

Coronary Stenting in Patients With Medically Resistant Vasospasm

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Formally described by Prinzmetal and colleagues in 1959, variant angina represents a syndrome of resting angina that results from severe coronary artery vasospasm associated with ST elevation. The majority of patients respond to nitrates or calcium channel blockers. However, medical treatment-resistant vasospasm can occur in up to 20% of cases, thus requiring further interventions. We present a rare instance of coronary vasospasm associated with complete heart block resistant to medical therapy that was successfully treated with stenting. This case example is followed by a detailed review of the literature with regard to percutaneous or surgical coronary revascularization of patients with medically resistant vasospasm.

[Rev Cardiovasc Med. 2010;11(4):264-270 doi: 10.3909/ricm0545]

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Key words: Prinzmetal angina • Vasospastic angina • High-grade AV block • Conduction defect • Stenting • Revascularization • ST elevation • Percutaneous coronary intervention • Spasm • CABG

Formally described by Prinzmetal and colleagues¹ in 1959, variant angina represents a syndrome that results from severe coronary artery vasospasm. Patients present with episodic angina that occurs at rest associated with ST elevation. The majority of patients respond to medical treatment in the form of calcium channel blockers (CCBs) and nitrates. However, in this case report, we present a rare instance of coronary vasospasm associated with complete heart

block that was resistant to medical therapy and successfully treated with stenting. This case is followed by a review of the literature.

Case Report

A 79-year-old man with a history of chronic obstructive pulmonary disease, hypertension, and previous tobacco use presented to the emergency department with a 1-week history of intermittent chest pain. The pain was described as a pressure sensation located in the substernal region radiating to the jaw. The pain occurred at rest and was associated with shortness of breath and nausea. The patient reported each episode lasting approximately 5 to 6 minutes with spontaneous resolution. However, on the day of the visit to the emergency department, he had a prolonged episode of chest pain lasting for 45 minutes. Upon initial assessment, the patient's vital signs were stable with a temperature of 37°C, pulse rate of 62 beats/min, and blood pressure of 130/92 mm Hg. The remaining physical examination results were all within normal limits. An initial electrocardiogram (ECG) during his episode of chest pain demonstrated sinus bradycardia and 1-mm ST elevation in leads II, III, and aVF with reciprocal ST depressions noted in the anterior leads (Figure 1). The patient was administered a heparin drip and 325 mg of aspirin. Before any nitroglycerin treatment, his chest pain resolved spontaneously with resolution of inferior ST elevation (Figure 2). Troponin I test results were negative. The patient was taken emergently for cardiac catheterization. Coronary angiography showed a dominant right coronary artery (RCA) which was a large vessel with a mild 20% proximal lesion. The left coronary system revealed 80% distal obtuse marginal stenosis that was very small

Figure 1. Initial electrocardiograph on presentation.



Figure 2. Follow-up electrocardiograph just prior to initial cardiac catheterization.

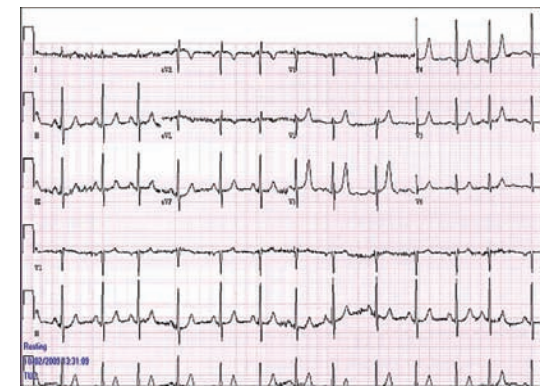
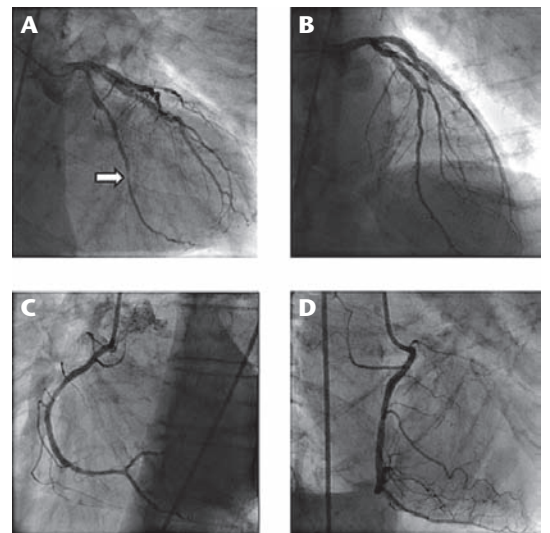


