The Incidence and Clinical Implications of Coronary Artery Spasm

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SUMMARY
The total incidence of coronary artery spasm during coronary angiography has been reported to be between 0.26% and 0.93%. The rarity of this phenomenon has been invoked to minimize its clinical significance. Review of a one-year experience in our catheterization laboratory showed that coronary spasm occurred in eight of 274 coronary angiograms (2.93%). In three instances, spasm could not be ascribed to catheter tip irritation, and was considered to be spontaneous. Since multiple factors during coronary arteriography might inhibit the occurrence of coronary spasm, it is believed that the incidence of spontaneous spasm may be higher than can be documented during angiography. Coronary spasm may have important clinical significance in various chest pain syndromes and greater methodical attention should be directed toward this phenomenon.

Although recent reports have documented coronary arterial spasm as a cause of Prinzmetal's variant angina,\(^1\)\(^-\)\(^8\) the clinical significance of this phenomenon has been underrated because of its rarity during selective coronary angiography and the frequent absence of associated symptoms.\(^9\)\(^-\)\(^11\) In order to determine the incidence and possible clinical significance of coronary artery spasm, we directed special attention to recognition of this phenomenon during coronary angiograms performed in our catheterization laboratory. This report presents our one-year experience.

Materials and Methods

Starting in January 1974 we directed special attention to recognition and documentation of coronary arterial spasm in our cardiac catheterization laboratory. The phenomenon was looked for prospectively in all patients undergoing selective coronary arteriography. This implied the following: 1) avoiding prophylactic administration of coronary vasodilators at the beginning of the procedure; 2) attempting to obtain two sets of coronary cineangiograms, before and after the sublingual administration of nitroglycerin (0.3–0.6 mg), if segmental narrowing was seen, when it was judged technically feasible and clinically safe; 3) careful review of films by experienced angiographers with attention directed to the recognition of spasm.

No attempts to artificially induce spasm by pharmacologic or mechanical stimuli were made in any case. The coronary angiograms were performed with Renographin-76 via the brachial artery approach\(^9\) or percutaneous femoral techniques.\(^10\)\(^-\)\(^14\)

Coronary artery spasm was considered to be present only when the evidence was unequivocal and satisfied two of the following three criteria: 1) appearance of transient narrowing in a coronary segment that initially or subsequently appeared to be angiographically normal; 2) occurrence of transient total obstruction in a normal coronary segment or at the site of partial narrowing due to an atheromatous lesion; 3) prompt response of the narrowing or obstruction to sublingual administration of nitroglycerin or its spontaneous relief, documented upon subsequent injections of the same coronary artery.

To be considered catheter-induced, the spasm phenomenon must be located within 1 to 2 cm of the coronary ostium and/or the operator must have recognized a cannulation during which the catheter tip touched the area of spasm. Instances where the phenomenon could not be attributed to the catheter were presumed to be spontaneous, despite the impossibility of certain exclusion of induction of spasm by catheters during selective coronary angiography.

All cases satisfying these criteria, whether spasm was believed to be spontaneous or catheter-induced, were included in this report. Cases in which it was difficult to interpret the degree of narrowing because of variation from one injection to another or before and after nitroglycerin were excluded, although it is recognized that these instances may represent examples of spasm.

Results

Two hundred and seventy-four coronary angiograms were performed during the period between January 1 and December 31, 1974. The Sones technique was used in 80% of these studies and 20% were performed via the percutaneous transfemoral approach. Two hundred and fourteen (78%) had evidence of atherosclerotic coronary artery disease with significant narrowing of one or more major vessels. Sixty (22%) had normal coronary angiograms or minimal nonobstructive irregularities. The latter

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group included patients with either chest pain syndromes where the procedure was performed to rule out coronary artery disease or valvular heart disease or cardiomyopathy where coronary angiograms were considered necessary.

Coronary arterial spasm satisfying our rigid criteria was encountered in eight cases (incidence of 2.93%).

Case 1
A 57-year-old Caucasian male presented with a six-year history of angina. During the two years before admission to the Houston VA Hospital, he had one episode of prolonged chest pain presumed to be due to myocardial infarction, and several other hospital admissions for unstable angina. His electrocardiogram showed poor R wave progression from V₁ to V₅ compatible with the diagnosis of old anteroseptal myocardial infarction. A treadmill test (Bruce protocol)¹⁸ showed poor exercise tolerance (3 minutes, 28 seconds) and was complicated by ventricular tachycardia and left bundle branch block.

