

The importance of excluding coronary artery vasospasm before percutaneous transluminal coronary angioplasty

A case report

J. Z. PRZYBOJEWSKI

Summary

It is important to exclude coronary vasospasm, the mechanism responsible for so-called 'dynamic' coronary stenosis, when selecting of patients for percutaneous transluminal coronary angioplasty (PTCA). Although cine angiographic demonstration of this frequently fleeting entity can sometimes be difficult, a strong suspicion should be aroused by a carefully taken history. The danger of PTCA in these cases of Prinzmetal's variant angina, as well as the frustration often encountered in drug management, is highlighted.

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Case report

A 39-year-old white woman was admitted to the Intensive Coronary Care Unit (ICCU) at Tygerberg Hospital on 24 August 1983. She had been asymptomatic until 1 week before admission, when she noted the onset of dull pain in the left arm, which radiated to the chest and was precipitated by effort. On the day of admission this pain had persisted for several hours and was associated with palpitations. She was otherwise well.

She was a heavy smoker (30 cigarettes a day for the past 22 years) and had a strong family history of ischaemic heart disease (IHD). Physical examination revealed nothing abnormal apart from elevated blood pressure (160/110 mmHg) and a fourth heart sound. A resting ECG, taken when the chest pain had subsided, was normal, as were a chest radiograph and results of sideroom investigations. Serial serum enzyme levels were normal and the patient had no further episodes of pain.

A diagnosis of type I unstable angina pectoris (normal resting ECG) and essential hypertension was made. The patient was discharged on 27 August on nifedipine 10 mg 3 times a day, transdermal nitroglycerin 5 mg/d and sotalolol 80 mg twice a day.

Approximately 1 month after discharge a maximal treadmill exercise test (Bruce protocol) was negative, and she claimed to be asymptomatic. However, her blood pressure was still raised (170/110 mmHg), so a diuretic was added to the therapeutic regimen. She was then discharged, to be followed up by the Day Hospital Organization.

The patient was admitted to the ICCU for the 2nd time on 13 August 1984, some 10 months later, with chest pain at rest radiating down the left forearm and not relieved by sublingual

nitrate. Blood pressure was normal at 130/80 mmHg, and physical examination was unremarkable. A resting ECG, taken during chest pain, revealed asymmetrical T-wave inversion in leads V1 - V6 (the anteroseptal and lateral leads). The chest pain was readily relieved by sublingual nifedipine 10 mg, and a repeat resting ECG after pain relief was normal. The patient remained asymptomatic on oral therapy. A diagnosis of type II unstable angina pectoris (abnormal resting ECG) was then made, and she was discharged on 15 August on nifedipine 10 mg 3 times a day, transdermal nitroglycerin 10 mg/d, and sublingual isosorbide dinitrate when required.

Two days later, on 17 August, the patient was admitted to the ICCU for the 3rd time. Since her previous discharge she had been experiencing nocturnal chest pain at rest not entirely relieved by sublingual isosorbide dinitrate or sublingual nifedipine. The blood pressure was 110/70 mmHg with no abnormal physical signs. She was maintained on the previous drug therapy. A resting ECG recorded while she was free of chest pain was normal, as were serial serum enzyme levels, and the patient had no further episodes of chest pain. A diagnosis of type I unstable angina pectoris was made. Because of these three admissions, a colleague performed cardiac catheterization and coronary angiography on 21 August. The patient was still taking all her medication.

First cardiac catheterization

The aortic and left ventricular (LV) pressures were within normal limits. LV cine angiography in the right anterior oblique (RAO) projection demonstrated normal contractility with no mitral valve prolapse or insufficiency. Injection of contrast material into the right coronary artery (RCA) in the left anterior oblique (LAO) and RAO views delineated an angiographically normal and dominant RCA. No retrograde filling of the left coronary artery (LCA) could be visualized. Selective angiography of the LCA demonstrated an isolated 50% smooth-walled luminal stenosis of the left anterior descending (LAD) coronary artery, and a very insignificant internal luminal narrowing of the left circumflex (LCx) coronary artery (Figs 1 and 2). The patient had no chest pain during this procedure.

A diagnosis of insignificant atherosclerotic coronary artery disease was then made. The possibility of a percutaneous transluminal coronary angioplasty (PTCA) on the LAD artery lesion was discussed, but it was felt that this lesion was not severe enough to warrant this procedure. The patient was reassured, strongly advised to stop smoking, and discharged on 22 August on nifedipine 20 mg 3 times a day, transdermal nitroglycerin 10 mg/d, atenolol 50 mg/d, a diuretic and a sedative, and sublingual isosorbide dinitrate when necessary.