Figure 3. Initial cardiac catheterization images. (A) 70% stenosis noted in the first obtuse marginal branch (arrow indicates high-grade lesion). (B) View of the left anterior descending artery. (C, D) Views of the right coronary artery.



in caliber, and did not explain his initial inferior ST elevation (Figure 3). A diagnosis of right coronary vasospasm was made without further coronary intervention at that time. The patient was started on nitroglyc-

erin drip, 5 mg of amlodipin, aspirin, and simvastatin. He was admitted to the intensive care unit for overnight observation.

Approximately 8 hours later, the patient had another episode of chest

pressure with radiation to his jaw associated with diaphoresis and shortness of breath. A repeat ECG once again showed ST elevations in the inferior leads but more pronounced at 3 mm, in addition to reciprocal changes in the anterior leads. Twenty minutes later, after initial resolution of his chest pain and ST elevation, he developed recurrent chest pain, severe bradycardia, hypotension, and third-degree atrioventricular block, with a heart rate as low as 28 beats/min and a blood pressure of 60/30 mm Hg, and required transcutaneous pacing (Figure 4). His chest pain as well as his ECG changes spontaneously resolved after 5 minutes with normalization of his heart rate and blood pressure.

The patient was urgently taken to the cardiac catheterization laboratory for repeat coronary angiography and intervention. After initial temporary transvenous pacemaker placement, repeat angiography revealed a right coronary spasm in the area of the previously documented 20% stenosis in the proximal RCA with improvement after intracoronary administration of 200 μ g of nitroglycerin (Figure 5). Intravascular ultrasound (IVUS) was subsequently performed in the area of spasm confirming mild atherosclerotic disease without significant stenosis (Figure 6). Considering the life-threatening arrhythmia associated with this severe vasospasm despite medical therapy, the decision was made to proceed with percutaneous

Figure 4. Electrocardiographs prior to second cardiac catheterization. Electrocardiograph showing pronounced ST elevations in the inferior leads with reciprocal changes anteriorly (top). Electrocardiograph showing evidence of complete heart block (bottom).

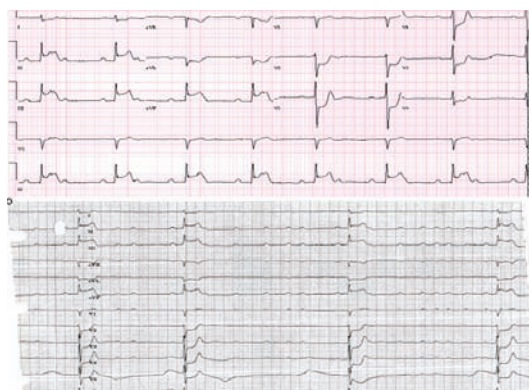


Figure 5. Images from the second cardiac catheterization. 70% stenosis noted in the mid right coronary artery (left). Resolution of the stenosis after intracoronary nitroglycerin administration (right). Arrow indicates coronary spasm.