The left ventricular angiogram showed mild anterior hypokinesis. Coronary angiography, however, showed minimal nonobstructive luminal irregularities. Spasm was noted at the tip of the catheter near the origin of the right coronary artery during one injection and disappeared during subsequent injections (fig. 1).

Case 2
A 48-year-old black male presented with nine-year history of chest pains suggestive of angina. A year before our study he was hospitalized and told that he sustained a myocardial infarction. He was subsequently hospitalized again because of unstable angina. His electrocardiogram showed small Q waves in leads II, III and aVF. A treadmill test showed decreased exercise tolerance (4 minutes, 28 seconds) but no ischemic ST shifts.

At angiography the left ventricle contracted normally and the coronary arteries appeared to be normal. Proximal right coronary spasm was noted at the catheter tip and responded to nitroglycerin administration.

Case 3
A 47-year-old black male with four-year history of angina and two well-documented myocardial infarctions was referred because of persistent classical angina pectoris. His treadmill test showed limited exercise tolerance (5 minutes, 8 seconds). The test was terminated because of moderately severe angina and ischemic ST shifts were noted.

Coronary arteriography showed a 70% obstructive atheromatous lesion in the proximal right coronary artery about 2.5 to 3 cm from the ostium and total occlusion of the atrioventricular groove branch of the left circumflex. Severe spasm of the right coronary artery in the vicinity of the organic lesion was seen in a later injection and resulted in transient complete occlusion of the vessel. Patency of the vessel was re-established readily following administration of nitroglycerin (fig. 2). This case was reported in detail elsewhere.¹⁶

Case 4
A 42-year-old Caucasian male was referred because of rheumatic heart disease with predominant mitral stenosis and minimal aortic valve disease. His main complaint was dyspnea on exertion. He denied history of angina. Treadmill tests repeatedly showed marked ST shifts with ischemic morphology. This finding persisted on retesting several weeks after discontinuance of all medications.

Figure 1
Cine frames of the right coronary artery of case 1. (A) and (B) show two views of the catheter-induced spasm and (C) shows the vessel after relief of the spasm.

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Coronary angiograms showed no evidence of narrowing except for proximal right coronary artery spasm, presumably catheter-induced, which responded readily to nitroglycerin administration (fig. 3).

Case 5

A 45-year-old Caucasian male with history of exertional angina of two to three years’ duration was admitted because of recent onset of resting and nocturnal angina. An exercise test was not performed because of the unstable nature of his disease.

At coronary angiography a 90% obstructive lesion was noted at the origin of the left anterior descending coronary artery. The rest of his coronary circulation appeared within normal limits except for multiple areas of spasm of the right coronary artery proximally near the origin of pulmonary conus branch and distally near the origin of a right ventricular branch. The vessel became fully patent following administration of nitroglycerin (fig. 4).

Case 6

A 53-year-old black male presented with a history of hypertension of more than 30 years and typical exertional angina pectoris of about three years’ duration. He denied past history of myocardial infarction. He was first referred to the Houston VA Hospital because of an episode of unstable angina which was treated conservatively with bed rest and isosorbide dinitrate. He improved slightly but kept complaining of angina during moderate activity for six weeks following his discharge. A treadmill test showed decreased exercise tolerance (4 minutes, 14 seconds). He stopped because of shortness of breath and mild chest pain and the electrocardiogram showed ST-segment elevation (injury pattern) followed by typical horizontal depression (ischemic morphology) (fig. 5). Serial electrocardiograms and enzymes failed to show evidence of necrosis following the exercise test.

Angiography revealed a hypertrophied and hyperdynamic left ventricle. The right coronary artery was preponderant and showed no evidence of atheromatous disease. Transient catheter-induced spasm at the ostium was noted during one injection (fig. 6). The left coronary angiogram showed patent left main and left anterior descending branches without significant disease. A noncritical (less than 50% narrowing) atheromatous lesion was noted in the proximal left circumflex branch before bifurcation into obtuse marginal and atrioventricular groove branches (fig. 6). During one injection of the left coronary artery, spasm occurred in the vicinity of the circumflex lesion and resulted in transient total occlusion of the vessel. ST-segment elevation was noted on the monitored electrocardiogram and nitroglycerin was administered promptly. Within two minutes repeat left coronary angiography showed a patent vessel including the distal branches of the circumflex and persistence of the noncritical atheromatous lesion (fig. 7). The patient tolerated the procedure without sequelae.

Case 7

A 41-year-old black male presented with a history of asymptomatic cardiomegaly since adolescence. Six
months before his admission to our hospital he developed symptoms and signs of left and right heart failure and was started on digitalis and diuretic therapy. He gave no history of angina.

