Case Study

Coronary spasm as a cause of recurrent chest pain : a case report

Abstract

Background:

Coronary artery spasm plays an important role in the pathogenesis of a wide variety of ischemic heart diseases, including myocardial infarction and sudden cardiac death-. However, the diagnosis of vasospastic angina is not always easy on the basis of symptoms alone-.

Case presentation:

A 36 year- old- man was evaluated due to recurrent left sided chest pain of 8 months duration. He is a smoker-, and otherwise physical examination was unremarkable. Electrocardiogram and blood tests were normal-, apart from elevated serum concentrations of triglycerides and low density lipoprotein cholesterol ~~concentrations~~. During the recovery phase of exercise treadmill test, the patient developed -progressive ST-segment elevation at inferior leads II, III and aVF together with progressive ST depression at precordial leads V1 to V5. (with inappropriately decreased heart rate till the development of complete heart block) (please rewrite this sentence). The patient collapsed with chest pain and hypotension. It took about 10 minutes for the ECG retuning to the baseline after medical management. The patient was referred to the coronary care unit for further management and underwent coronary angiogram. Coronary spasm -was observed in the proximal segment of the right coronary artery. The patient received medical treatment after coronary angiogram and stood well for more than one year follow up.

Conclusion

Coronary spasm may lead to both recurrent chest pain and significant arrhythmia. The diagnosis of coronary spasm often requires high index of suspicion and lab documentation.

Background:

Coronary artery vasospasm, or smooth muscle constriction of the coronary artery, is an important cause of chest pain syndromes that can lead to myocardial infarction, ventricular arrhythmias, and sudden death. Although it can occur in vessels distressed by atherosclerosis, traditionally it has been associated with variant or Prinzmetal's angina, which was first described in 1959 (1). The diagnosis of vasospastic angina (VSA) is not always easy on the basis of symptoms alone and often requires high index of suspicion and lab documentation as well.

Case presentation:

A 36 year -old- man was evaluated at our out-patient clinic complaining of recurrent left sided chest pain of 8 months duration. The pain occurred at rest and was precipitated sometimes with effort, which could be lasted for few minutes, diffuse, vague in nature but not referred. The patient is a current smoker for more than 10 years and did not have past history of diabetes, hypertension, dyslipidemia or family history of CAD.

Physical examination was unremarkable with BMI at 24 kg/m^2, waist circumference at 95 cm, and blood pressure was 140 /85 mmHg.

Chest x-ray and resting electrocardiogram (ECG) were normal and blood tests showed low density lipoprotein cholesterol 3.99 mmol/L, high density lipoprotein cholesterol 1.1 mmol/L, total cholesterol 5.72 mmol/L, triglycerides 3.13 mmol/L-, and HbA1c 5.0%. All other blood tests were normal.

We decided to perform exercise stress test using CAEP protocol (The **C**hronotropic **A**ssessment **E**xercise **P**rotocol).(reference) Blood pressure, heart rate (HR) and 12-leads ECG were recorded at rest, at two-minute intervals during exercise, at peak exercise, and through the recovery phase. The ECG ~~and ST-segment~~ wasere continuously displayed and ST-segment was measured automatically by a computer-assisted system in all 12 leads. We decided to stop the test because the patient got fatigue with achievement of 89 % of age-predicted maximal HR for age. No significant hemodynamic abnormalities or chest pain occurred with rapid upsloping ST-segment depression seen at maximal exercise. Achieved METs was 12.1 and RPP was 27,710 beats x mmHg-. At minute 2 in the recovery-, we noticed early ST-segment elevation in the inferior leads-. HR was 122 beats/min, and then HR inappropriately decreased with progressive ST--segment elevation in the inferior leads together with progressive ST depression in the precordial leads V1 to V5. The patient started to get chest pain and feels dizzy. The ECG showed sinus bradycardia with 1st degree heart block followed by Mobiz-type II heart block and then complete heart block (CHB). It took ~~takes~~ about 4 min from cessation of exercise to develop CHB. HR was 30 beats/min, and BP was 65 /30 mmHg. At the start-, the patient received oxygen and sublingual NTG-. After the development of CHB-, he received 1-mg atropine iv push-, and started fluid resuscitation. A random blood sugar was normal-.After that

by about 7 min-, the ECG showed junctional escape rhythm with HR 45 b/min , followed rapidly by accelerated junctional rhythm with HR 101 beats/min then sinus tachycardia-. Also, ST-segment changes in the inferior leads and precordial leads gradually improved till complete resolution after about 10 minutes from its start-, together with disappearance of chest pain and normalization of BP.

