Dynamic Coronary Thrombosis: A Possible Cause of Prinzmetal's Variant Angina

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Two patients presented with features typical of Prinzmetal's variant angina: recurrent episodes of chest discomfort at rest associated with transient ST segment elevation. Episodes of recurrent ischemia persisted despite treatment with intravenous nitroglycerin. Coronary arteriography disclosed a high grade stenotic lesion and intracoronary thrombus in both patients. Coronary spasm was not demonstrated. These observations suggest that "dynamic thrombosis" may have a more important role than heretofore recognized in some patients with Prinzmetal's variant angina. (J Interven Cardiol 1990:3:1)

Introduction

Since the description by Prinzmetal in 1959 of chest pain associated with transient ST segment elevation, the syndrome of variant angina has stood as a distinct, clinically recognizable entity.[1] Coronary arteriograms performed during episodes of ST segment elevation have demonstrated spasm of the coronary artery.[2–6] As such, the pathogenesis of this clinical entity is assumed to be coronary artery spasm, with or without underlying critical coronary atherosclerotic disease.[7–9] Yet, since ST segment elevation is an indicator not of spasm, per se, but of transmural myocardial ischemia,[10] it is reasonable to consider that other pathogenetic mechanisms may be responsible for some instances of variant angina. Herein, we report two patients presenting with a typical picture of Prinzmetal's variant angina in whom coronary arteriograms disclosed intracoronary thrombus causing subtotal occlusion. These observations suggest that the pathophysiological mechanism of variant angina may not always be coronary spasm and may open up the potential for other therapeutic interventions, in addition to spasmolytic agents, in the treatment of some patients with this disorder.

Case 1. A 69-year-old male had a 10-year history of exertional chest pain considered to represent stable effort angina. He required hospitalization for a spontaneous pneumothorax that was treated with chest tube insertion. This resolved, and plans were made to discharge the patient when he developed severe chest pain associated with ST segment elevation in leads II, III, and aV_F (Fig. 1 left). He was given sublingual nitroglycerin with resolution of the pain and return of the ST segments to normal (Fig. 1 right). This episode lasted 15 minutes. Cardiac enzymes were equivocally elevated; MB-CK on one determination was 16 (normal up to 14) IU/L, but total CPK remained within normal levels. The diagnosis of variant angina was entertained and he was transferred for further management. He was placed on an intravenous infusion of nitroglycerin, but on the following day had two more episodes of chest pain. Each episode was associated with ST segment elevation in the same ECG leads, which returned to baseline in 15 minutes. Additional cardiac enzyme determinations remained within normal levels. He appeared to sta-

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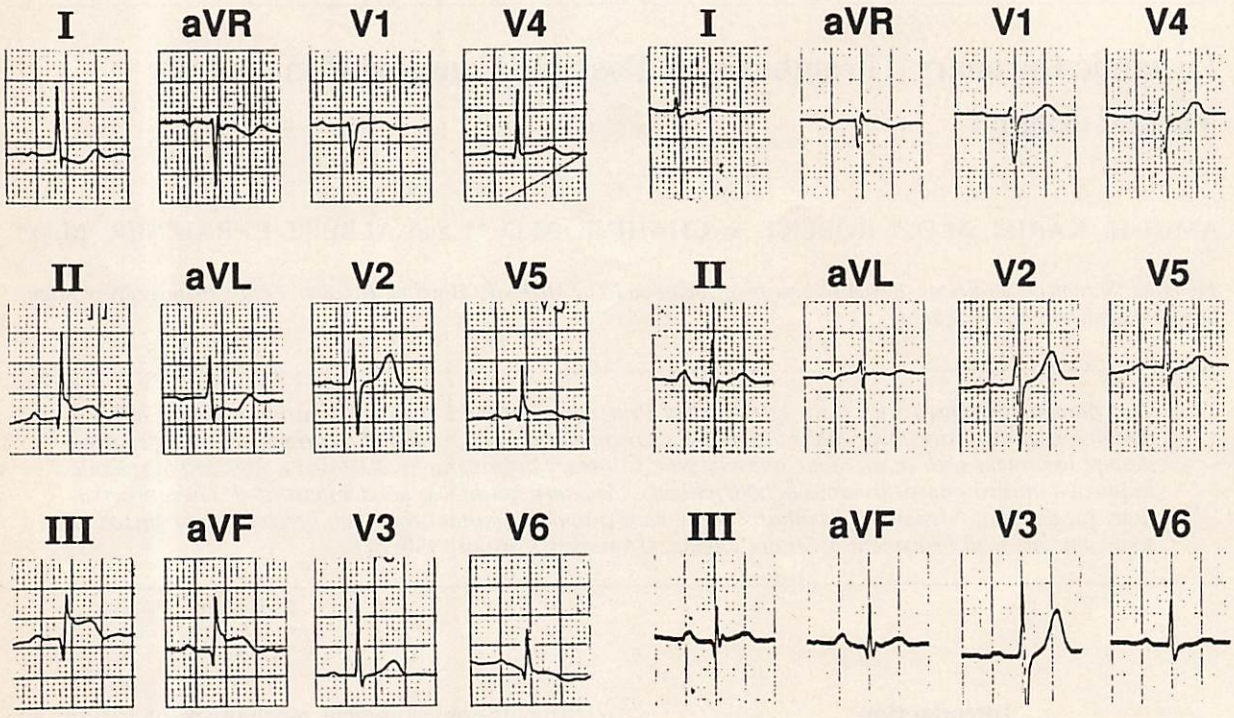