Cardiac catheterization and coronary angiography were performed to document the diagnosis of congestive cardiomyopathy. The left ventricle was diffusely hypokinetic. The coronary arteries appeared within normal limits except for the occurrence of proximal spasm of the right coronary artery near the catheter tip. The spastic segment relaxed promptly following administration of nitroglycerin.

Case 8

A 62-year-old black male presented with the clinical picture of congestive cardiomyopathy presumably secondary to chronic alcohol ingestion. There was no history of chest pain.

Cardiac catheterization and angiography were performed to document the clinical diagnosis. The study revealed a dilated, diffusely hypokinetic left ventricle and angiographically normal coronary arteries except for transient spasm of the right coronary artery near the catheter tip which responded readily to nitroglycerin.

Summary

It is our opinion that in five of these cases (cases 1, 2, 4, 7 and 8), the spasm was catheter-induced. In case 3, spasm seemed to be unrelated to the catheter tip and cases 5 and 6 appeared to represent a combination of catheter-induced and spontaneous spasm of the right coronary artery (case 5) and catheter-induced spasm of the right and spontaneous spasm of the left circumflex artery (case 6). Only one case (case 6) was studied via the percutaneous femoral approach. The rest were studied using the Sones technique.

There were no typical cases of Prinzmetal's variant angina studied during this period of time. Two cases with some features suggestive of Prinzmetal's variant were catheterized. None had chest pain during the procedure and no spasm was visualized.

Discussion

The role of coronary arterial spasm in the production of angina pectoris has long been of interest. Sir William Osler believed it would constitute the best explanation for the mechanism of angina:

Let us now consider in what condition we actually see spasm of the arteries; and by spasm I mean a persistent contraction leading to ischemia, with disturbance of function of the parts supplied. The spasm is not always painful, but it may be associated with intense pain. Spasm or narrowing of a coronary artery, or even of one branch, may so modify the action of a section of the heart that it works with disturbed tension, and there are stretching and strain sufficient to arouse painful sensations. I do not know of any better explanation of anginal pain.

Yet in the last decade there has been less enthusiasm about the possible role of spasm in the production of myocardial ischemia for two important reasons: the overwhelming association of angina with atheromatous narrowing of coronary arteries and the failure to find coronary spasm with significant frequency in coronary angiograms. The reported incidence of coronary arterial spasm during coronary arteriography varies between 0.26% to 18%.

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**Figure 4**

Cine frames of the right coronary artery of case 5. (A) shows spasm near the origin of the right ventricular branch (arrow). (B) shows spasm near the origin of pulmonary conus branch (arrow), presumably catheter-induced. The spasm near the right ventricular branch is already relaxed. (C) After nitroglycerin, note relaxation of both spastic segments.

**Figure 5**

Electrocardiographic strips of the monitored lead (modified bipolar V5) of case 6. Note initial ST elevation (injury pattern) followed by ST depression (ischemic morphology).
and 0.93%9-11 and it is generally ascribed to mechanical irritation of the vessel by the catheter tip. Lavine and co-workers11 recognized the evidence implicating coronary artery spasm as one cause of Prinzmetal's variant angina, but questioned the clinical importance of spasm by stressing its rarity and the frequent absence of associated symptoms. They stressed the assumption that direct irritation of the catheter tip is the usual underlying mechanism and speculated that spontaneous coronary spasm may be rarer.

The incidence of coronary spasm in our one-year review is significantly higher than that reported by others.9-11 Such differences may be attributed to: 1) our systematic, prospective search for the phenomenon; 2) avoidance of vasodilators when feasible until one set of coronary angiograms were obtained; and 3) repeating several views after nitroglycerin was administered. The catheter techniques and contrast media were those generally employed and could not account for the higher incidence of spasm in our series. The catheterization was performed on all patients in fasting state. Very few patients received premedication, which usually consisted of Valium 10 mg orally. During the procedure, nitroglycerin was used routinely between two sets of coronary cineangiograms or when patients developed chest pain. Atropine (0.4-1.0 mg) was used in a few cases where severe bradycardia occurred during coronary angiography, and morphine sulfate (8-10 mg) was administered in rare cases where chest pain failed to respond readily to nitroglycerin.

Although catheter tip irritation may account for the majority of instances of spasm, it cannot be implicated in every case. It should be recognized that it is not possible to exclude a catheter factor in any case where the coronary artery is cannulated. In three of our cases, spasm occurred in locations remote from the catheter tip and hence it is unlikely that spasm resulted from catheter tip irritation. In addition, Oliva and co-workers9 demonstrated clearly that spasm in their patient correlated more with the presence of chest pain than with the presence of a catheter in the coronary ostium, thus supporting the contention that spasm does not always have to be catheter-induced during coronary angiography. MacAlpin et al.22 reported observing spasm of the right coronary artery on the operating table, further demonstrating that spasm can occur without intraluminal irritation by a catheter. Three of our patients (cases 3, 5, 6) exhibited spasm that could not be ascribed to catheter irritation.