Subsequent course

The patient was asymptomatic for approximately 2½ months, but on 28 October she was admitted for the 4th time, with a 1-week history of chest pain at rest. During this period she had run out of the transdermal nitroglycerin preparation and substituted oral isosorbide dinitrate. On the day of admission the chest pain had lasted several hours. She was extremely anxious but had a normal blood pressure of 110/80 mmHg and a fourth heart sound but no other signs. A resting ECG recorded during chest pain

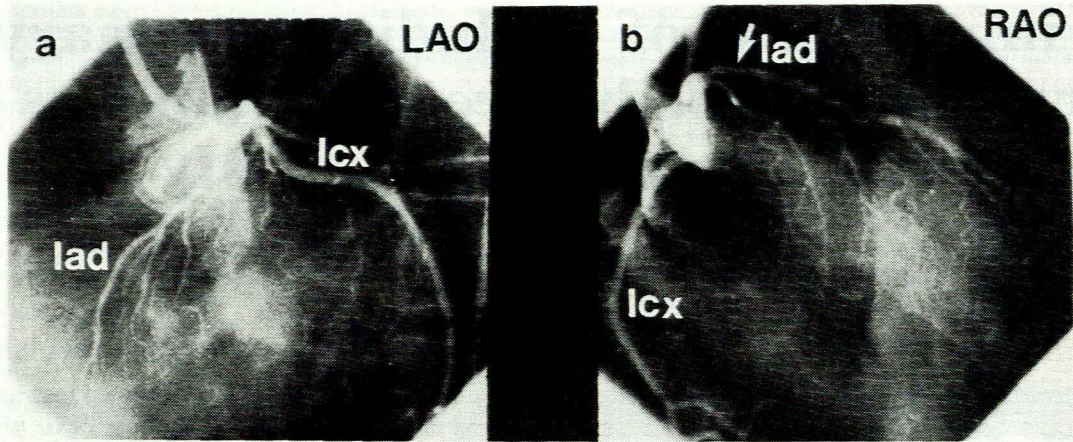


Fig. 1. Left coronary cine angiograms in (a) LAO and (b) RAO projections. A 50% smooth-walled stenosis (arrowed) can be seen in the proximal portion of the LAD coronary artery. Insignificant internal luminal irregularities are present in the LCx coronary artery.

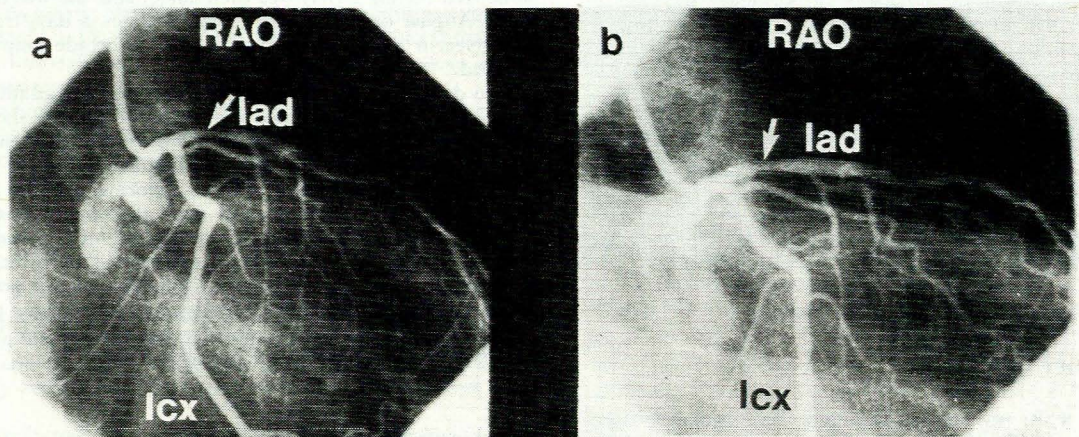


Fig. 2. Left coronary cine angiograms in (a) shallow RAO view with cranial angulation and (b) shallow RAO view with caudal angulation. The 50% LAD coronary artery stenosis (arrowed) and insignificant LCx coronary artery luminal irregularities are better seen in these views.

revealed asymmetrical T-wave inversion in leads V1 - V6; after relief of pain by sublingual nifedipine the ECG was normal. Apart from increasing the nifedipine to 30 mg 3 times a day therapy was left unaltered, and the patient had no further episodes of chest pain. Serial resting ECGs, serum enzyme levels and a fasting lipogram were normal. A diagnosis of type II unstable angina pectoris was again made. An exercise thallium-201 scintiscan failed to show any myocardial ischaemia. The patient was discharged on 31 October.