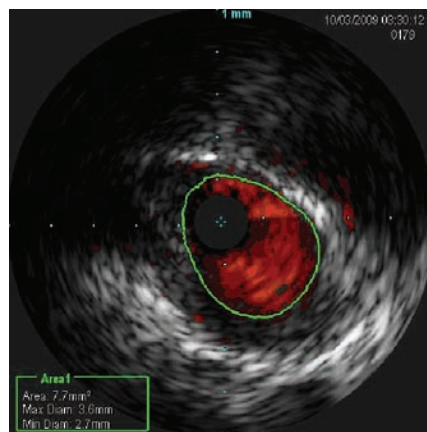
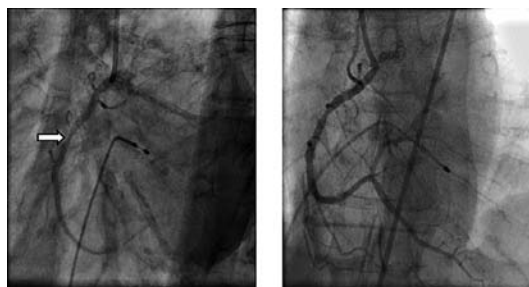


Figure 6. Intravascular ultrasound image of the right coronary artery during the second cardiac catheterization.

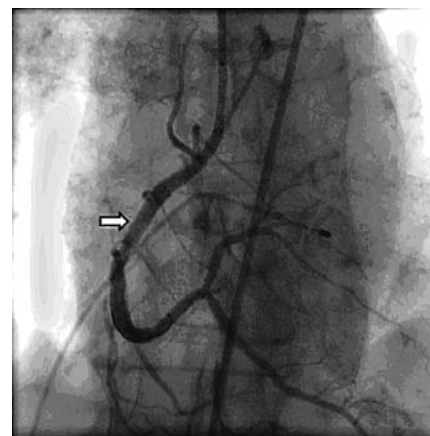


Figure 7. Right coronary artery after stent placement. Arrow points to stented segment.

Considering the life-threatening arrhythmia associated with this severe vasospasm despite medical therapy, the decision was made to proceed with percutaneous coronary intervention (PCI) and stenting of the documented area of vasospasm in the proximal RCA.

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using a 3.5 \times 18 Endeavor[®] stent (Medtronic, Minneapolis, MN), up-sizing using a 4.0 \times 15 Apex balloon

catheter (Boston Scientific, Boston, MA) with excellent results (Figure 7). Stenting with a 2.25 \times 12 mm TAXUS[®] Liberté[®] Atom[™] (Boston Scientific) was also performed on the 80% distal first obtuse marginal branch with excellent results (Figure 8). The patient responded well to the intervention with no

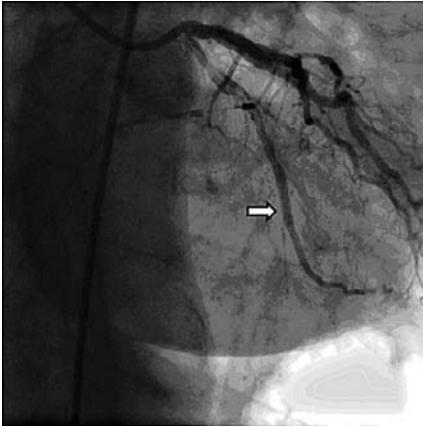


Figure 8. Obtuse marginal branch after stent placement. Arrow points to stented segment.

further episodes of chest pain or bradycardia and was discharged home several days later. The patient was seen in an outpatient clinic approximately 6 weeks later and reported being symptom free.

Review

Epidemiology and Treatment Dilemma

Coronary artery vasospasm is an entity that on most occasions responds well to medical treatment in the form of CCBs and long-acting nitrates.^{2,3} Yet, it has been shown that approximately 20% of patients with coronary artery vasospasm remain refractory to medical therapy.^{4,5} Although no specific guidelines currently exist, in practice, the use of PCI in resistant focal spasm and minimally obstructive disease is controversial.

The Role of IVUS

Previous studies have shown that the degree of atherosclerosis at sites of focal vasospasm may be grossly underestimated when relying solely on angiographic data; thus, the use of IVUS in such cases proves advantageous.^{6,7} This becomes important because studies have shown that the degree of organic stenosis can pro-

vide prognostic value. Nishizawa and colleagues⁸ analyzed a cohort of patients in which a fixed stenosis was present at the site of provoked coronary artery vasospasm. Comparing these patients with fixed stenosis to those with no apparent organic stenosis, it was shown that intermediate fixed stenosis serves as an independent risk factor for major adverse cardiac events in patients with underlying variant angina. More recently, IVUS data have helped show

rarely considered for the treatment of medically resistant vasospastic angina anymore.