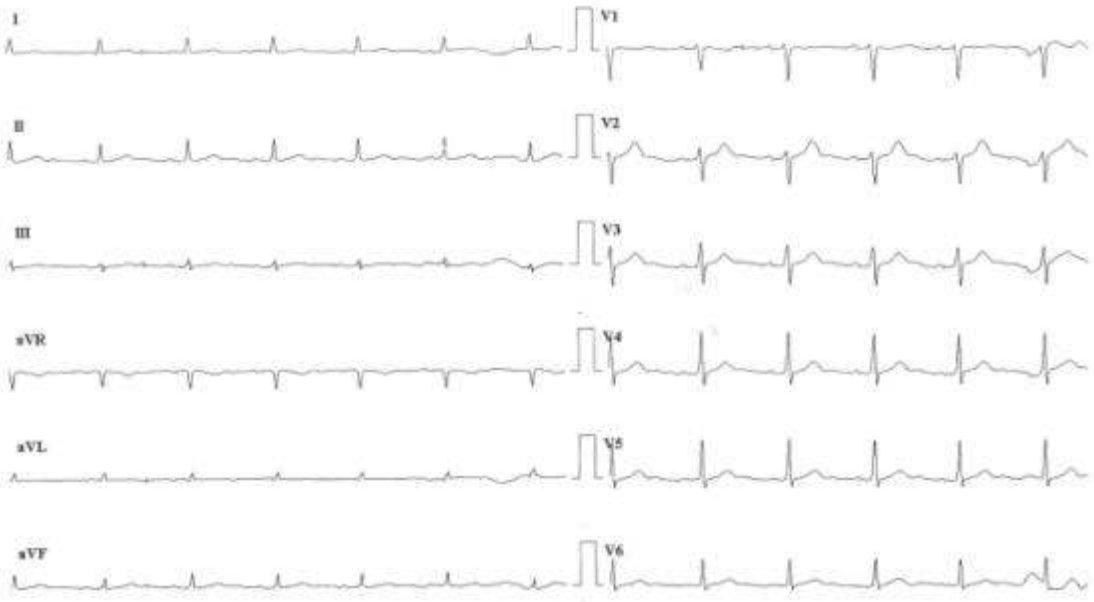

Figure 1. Resting ECG

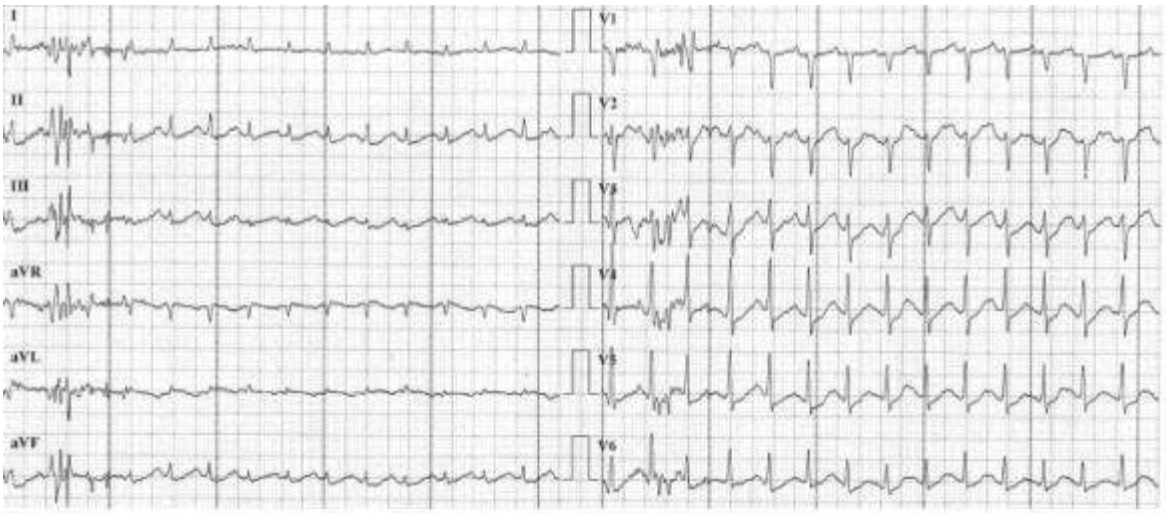

Figure 2. Maximal exercise treadmill test with normal response

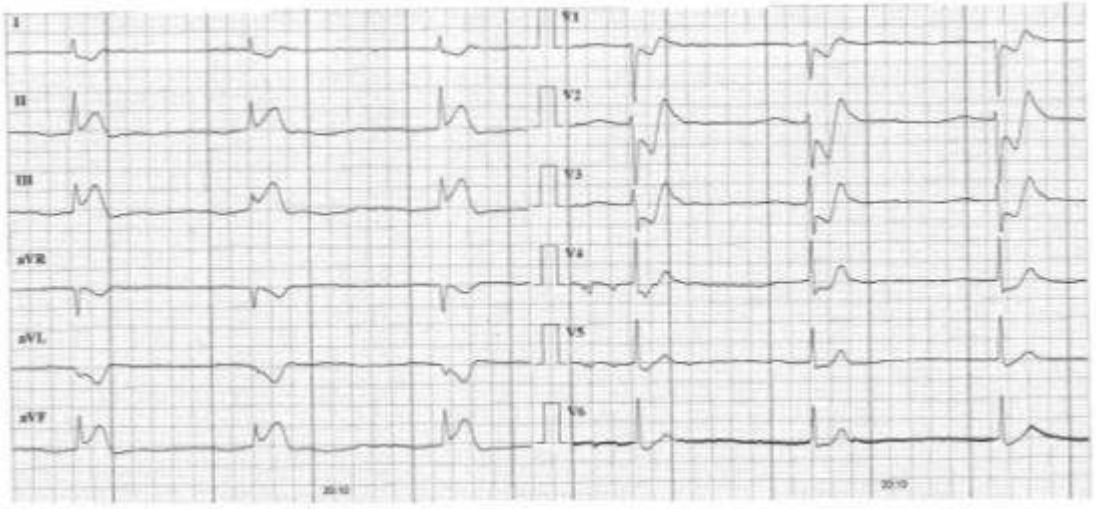

Figure 3. Recovery phase of exercise treadmill test with the development of CHB and ST elevation at inferior leads together with ST depression at precordial leads

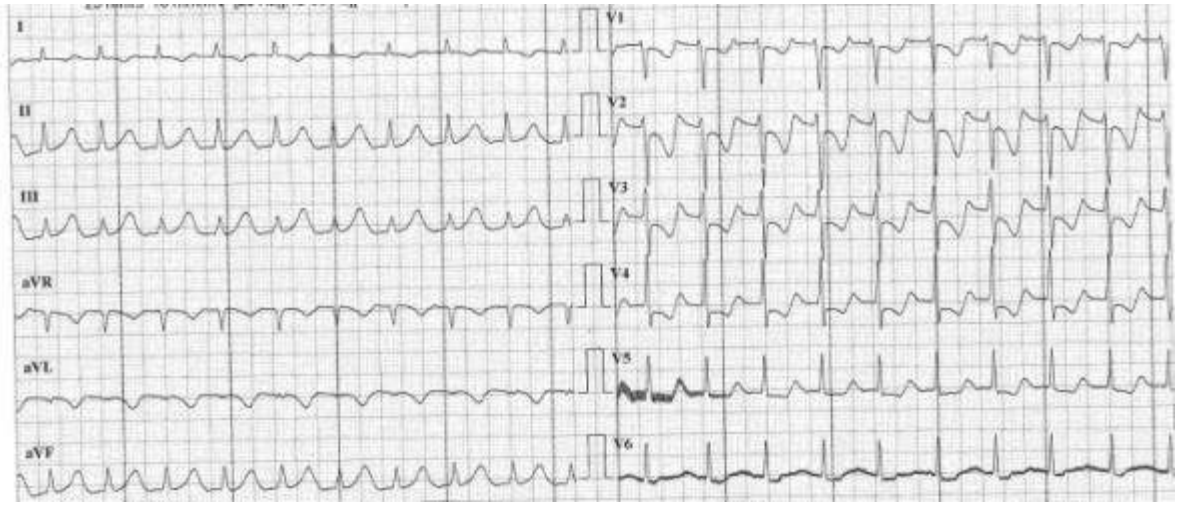

Figure 4. Resolving ST changes after IV atropine

The patient was transferred to the coronary care unit for observation and further evaluation. Cardiac enzymes ~~on admission ,after 6 and 12 h~~ were checked at baseline, 6, and 12 hours, ~~ordered~~ and echo~~-D~~doppler evaluation was done where the results were normal. Coronary angiography and left

ventriculography were performed in the following day. The left coronary system was imaged at left and right oblique, right cranial and caudal and anteroposterior cranial positions. The left coronary artery and left ventriculography were normal .The right coronary artery showed significant focal spasm at its proximal segment without provocation that relieved completely by 100 ug intracoronary NTG .