Figure 1. The electrocardiogram of patient 1 is shown during a chest pain episode (left) and after the pain resolved (right). The transient ST segment elevation in leads II, III and aV_F is typical of Prinzmetal's variant angina.

bilize on a higher dose of intravenous nitroglycerin. Diltiazem was added to the medical regimen.

On the following day, he underwent cardiac catheterization. Left ventriculography showed normal left ventricular contraction. Coronary arteriography disclosed noncritical plaques in the circumflex and left anterior descending coronary arteries, but with a 70% stenosis of the first diagonal branch. The right coronary artery contained a 90% stenosis in the middle segment. A distinct intraluminal filling defect was apparent at the site of the critical stenosis, indicative of an intracoronary thrombus (Fig. 2). In view of this, ergonovine was not administered. Percutaneous transluminal coronary angioplasty of the right coronary artery lesion was successfully performed. The thrombus was not seen after dilatation. The patient had an uneventful hospital course thereafter, without further chest pain or ST segment alterations, and was discharged on diltiazem and aspirin.

Case 2. A 59-year-old male without prior cardiac history presented to a hospital having had several episodes of transient chest pain at rest. An ECG showed ST segment elevation in leads II, III, and aV_F (Fig. 3 left). The chest pain subsided within 10 minutes after the administration of sublingual nitroglycerin and a follow-up ECG showed normal ST segments (Fig. 3 right). He was transferred to our institution where cardiac enzymes were normal and he was considered to have variant angina. He was started on an intravenous nitroglycerin infusion, but had further chest pain episodes. A continuous intravenous heparin infusion was begun. Cardiac catheterization was performed. Left ventriculography was normal. The right coronary artery had a 70% narrowing in the middle segment. At the site of stenosis a filling defect was apparent, compatible with thrombus, causing subtotal occlusion of the artery (Fig. 4). In addition, there was a 90% stenosis of the middle segment of the left anterior descending coronary artery. Percutaneous transluminal coronary angioplasty was successfully carried out, with resolution of the stenosis. No thrombus was angiographically detected after this

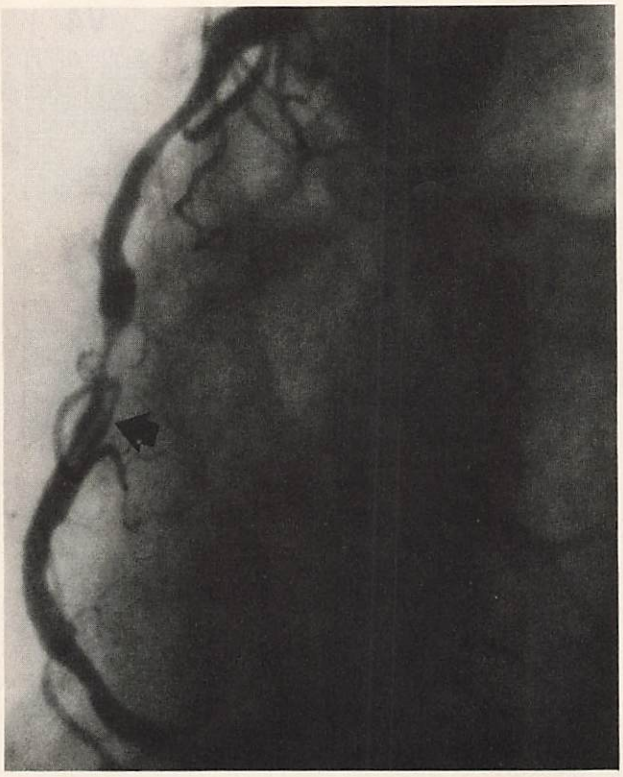

Figure 2. Arteriogram of the right coronary artery of patient 1 shows a high grade stenosis and an intracoronary thrombus (arrow).

procedure. He was placed on a continuous intravenous heparin infusion for 48 hours after angioplasty and subsequently discharged on diltiazem, aspirin, and dipyridamole.