PCI and Stenting

The advent of the intracoronary stent provided a less invasive option for treatment of refractory vasospasm. Lopez and coworkers¹¹ reported the use of a Gianturco-Roubin stent for refractory vasospasm; the patient remained asymptomatic at 3-month follow-up and had a negative exercise

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that the composition of underlying plaques differs in those patients with coronary artery vasospasm and unstable angina. Plaques in patients with vasospasm tend to be less calcified and contain less fibrous tissue.⁹ Such findings may help us to better understand the underlying mechanisms responsible for refractory vasospasm.

Coronary Artery Bypass Grafting

Reports have shown that coronary intervention in patients with medical therapy refractory vasospasm may be beneficial. Prior to the existence of coronary stents, Sussman and associates¹⁰ reported on the utilization of coronary artery bypass grafting (CABG) for refractory variant angina. The authors discuss 2 patients who were refractory to standard medical management who underwent CABG to bypass the area of severe vasospasm; both patients were asymptomatic at 24- and 66-month follow-up. With the exception of anecdotal case reports, there are no studies comparing surgical versus percutaneous treatment of refractory coronary spasm. With the advent of PCI and stenting, CABG is

myocardial perfusion study result. Similarly, Kültürsay and colleagues¹² reported the use of a Palmaz-Schatz stent for persistent refractory coronary vasospasm. The patient remained asymptomatic at 3-month follow-up, with negative results on exercise stress test and myocardial perfusion study. Gupta and coauthors¹³ also showed successful results with stenting of severe vasospasm of the left anterior descending artery (LAD) that was refractory to triple-drug therapy; the patient remained asymptomatic with negative provocative test results at 4-month follow-up. Khatri and associates¹⁴ evaluated 9 patients with clinically severe coronary artery vasospasm documented by coronary angiography who were refractory to aggressive medical management. All 9 patients were free of any significant angiographic obstructive coronary artery stenosis on baseline cardiac catheterization. Five of the 9 patients remained symptom free after PCI with stenting. Complications noted in the follow-up period included in-stent restenosis and recurrent vasospasm. Gaspardone and coworkers¹⁵ performed a similar study evaluating 9 consecutive patients found to have

medically refractory vasospasm associated with mild to moderate coronary disease. Results revealed 6 out of 9 patients to be symptom free at follow-up approximately 10 months after stent implantation. However, it is important to note that coronary stenting is not free from complications. In-stent restenosis and coronary vasospasm proximal to the implanted stent have occurred in some patients. Martí and colleagues¹⁶ studied a cohort of 5 patients who were found to be refractory to medical therapy. All 5 patients underwent coronary artery stenting; 3 of the 5 patients required further stenting in the poststent period secondary to recurrent coronary artery vasospasm. Follow-up at approximately 30 months revealed 3 out of the 5 patients to be asymptomatic. The remaining 2 patients experienced complications, including in-stent restenosis and a de novo lesion in the treated vessel. Some reports have shown that the stent restenosis rate in those patients treated for variant angina is significantly higher than in those stented for other indications.¹⁷ Tanabe and coauthors¹⁸ demonstrated poststent spasm occurring at a site different from the initial stenosis. A total of 45 patients with clinically significant coronary vasospasm and severe baseline organic stenosis who underwent PCI were included in the study. No restenosis was observed at 7-month follow-up. Despite lack of coronary vasospasm at the original site of intervention, spasm at a site proximal or distal to the stent or in another coronary artery occurred in 77% of the patients, whereas multivessel spasm was evident in 62%. The data from this study suggest that medical management with CCBs and nitrates should be continued even after successful stenting given the high risk of continued vasospasm at different locations.

Such complications are illustrated eloquently by Nishtar and colleagues,¹⁹ who describe a case of severely refractory vasospastic angina.

Unique to our patient was the development of complete heart block in the face of severe coronary vasospasm.