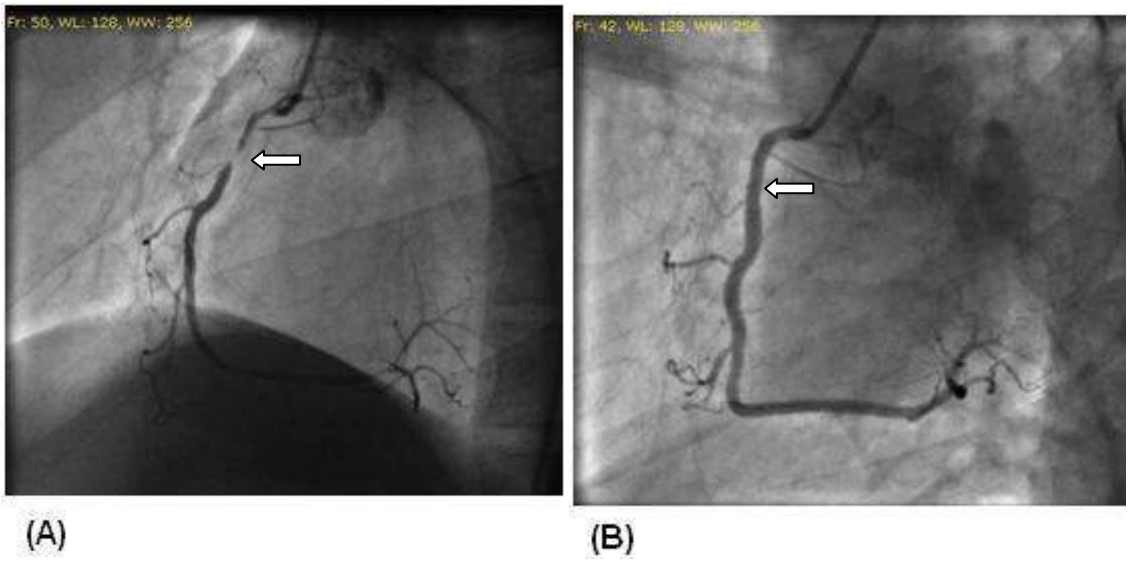

Figure 5. RCA angiogram during spasm (A) and after using NTG (B).

The patient was advised to stop smoking and discharged with LA isosorbide mononitrate 100 mg per day-, amlodipine 5 mg per day-, atorvastatin 20 mg per day. With follow up of more than one year-, the patient feels much better with little symptoms ~~, if any~~.

Discussion:

Coronary vasospasm is a transient abnormal contraction of an epicardial coronary artery which can instigate myocardial ischemia.
Coronary arterial tone varies normally via physiologic mechanisms, but the degree of vasoconstriction can range along a spectrum extending from undetectable constriction to complete arterial occlusion.
Many observers use the presence of constriction-induced ischemia as the threshold for defining clinical coronary artery vasospasm (2) ,which has also been called vasospastic angina or variant angina.

It is an important cause of morbidity, but rarely causes mortality.
Coronary spasm is caused by abnormal coronary smooth muscle activity which is not a rare occurrence limited to a particular form of variant angina, but a common pathogenic element in ACS (2). It is predominantly occurring at rest and usually associated with transient ST-segment elevation on the ECG.

Multiple mechanisms involved as chronic low grade inflammation with increased mast cells level (3) and C-reactive protein (CRP) concentrations (4) , and endothelial dysfunction (5) that may enhance vascular smooth muscle reactivity to agonists as serotonin ,histamine and endothelin (6,7) .

Other possible mechanisms include primary vascular smooth muscle cell hyperreactivity (8)-, increase in autonomic nervous activity (9)-, magnesium deficiency (10)-,and genetic predisposition (11). Nevertheless-, the exact cellular mechanisms responsible for the spasm remain elusive.

Before doing coronary angiography ,there was high probability that our patient has coronary spasm because there was no obvious CAD risk factors apart from smoking and mildly increased LDL-C, together with patient's atypical chest pain .Moreover, the patient developed ST-segment elevation complicated with serious arrhythmia after termination of exercise that takes few minutes before completely resolved.

