66. doi: 10.1093/europace/euj054. Epub 2006 Feb 3. PMID: 16627451.
7. **Miwa K, Kambara H, Kawai C**. Effect of aspirin in large doses on attacks of variant angina. *Am Heart J*. 1983 Feb;105(2):351-5. doi: 10.1016/0002-8703(83)90548-3. PMID: 6823827.
8. **Yasue H, Takizawa A, Nagao M, Nishida S, Horie M, Kubota J, Omote S, Takaoka K, Okumura K**. Long-term prognosis for patients with variant angina and influential factors. *Circulation*. 1988 Jul;78(1):1-9. doi: 10.1161/01.cir.78.1.1. PMID: 3260150.
9. **He Z, Xu X, Zhao Q, Ding H, Wang DW**. Vasospastic angina: Past, present, and future. *Pharmacol Ther*. 2023 Sep;249:108500. doi: 10.1016/j.pharmthera.2023.108500. Epub 2023 Jul 22. PMID: 37482097.
10. **Ahn JM, Lee KH, Yoo SY, Cho YR, Suh J, Shin ES, Lee JH, Shin DI, Kim SH, Baek SH, Seung KB, Nam CW, Jin ES, Lee SW, Oh JH, Jang JH, Park HW, Yoon NS, Cho JG, Lee CH, Park DW, Kang SJ, Lee SW, Kim J, Kim YH, Nam KB, Lee CW, Choi KJ, Song JK, Kim YH, Park SW, Park SJ**. Prognosis of Variant Angina Manifesting as Aborted Sudden Cardiac Death. *J Am Coll Cardiol*. 2016 Jul 12;68(2):137-45. doi: 10.1016/j.jacc.2016.04.050. PMID: 27386766.
11. **Williams MJA, Barr PR, Lee M, Poppe KK, Kerr AJ**. Outcome after myocardial infarction without obstructive coronary artery disease. *Heart*. 2019 Apr;105(7):524-530. doi: 10.1136/heartjnl-2018-313665. Epub 2018 Sep 29. PMID: 30269079.
12. **Mehta PK, Thobani A, Vaccarino V**. Coronary Artery Spasm, Coronary Reactivity, and Their Psychological Context. *Psychosom Med*. 2019 Apr;81(3):233-236. doi: 10.1097/PSY.0000000000000682. PMID: 30747790; PMCID: PMC6443496.