For the next 6 months the patient remained entirely free of chest pain, but on 5 May 1985 she was admitted for the 5th time with a 3-day history of chest pain at rest, of increasing severity and frequency and unresponsive to drug therapy. She had a loud fourth heart sound and a normal blood pressure of 120/80 mmHg. A well-localized and firm nodule was palpated in the left lobe of the thyroid gland, but she was clinically euthyroid. A resting ECG recorded during chest pain highlighted asymmetrical T-wave inversion in leads V1 - V6 (Fig. 3a). Nitroglycerin was administered by intravenous infusion and the patient was also given sublingual nifedipine. The chest pain subsided after approximately 10 minutes, at which time a resting ECG was normal (Fig. 3b). A diagnosis of type II unstable angina pectoris was again made. Serial serum enzyme levels were normal, the patient had no more chest pain, and the results of thyroid function tests were all within normal limits.

Management was thus proving extremely difficult, and recurrent myocardial ischaemia, as demonstrated by ECGs during episodes of chest pain, seemed a real possibility. The initial coronary angiography 9 months previously had clearly demonstrated a

lesion in the proximal part of the LAD coronary artery. This did not appear haemodynamically significant, but its location corresponded to the region of intermittent myocardial ischaemia documented electrocardiographically. In view of this diagnostic dilemma, the author decided to undertake cardiac catheterization on 9 May while the patient was being maintained on all her drug therapy.

Second cardiac catheterization

Left-sided intracardiac pressures were all normal. The RCA was still angiographically free of disease. Injection of contrast medium into the LCA immediately demonstrated that the previous 50% proximal LAD coronary artery lesion was no longer present (Fig. 4), although two insignificant lesions were now observed in the LCx coronary artery (Fig. 5). It now seemed extremely likely that coronary vasospasm was the major cause of the patient's clinical features. In order to exclude the possibility of coronary vasospasm of the LCx coronary artery, isosorbide dinitrate 10 mg was administered sublingually and LCA angiography was repeated 10 minutes later. This now showed some general vasodilatation of the coronary vasculature without any real change in the two luminal narrowings of the LCx coronary artery (Fig. 6, a). The patient was therefore given nifedipine 10 mg sublingually and LCA angiography was repeated 15 minutes later. This demonstrated a greater degree of generalized coronary vasodilatation without any significant alteration in the two LCx coronary artery lesions (Fig. 6, b). Throughout catheterization there was no evidence of myocardial ischaemia on the ECG or any chest pain.