Unlike atherosclerotic CAD-, patients with variant angina tend to be younger in age (12) and chest pain is commonly severe and may be accompanied by palpitations or syncope secondary to arrhythmia. As stable angina, vasospasm responds by nitrate medication. Serum cardiac troponins may also prove unreliable as they may or may not be raised-.

There is no independent predictor of severity of vasospasm and its occurrence. It occurs most often from midnight to early morning and is usually not induced by exercise in the daytime (13&14)-. Some studies have shown that mild stage exercise is enough to induce variant angina in early hours of the morning even multistage exercise fails to do so in the afternoon (2, 13) as was the case of our patient.

Is it by nitrate-, atropine or by itself coronary spasm was relieved?

Our patient's hemodynamic decompensation, which developed during the exercise recovery phase, was relieved after intravenous administration of atropine, a parasympatholytic agent-, that was preceded with using sublingual NTG. Patients with coronary artery vasospasm appear to have a heightened vasoconstrictor response to acetylcholine as well as an enhanced response to

the vasodilator effects of nitrates, an observation that is consistent with a deficiency of endogenous nitric oxide activity (2) .

During strenuous exercise, sympathetic discharge is maximal, and parasympathetic stimulation is withdrawn. In our patient, bradycardia and hypotension in the presence of ongoing ischemia due to coronary arterial spasm occurred during the early recovery phase that may resulted from sudden parasympathetic hyperactivity immediately after exercise which could be abolished with atropine.

Previously, Yasue and colleagues (15) found that pretreatment with intravenous atropine blocked acetylcholine-induced coronary spasms, and they suggested that parasympathetic tone might play a role in the pathogenesis of coronary arterial spasm.

On the other hand, Wang and associates (16) reported that the isoproterenol head-up tilt test could provoke coronary arterial spasm, and they speculated that both increased basal parasympathetic tone and strong sympathetic stimulation are important in causing coronary arterial spasm.

Definitive diagnosis is made by angiographically demonstrated coronary artery vasoconstriction either naturally or with provocative tests which reverses with intravenous or intra arterial NTG. In most case reports, the diagnosis was based on the clinical and laboratory findings without provocation (17) . A recent guideline by the Japanese Circulation Society Joint Working Group advocated that the diagnosis can be solely established on clinical ground (18).

Its management remains a debate with absence of hard scientific evidences and guidelines. The therapy for vasospastic coronaries can be difficult; up to 25% of patients continue to have intractable angina despite optimal treatment (19).These episodes can be detrimental and occasionally life-threatening when myocardial infarction or arrhythmias occur.

Failing medical therapy, mechanical revascularization has been tried successfully. Scattered reports of coronary stenting suggest that a percutaneous strategy may be feasible in such patients (20).

In spite that stent implantation on vasospastic artery bears the danger of in-stent restenosis and recurrent spasm ,drug-coated stents is favourable as it is safer and limits the risk of restenosis. The results for surgical revascularization have been variable, but overall, bypass surgery appears to provide clinical benefit to less than 50% of patients (21).

In these patients, adding complete plexectomy to the procedure may provide additional benefit (22).

Mortality though rare, is not uncommon. Long-term survival is believed to be good, especially in patients who tolerate calcium antagonists and avoid smoking (23). Predictors of poorer prognosis include the presence of concurrent coronary atherosclerosis (21),ongoing smoking, intolerance of calcium antagonists, and spasm of multiple coronary arteries (24).

In conclusion,variant angina can be readily diagnosed by clinical criteria and/or provocative testing, yet it is often not considered. Traditionally, such patients have been reassured that they do not have heart disease despite persistent symptoms and re-hospitalization .

Given that it can have life-threatening sequelae that are preventable with readily available therapies, it is essential that clinicians are vigilant in considering this condition.

Abbreviations

CAD: coronary artery disease; ECG: electrocardiogram; RPP : rate-pressure product; CHB: complete heart block; NTG: nitroglycerine; CXR: Chest x-ray; BMI: Body mass index; BP : Blood pressure; HR: Heart rate; HDL-C: High density lipoprotein-cholesterol; LDL-C: Low density lipoprotein-cholesterol; TG: Triglycerides; HBA1c: Glycosylated hemoglobin; NTG: nitroglycerin.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Declaration of Interest

The authors report no conflicts of interest

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; 27: 375-388.

2. Yasue H, Nakagawa H, Itoh T, Harada E, Mizuno Y. Coronary artery spasm-cinical features, diagnosis, pathogenesis, and treatment. J Cardiol 2008; 51: 2-17.