Standard coronary angiography techniques probably reduce the likelihood of observing coronary arterial spasm. Angiographic contrast media produce coronary vasodilatation which minimizes the opportunity for spasm. In many laboratories, nitroglycerin...
or other vasodilator drugs are given routinely at the beginning of the procedure. Most angiographers employing the Judkins technique are reluctant to change from right to left coronary artery catheters solely to avoid giving nitroglycerin before both coronary arteries are initially opacified. Also, most angiographers are understandably reluctant to inject into the coronary arteries during chest pain, when spontaneous spasm may be most likely present. It is possible to confuse spasm with structural obstruction, particularly in diseased vessels, unless the phenomenon is carefully looked for and cineangiograms are obtained in the same projection before and after vasodilator drug administration. It is important to stress that our data may underestimate the actual incidence of spasm because of our rigid criteria and the factors minimizing the likelihood of detecting spasm.

In two of the cases where spontaneous spasm occurred (3 and 6), it is reasonable to implicate it in the production of the patients' symptoms, particularly in case 6 where critical atheromatous obstruction could not be demonstrated anywhere in the coronary tree. Critical obstruction usually implies a decrease in lumen cross sectional area of 75% or more. Clearly, spontaneous spasm has been recognized as a cause of anginal pains in some cases of Prinzmetal's variant angina. Coronary spasm has been implicated also in the pathophysiology of angina, myocardial infarction and sudden death in cases of withdrawal from industrial exposure to nitroglycerin. More recently a case was described where spontaneous spasm was invoked as a possible cause of cardiac arrest. Patients with classical Heberden angina may also manifest spontaneous spasm, as our case 3 demonstrates. One may speculate that spasm in such patients plays a role in phasic worsening of their disease, e.g., unstable angina, myocardial infarction, or sudden death. In addition, cases 3 and 6 demonstrate that spasm can occur in the vicinity of atheromatous lesions and may be more serious than when it occurs in normal coronaries, since it results in total occlusion of the vessel.

Whereas spontaneous coronary artery spasm appears to be a documentable phenomenon with probable clinical importance, the clinical significance of catheter-induced spasm is not generally accepted. This is understandable since such spasm is iatrogenic. Nevertheless, it is of interest that in some of the earlier reports of patients with Prinzmetal's variant angina where coronary spasm was documented, it occurred in locations where it could be attributed to mechanical catheter irritation. In this regard, two of our three patients with spontaneous spasm also demonstrated catheter-induced spasm; and the possibility that there is a predisposition to coronary spasm in certain individuals cannot be excluded. Review of the reported cases of catheter-induced spasm shows that it is most commonly observed in patients with angina or chest pain syndromes and normal coronary arteriograms. Cases 1 and 2 in our series also belong in this category. One wonders if predisposition to spontaneous coronary spasm is not the basic pathophysiology in such cases. Variable predisposition to spasm may exist in different parts of the coronary tree. Of 45 instances of coronary spasm (spontaneous and catheter-induced) described in the literature (including our cases), 35 (78%) occurred in the right coronary artery. The left circumflex artery is least often involved (4%). Left anterior descending branch involvement occurred in 7% and main left coronary artery in 11%. It may be tempting to ascribe this distribution to the possibility that the right coronary artery is more vulnerable to catheter tip irritation. Yet in nine of the 12 instances where coronary spasm was presumed to be spontaneous it occurred also in the right coronary at various other points of its course. Possibly a difference in innervation may make one coronary artery more prone to spasm than the other. Further studies, using larger series of patients with critical attention paid to the phenomena of catheter-induced and spontaneous spasm, are necessary to further elucidate these speculations.

It is concluded that coronary artery spasm during coronary angiography may be more common than generally recognized. In the majority of instances, it may be attributed to catheter tip irritation; yet spontaneous coronary spasm occurs and its true incidence may be higher than is angiographically demonstrable. Catheter-induced spasm may occur only in patients with predisposition to spasm. Further studies on these patients and long-term follow-up are warranted to determine the significance of the spasm. Since elucidation of the possible role of spasm may help in the understanding of unstable angina, myocardial infarction, sudden death, and angina with normal coronary angiograms, more attention should be directed toward this phenomenon.

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References


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