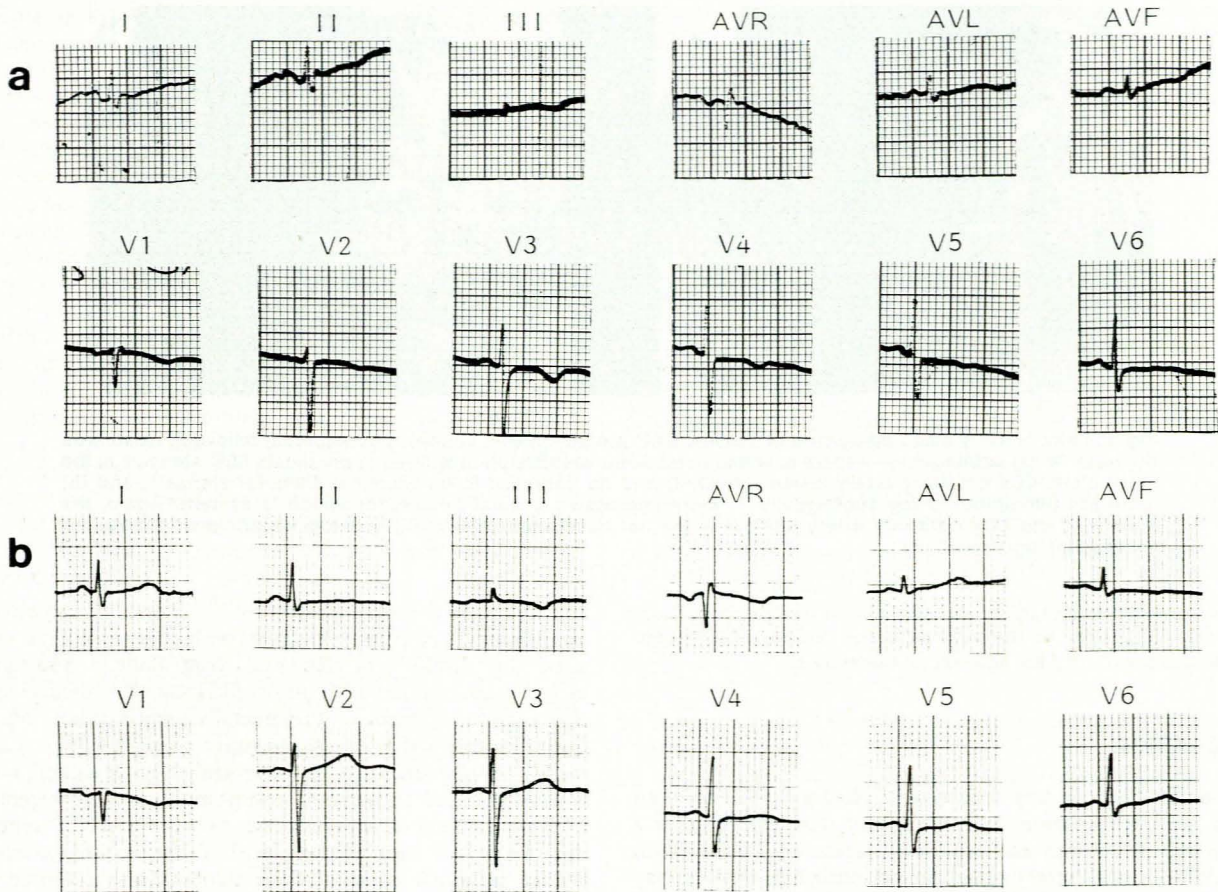


Fig. 3. Resting 12-lead ECGs recorded on full standardization: (a) during chest pain — asymmetrical T-wave inversion is evident in the anteroseptal (V1 - V3) and lateral (V4 - V6) leads; and (b) following relief of chest pain by nitroglycerin and nifedipine — the ECG is now normal.

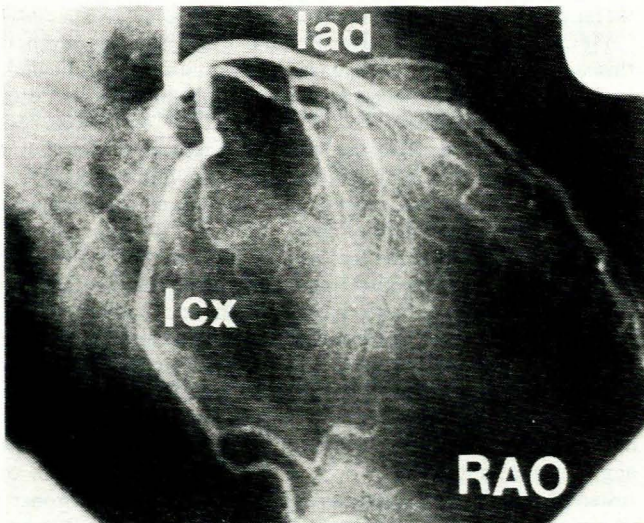


Fig. 4. Left coronary cine angiogram in RAO projection. The proximal 50% LAD coronary artery stenosis is no longer evident. However, there are internal luminal irregularities in the LCx coronary artery.

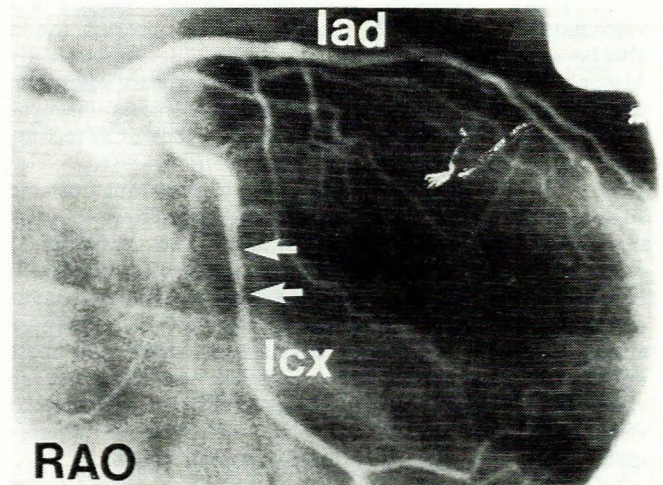


Fig. 5. Left coronary cine angiograms in shallow RAO view with caudal angulation. The LAD coronary artery appears normal. There are two insignificant lesions (arrowed) in the LCx coronary artery.