Discussion

In 1959, Prinzmetal and co-workers described a syndrome that differed from classic effort angina and termed this entity "a form of variant angina."[1] It is clinically characterized by chest pain occurring at rest and associated with ST segment elevation. The underlying coronary anatomy in Prinzmetal's variant angina is quite variable and ranges from angiographically normal coronary arteries to severely stenotic atherosclerotic disease of one or more arteries.[11]

The pathophysiological mechanism responsible for the attacks of resting ischemia in variant angina patients was first decisively documented by Oliva et al.[2] These investigators demonstrated spasm of the coronary artery during the ischemic phases. The causal relationship of coronary artery spasm to variant angina was subsequently confirmed by others.[3–6] As a result, the finding of transient ST segment elevation associated with resting chest pain has become accepted as prima facie evidence that coronary artery spasm is present.[7–9] Since patients with variant angina are assumed to have coronary spasm and are uniformly treated with vasodilators, the role of coronary arteriography in current clinical practice is primarily to assess the presence and severity of underlying atherosclerotic occlusive disease and, hence, the need for more aggressive intervention such as angioplasty or bypass surgery.

Our patients presented with the classic features of variant angina and in both the diagnosis was made prior to cardiac catheterization. Coronary arteriography in these patients disclosed intracoronary thrombus adherent to a severely stenotic atherosclerotic plaque and causing subtotal obstruction of the artery. Since no attempt was made to induce coronary artery spasm in these patients because of the high grade stenosis and the presence of clot, we cannot rule out the possibility that spasm, superimposed on thrombus, contributed to the episodic ischemia. However, the persistence of chest pain episodes despite intravenous nitroglycerin would mediate against spasm playing the sole or predominant role in the production of the recurrent ischemia.

In the absence of angiographic evidence of coronary artery spasm, the possibility that the thrombus provoked the patients' clinical manifestations must be considered. It is widely accepted that a clot within an artery can serve as a nidus for additional clots that might result in complete obstruction of the artery and severe ischemia.[12,13] Conversely, partial lysis of the thrombus can lessen the degree of obstruction imposed by the clot and hence the degree of ischemia.[14–16] Thus, thrombus, like vasospasm, can be dynamic in nature[13,14] and may be the cause of transient severe ischemia in some patients with typical Prinzmetal's variant angina.

It is not surprising that the clinical presentation of variant angina may be attributed to incomplete thrombosis in some patients. It is recognized that