The authors describe a 27-year-old man with multiple hospital admissions secondary to symptomatic chest pain and troponin-positive myocardial infarction. The patient eventually underwent coronary artery stenting of the RCA but suffered severe in-stent stenosis. Given the severity and persistence of symptoms, the patient was referred to cardiothoracic surgery and underwent bypass surgery. The postsurgical period was complicated by episodes of ventricular fibrillation requiring implantation of a cardiac defibrillator. The patient continued to complain of chest pain, and was eventually found to have spastic disease of his LAD, which responded well to PCI with stent placement. Burns and associates²⁰ described a case of a 54-year-old man with chest pain and bradycardia who was found to have inferior ST elevations and was treated

Unique to our patient was the development of complete heart block in the face of severe coronary vasospasm. Previous reports have been published

on the development of bifascicular block, complete heart block, and even asystole related to severe coronary vasospasm.²¹⁻²⁶ Jeong and coworkers²⁴ reported on a similar case of severe refractory coronary vasospasm of the LAD successfully treated with coronary artery stent placement; the patient was symptom free at 3-year follow-up. However, this is the first case report to our knowledge in which complete heart block induced by refractory RCA vasospasm was successfully treated with implantation of a single coronary artery stent. Another unique aspect to this case was the severity of focal vasospasm with only mild atherosclerotic disease shown by IVUS examination.

These reports help demonstrate that stent-based PCI in carefully selected patients who are refractory to medical management may provide an additional means of treat-

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with stent placement to the RCA. The patient returned with continued chest pain a few months later and was eventually found to have vasospastic disease distal to the stent that had been placed. The patient underwent extensive stenting of the RCA and remained symptom free at 24-month follow-up. Such cases help to demonstrate the complexity and intricacies involved in coronary artery vasospasm.

ment. However, because of significant risk of stent restenosis, thrombosis, and recurrent vasospasm in different sites, aggressive medical management still remains the gold standard for the treatment of coronary vasospasm; PCI with stenting may be considered in refractory cases. A synopsis of major studies involving patients undergoing PCI for medically refractory coronary vasospasm can be seen in Table 1.

Table 1
Synopsis of Major Studies Involving Patients Undergoing PCI
for Medically Refractory Coronary Vasospasm

Study	Patients (N)	Patients Presenting With ST Elevation (%)	Patients With Cardiac Enzymes (%)	Patients Presenting With Associated Arrhythmia (%)
Lopez JA et al. ¹¹	1	+	—	—
Kültürsay H et al. ¹²	1	—	—	—
Gupta S et al. ¹³	1	+	—	+
Khatrī S et al. ¹⁴	9	78	—	22
Gaspardone A et al. ¹⁵	9	+	—	—
Martí V et al. ¹⁶	5	+	—	80
Nishtar SS et al. ¹⁹	1	+	+	+
Burns A et al. ²⁰	1	+	+	+
Ortega-Carnicer J et al. ²¹	1	+	—	—
Unverdorben M et al. ²²	1	+	—	+
Van Spall HG et al. ²⁵	1	+	—	—
Sosnowski C et al. ²⁶	5	+	40	20

PCI, percutaneous coronary intervention.

Conclusions

The utilization of PCI for severe refractory coronary vasospasm appears to be a promising adjunct to current therapies. The complications associated with stent implantation in such a scenario must be carefully considered, and the risks and benefits should be weighed on an individual basis. Larger cohort studies are needed to further investigate the

routine use of stenting in refractory disease. ■

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Main Points

- Variant angina represents a syndrome that results from severe coronary artery vasospasm. The majority of patients respond to medical treatment in the form of calcium channel blockers and nitrates; yet, it has been shown that approximately 20% of patients remain refractory to medical therapy.
- Because of significant risk of stent restenosis and recurrent vasospasm in different sites, aggressive medical management still remains the gold standard for the treatment of coronary vasospasm.
- The advent of the intracoronary stent provides a less invasive option for the treatment of refractory vasospasm.
- The utilization of percutaneous intervention for severe refractory coronary vasospasm appears to be a promising adjunct to current therapies.

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