Follow-up

The author was convinced that the lesion of the LAD coronary artery seen on the first cardiac catheterization was due to coronary vasospasm and that there were fixed but haemodynamically insignificant atherosclerotic lesions in the LCx coronary artery. How-

ever, the 'fixed' stenoses in the LCx coronary artery could have been aggravated by a 'dynamic' or 'functional' component caused by coronary vasospasm, since this could be partially explained by the ECG changes in the lateral leads V5 and V6. Since the patient still had symptoms and signs of intermittent myocardial ischaemia on medication, almost certainly due to coronary vasospasm, the

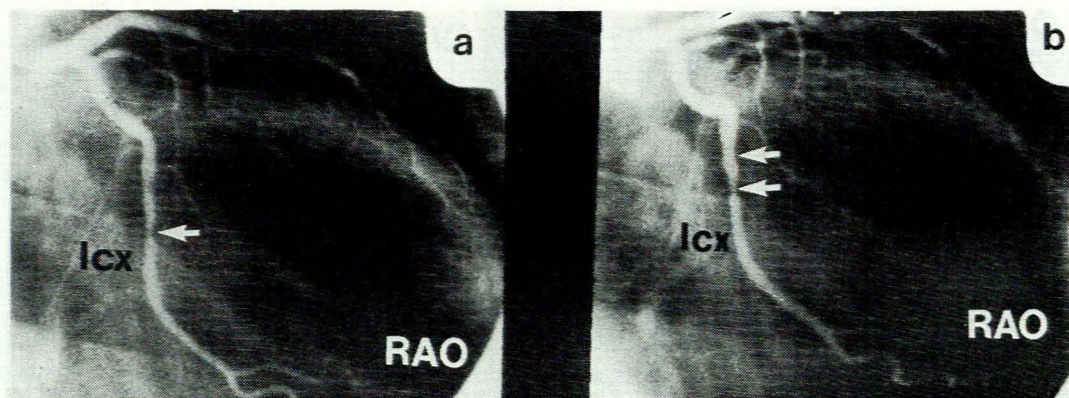


Fig. 6. Left coronary cine angiograms in shallow RAO projection with caudal angulation: (a) following isosorbide dinitrate 10 mg sublingually — there is some generalized vasodilatation with an approximate 50% stenosis of the more distal LCx coronary artery lesion (arrowed) and no decrease in transluminal diameter stenosis; and (b) following nifedipine 10 mg sublingually — more impressive generalized vasodilatation is evident. Again, the lesions in the LCx coronary artery (arrowed) are not decreased in severity, making superimposed coronary vasospasm highly unlikely.

calcium antagonist nifedipine was replaced with another calcium antagonist diltiazem, in the hope of better control. The patient was discharged on 10 May and will be followed up.

Discussion

The main object of this report is to illustrate the ease with which misinterpretation of investigative data can lead to a potentially deleterious decision on management. The lesion in the LAD coronary artery visualized on initial cine angiography was interpreted as a 'fixed' stenosis, a clearly erroneous deduction, since the second examination demonstrated a normal LAD coronary artery, despite the complaint of chest pain. The lesion therefore had to be a 'dynamic' stenosis caused by intermittent coronary vasospasm. PTCA on the LAD lesion could not have been in the patient's best interests.

The patient's symptoms indicated a strong likelihood of a vasospastic component.¹ Her heavy cigarette smoking would also be a risk factor for spasm, as elegantly demonstrated by Maouad *et al.*² Further clinical evidence for coronary vasospasm in this young woman was the transient non-transmural myocardial ischaemia at rest visualized on numerous ECG recordings,³ although these changes are sometimes absent.⁴ Her clinical features were essentially those of recurrent unstable angina pectoris, a syndrome in which coronary artery spasm is thought to play a most important role.⁵ The possibility of catheter-induced coronary vasospasm⁶ must also be considered. However, the fact that she suffered recurrent transient myocardial ischaemia in the ECG distribution of the LAD coronary artery, unrelated to coronary angiography, makes this most improbable. Recurrent episodes of catheter-induced coronary vasospasm would not negate the possibility of spontaneous vasospasm, since there appears to be a link between catheter-induced coronary artery spasm and vasospastic angina.⁷