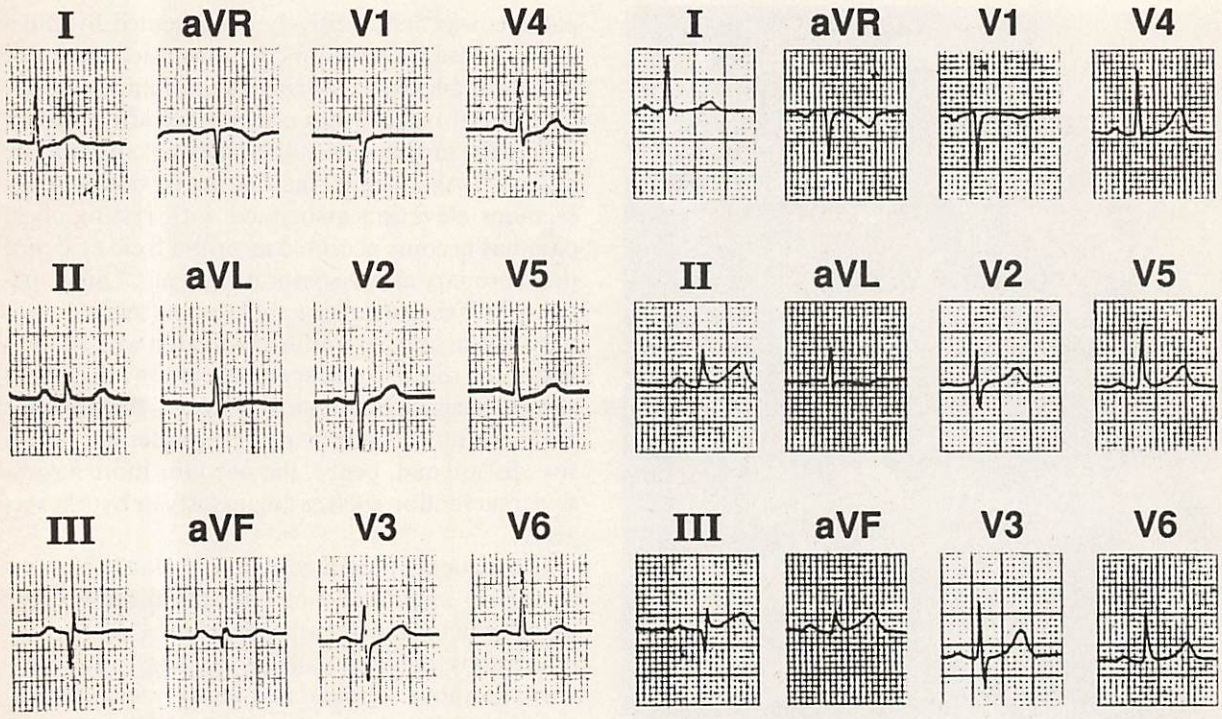

Figure 3. The electrocardiogram of patient 2 during (left) and after (right) chest pain.

thrombosis with complete coronary artery occlusion is the critical event initiating acute myocardial infarction,[17] a syndrome characterized by persistent resting chest pain and ST segment elevation. It is certainly reasonable to consider that some, perhaps even many such patients, may undergo spontaneous partial lysis of the thrombus and thereby abort the myocardial infarction. Such a situation would be clinically indistinguishable from Prinzmetal's variant angina, with the exception that coronary arteriography performed soon after the episode might reveal residual thrombus at the site of what moments before may have been complete or nearly complete thrombotic occlusion.

In this regard, previous reports have linked variant angina to coronary thrombosis and acute myocardial infarction. Myocardial cell damage, as reflected by the release of small amounts of MB-CK, may occur in variant angina patients who have prolonged attacks.[18] Zelinger et al. described a patient who presented with variant angina but then developed acute myocardial infarction.[19] Coronary arteriography performed shortly after the onset of infarction disclosed thrombus. Although the authors presumed that the episodes of variant angina were due to coronary vasospasm, spasm could not be demonstrated during arteriography. It is possible that "dynamic thrombosis" produced the variant angina and subsequent myocardial infarction in their patient. Intracoronary thrombus and coronary spasm were observed in a patient with variant angina without underlying atherosclerotic obstructive disease reported by Chahine and Mallon.[20] While it was speculated that spasm induced the thrombosis, the reverse sequence is also plausible.

The demonstration of Prinzmetal's variant angina associated with intracoronary thrombus has an important clinical implication. A patient with such a clinical presentation should probably not be presumed to have coronary spasm alone, particularly if ischemic episodes persist despite aggressive treatment with coronary vasodilators. Such a patient may in fact have thrombus, with or without spasm, and therefore may be at greater risk for the subsequent development of complete thrombosis and acute myocardial infarction. Coronary arteri-

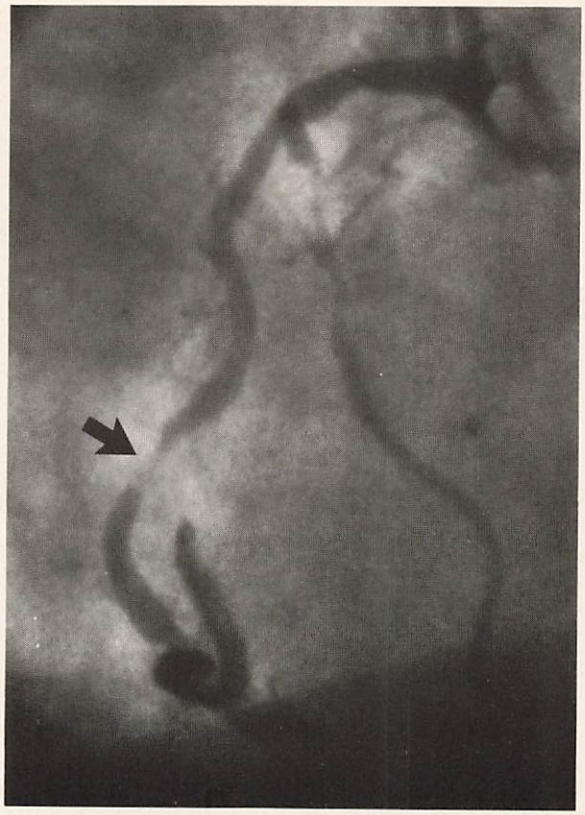

Figure 4. Coronary arteriogram of patient 2 showing a discrete cutoff and filling defect (arrow) indicative of intracoronary thrombus.

ography is still important to clarify the pathophysiology of transient ischemia, in addition to assessing the severity of underlying atherosclerotic disease. Although our patients were treated with balloon angioplasty with good results, the use of heparin, aspirin, and a thrombolytic agent may be useful in some patients in whom dynamic thrombosis may be operative.

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