3. Forman MB, Oates JA, Robertson D, Robertson RM, Roberts LJ, Virmani R. Increased adventitial mast cells in patients with

coronary spasm. N Engl J Med 1985; 313:1138-1141.

4. Hung MJ, Cherng WJ, Yang NI, Cheng CW, Li LF. Relation of high-sensitivity C-reactive protein level with coronary vasospastic angina pectoris in patients without hemodynamically significant coronary artery disease. Am J Cardiol 2005; 96: 1484-1490.

5. Murad F. Nitric oxide and cyclic GMP in cell signaling and drug development. N Engl J Med 2006; 355: 2003-2011.

6. Stanley K. Coronary artery spasm: multiple causes and multiple roles in heart disease. Biochem Pharmacol 1995; 49:859-871.

7. Kalsner S. Coronary artery spasm and no spasmogens? Med Hypotheses 1993; 40: 186-195.

8. Kaski JC, Tousoulis D, Gavrielides S, McFadden E, Galassi AR, Crea F, Maseri A. Comparison of epicardial coronary artery tone and reactivity in Prinzmetal's variant angina and chronic stable angina pectoris. J Am Coll Cardiol. 1991;17:1058 –1062.

9. Kugiyama K, Yasue H, Okumura K, et al. Nitric oxide activity is deficient in spasm arteries of patients with coronary spastic angina. Circulation 1996; 94:266-72.

10. Goto K,Yasue H, Okumura K, et al. Magnesium deficiency detected by intravenous loading test in variant angina pectoris. Am J Cardiol 1990; 65: 709–712.

11. Miwa K, Fujita M, Sasayama S. Recent insights into the mechanisms, predisposing factors, and racial differences of coronary vasospasm. Heart Vessels 2005; 20: 1–7.

12. Yasue H, Omote S, and Takizawa A. Circadian variation of exercise capacity in patients with Prinzmetal's variant angina: role of exercise-induced coronary arterial spasm. Circulation, vol. 59, no. 5, pp. 938–948, 1979.

13. Yasue H, Kugiyama K. Coronary spasm: clinical features and pathogenesis. Intern Med 1997; 36: 760-765.

14. Kishida H, Tada Y, Fukuma N, et al.: Significant characteristics of variant angina patients with associated syncope. Jpn Heart J 1996; 37: 317–326.

15. Yasue H, Horio Y, Nakamura N, Fujii H, Imoto N, Sonoda R, et al. Induction of coronary artery spasm by acetylcholine in patients with variant angina: possible role of the parasympathetic nervous system in the pathogenesis of coronary artery spasm. Circulation 1986;74:955–63. [PubMed]

16. Wang CH, Lee CC, Cherng WJ. Coronary vasospasm induced during isoproterenol head-up tilt test. Am J Cardiol 1997;80:1508–10.[PubMed]

17. Tun A, Khan IA. Myocardial infarction with normal coronary arteries: the pathologic and clinical perspectives. Angiology 2001; 52:299-304.

18. JCS Joint Working Group Guidelines for diagnosis and treatment of patients with vasospastic angina (coronary spastic angina) (JCS2008): digest version. *Circ J.* 74 2010:1745-1762.CrossRef | PubMed

19. Nakamura M, Takeshita A, Nose Y. Clinical characteristics associated with myocardial infarction, arrhythmias and sudden death in patients with vasospastic angina. Ciculation 1987; 75:1110-6.

20. Khitri A, Jayasuriya S, Habibzadeh MR, Movahed MR. Coronary stenting in patients with medically resistant vasospasm. Rev Cardiovasc Med. Fall 2010;11(4):264-70. [Medline].
21. Mishra PK. Variations in presentation and various options in management of variant angina. Eur J Cardiothorac Surg. May 2006;29(5):748-59. [Medline].
22. Bertrand ME, Lablanche JM, Rousseau MF, Warembourg HH Jr, Stankowtak C, Soots G. Surgical treatment of variant angina: use of plexectomy with aortocoronary bypass. Circulation. May 1980;61(5):877-82. [Medline].
23. Bory M, Pierron F, Panagides D, Bonnet JL, Yvorra S, Desfossez L. Coronary artery spasm in patients with normal or near normal coronary arteries. Long-term follow-up of 277 patients. Eur Heart J. Jul 1996;17(7):1015-21.
24. Yasue H, Takizawa A, Nagao M, Nishida S, Horie M, Kubota J, et al. Long-term prognosis for patients with variant angina and influential factors. Circulation. Jul 1988;78(1):1-9. [Medline].