Of considerable interest is the lack of response to relatively high doses of nifedipine and a moderate dose of transdermal nitroglycerin; this is particularly surprising since nifedipine has been shown to be most efficacious in vasospastic or Prinzmetal's angina^{8,9} and the combination of nifedipine and nitrates has been particularly beneficial in this type of angina.¹⁰ The patient was also given a β -blocker, atenolol, since there were episodes of exercise-induced chest pain. Effort-related coronary vasospasm is known to occur,¹¹ but is far less frequent than spasm at rest. The administration of β -blockers to patients with vasotonic or Prinzmetal's variant angina has been reported to exacerbate their symptoms through unopposed α -adrenergic

activity on the coronary vasculature.^{12,13} However, combination of diltiazem (a calcium antagonist) with propranolol has countered this ill-effect of the latter drug alone.¹³ Addition of propranolol to a combination of diltiazem and nifedipine has also achieved control of Prinzmetal's angina when this was unsatisfactory with calcium antagonist therapy alone.¹⁴ Carver *et al.*¹⁵ have documented the beneficial effect of a combination of nifedipine and diltiazem in vasospastic angina not responding to either calcium antagonist alone. Schroeder *et al.*¹⁶ reported the efficacy of monotherapy with diltiazem in vasospastic angina, although some of their patients also required oral nitrates. Verapamil too has been shown to be beneficial in Prinzmetal's angina.¹⁷ It was therefore decided to discontinue the β -blocker and attempt substitution of nifedipine with diltiazem, and to continue maintenance nitrate therapy. Follow-up will determine whether more extensive combination therapy will be needed for control.

PTCA on the 50% LAD coronary artery stenosis, even if this were a fixed atheromatous lesion, would not be indicated; Ischinger *et al.*¹⁸ demonstrated a markedly increased rate of restenosis after primary success with PTCA on lesions less than 60% stenosed. The angiographic features of the LAD coronary artery stenosis in this patient were highly suggestive of coronary vasospasm despite the absence of chest pain, a situation very rare in cardiological practice.¹⁹ Attempts should therefore have been made to exclude spasm at the first cardiac catheterization by administering drugs (including directly into the affected coronary artery) known to relieve dynamic stenosis. Nowadays there is an increasing tendency to carry out PTCA during the first cardiac catheterization rather than follow it with a second catheterization combined with PTCA.

Several workers have reported on the unsatisfactory results obtained with PTCA in patients with Prinzmetal's variant angina, especially with respect to the increased incidence of restenosis.²⁰⁻²² The pathophysiology and association of coronary vasospasm with PTCA has been described in detail by Przybojewski and Weich.²³⁻²⁵

Comparison of the coronary cine angiograms taken 9 months apart revealed an extremely rapid progression of the two lesions in the LCx coronary artery. Their angiographic appearance was very different from that of the LAD coronary artery lesion, in that they appeared irregular and resembled a fixed atherosclerotic stenosis. Administration of both nitrate and nifedipine during coronary angiography did not change the degree of stenosis of these lesions, a feature opposing coronary vasospasm (either in a normal or a diseased vessel). It is true that LCx coronary artery ischaemia could give rise to lateral

ischaemia on the ECG, but this does not explain the antero-septal and apical myocardial ischaemia documented on repeated resting ECGs. The likelihood of LCx coronary artery vasospasm therefore appears remote. As with the LAD coronary artery 'stenosis', it was felt that PTCA was not indicated for the LCx coronary artery lesions. Ergometrine maleate provocation²⁶ was not undertaken during repeat coronary cine angiography since the patient was on large doses of nifedipine, nitrates and β -blockers, medication that would interfere with the performance and interpretation of this test. However, Waters *et al.*²⁷ utilized ergometrine maleate provocation in order to determine any spontaneous remissions in patients with Prinzmetal's angina on long-term therapy with calcium antagonists. Winniford *et al.*²⁸ also employed provocation to analyse the effect of calcium antagonists in these patients.

In conclusion, we recommend that when PTCA is contemplated great care be taken to exclude coronary vasospasm, particularly in view of the recent trend of performing PTCA at the same session as diagnostic coronary cine angiography. The successful outcome of such a procedure will depend directly upon the presence or absence of this important pathogenetic mechanism in IHD.

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