Ergometrine-provoked coronary vasospasm on angiography without angina or ischaemia on ECG

A case report

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Summary

A 32-year-old White man suffered a large transmural inferoposterior myocardial infarction (MI). Coronary vasospasm is strongly suspected of having caused this MI since the ergometrine maleate provocation test gave rise to severe coronary vasospasm resulting in total occlusion of the dominant right coronary artery, without angina or ECG or haemodynamic features of myocardial ischaemia. This is a most unusual response to ergometrine maleate. Possible explanations are suggested and the implications are briefly discussed.

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Case report

A 32-year-old White man was completely asymptomatic until the night of 11 June 1983 when he experienced a sudden severe crushing precordial pain which radiated down his left arm. This episode occurred while he was sitting on the toilet smoking a cigarette. He noticed marked associated nausea and sweating and soon collapsed. Luckily he had not locked the toilet door and his wife soon came to his assistance. He was helped to his bed and soon regained consciousness. Nevertheless, the chest pain did not lessen over a period of a few hours and the patient's wife decided to call in their general practitioner, who found the patient in distress and immediately arranged for his transfer to the Intensive Coronary Care Unit (ICCU) at Tygerberg Hospital. On admission to the ICCU in the early hours of the morning of 12 June 1983 the patient was not shocked and there were no signs of cardiac failure. The radial pulse was regular and the blood pressure 100/70 mmHg. There were no features of hyperlipo-proteinaemia or of any other general disease. Results of clinical examination were normal. The patient claimed to be a very fit sportsman who was not aware of any history of ischaemic heart disease, hypertension or diabetes in his family. His only risk factor was that he had smoked some 15 cigarettes daily for several years.

On admission a 12-lead resting ECG demonstrated a sinus rhythm of 65 beats/min, a P-R interval of 0,15 second and a mean QRS axis of +35°. There were pathological Q waves in leads II, III and aVF with hyperacute ST-segment changes in

these leads. Slight upward-sloping ST-segment depression was visualized in the anterolateral leads. A striking feature was the presence of dominant R waves over the right precordial leads. This ECG was interpreted as showing features of a hyperacute transmural inferior myocardial infarction (MI) with true posterior extension. A chest radiograph delineated a normal cardiac silhouette. Results of side-room investigations and haematological screening tests and serum electrolyte values were within normal limits.

The patient was given routine anticoagulation therapy and oral nifedipine 10 mg 3 times daily as well as nitroglycerin 16 mg transdermally. Daily resting 12-lead ECG tracings and serial enzyme estimations (Table I) confirmed the presence of a transmural inferoposterior MI. A technetium-99m pyro-phosphate scintiscan (hot-spot scan) carried out on 14 June (3 days after admission) demonstrated a clear area of increased isotope uptake in the inferior area in keeping with an acute transmural inferior MI. The patient's clinical course was uncomplicated and he was discharged on 21 June; he was given maintenance doses of nifedipine and nitroglycerin 16 mg and advised to discontinue cigarette smoking.

When followed up as an outpatient at the Cardiac Clinic 2 weeks later he complained of continuing episodes of chest pain at rest as well as on moderate effort, with occasional palpitations at rest but no presyncope or syncope. Apart from a loud fourth heart sound, clinical examination revealed no abnormal features and a resting 12-lead ECG had not changed. Holter monitoring over 24 hours failed to demonstrate any arrhythmia or obvious intermittent ST-segment or T-wave changes. Because of his history he was subjected to submaximal treadmill effort testing (modified Bruce protocol) while still taking nifedipine and nitrates, but this failed to demonstrate any myocardial ischaemia. This investigation was then followed by an exercise thallium-201 stress test (keeping the drug therapy unchanged) to gain further insight into possible post-infarction ischaemia. An adequate level of exercise was achieved and immediately after this there was a definite area of reduced isotope activity in the inferior position of the left ventricle. However, a repeat scintiscan 4 hours later showed no change in the area of defect. Results of this investigation therefore further confirmed the previous transmural MI but failed to demonstrate any areas of reversible myocardial ischaemia.

In view of the possibility of coronary vasospasm, as well as the continuing episodes of chest pain despite the negative exercise stress test, he was admitted on 13 July for cardiac catheterization and selective coronary angiography. It was also anticipated that an ergometrine maleate provocation test would be carried out, and he was therefore advised to reduce the nifedipine dosage slowly during the week preceding admission. During this reduction he experienced no increase in the frequency of chest pain although he still continued to use the nitroglycerin formu-lation (increased to 32 mg). Cardiac catheterization was carried out by the Seldinger technique from the groin. All the intracardiac pressures and indices of left ventricular contractility were

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TABLE I. SERIAL SERUM ENZYME ESTIMATIONS

Enzyme	June 12	13	14	15	16	Normal range
CK	1 246	1 085	387	8	33	0 - 50
AST	666	900	204	62	40	0 - 40
ALT	69	97	58	41	26	0 - 53
LD	1 345	2 086	1 560	1 447	1 261	100 - 350

All values given in units per litre.
CK = creatinine kinase; AST = aspartate transaminase; ALT = alanine transaminase; LD = lactate dehydrogenase.

normal. Left ventricular cine angiography in the right anterior oblique (RAO) projection demonstrated inferoposterior akinesia due to previous MI, but there was no evidence of mitral insufficiency or mitral valve prolapse. Baseline selective coronary arteriography carried out in multiple projections delineated a very dominant right coronary artery with a 40% obstructive lesion in its second part (Fig. 1). The left coronary artery displayed a 20% lesion in the left anterior descending branch (Fig. 2) but no other lesions. The ergometrine maleate provocation test was then carried out by injection of an initial bolus of 0,025 mg into the main pulmonary artery while monitoring the central aortic pressure and standard leads II and V2 on the oscilloscope. A full 12-lead ECG was recorded every 4 minutes while standard leads I, II and III were recorded every 30 seconds. The patient was instructed to notify the operator of any onset of chest pain or any other symptom during the provocation. A further bolus of 0,025 mg of ergometrine maleate was given after 4 minutes. After this boluses of 0,05 mg were administered every 4 minutes to a total dose of 0,40 mg. During the entire period the patient had no chest pain or other symptom, and no features of myocardial ischaemia or cardiac arrhythmias were noted on the ECG or oscilloscope. Four minutes after the last bolus of ergometrine maleate left coronary cine angiography demonstrated only diffuse narrowing of the vessels without any definite localized area of vasospasm (Fig. 3). However, right coronary cine angiography delineated total occlusion of the vessel in its second part where the initial 40% lesion had been located (Fig. 4). At this stage the patient still did not state that he was experiencing any chest pain and there was no evidence of myocardial ischaemia on ECG monitoring. Because of the severe degree of coronary vasospasm a bolus of 200 μg of nitroglycerin was slowly infused directly into the right coronary artery. Right coronary cine angiography was then repeated after 5 minutes; at this time the total occlusion had been relieved to leave a 50% narrowing at the initial site of obstruction (Fig. 5). Diffuse dilatation was also seen in the right coronary artery. The patient still had no chest pain, and the ECG remained normal. Aortic pressure monitoring demonstrated no change after the intracoronary nitroglycerin injection. Cardiac catheterization was then completed without complication and the patient was returned to the ICCU for monitoring. Over the succeeding 3 days serial enzyme values remained normal and resting 12-lead ECGs failed to show any significant change. The patient also remained free of angina and was continued on nitroglycerin 32 mg transdermally as well as nifedipine 10 mg 8-hourly. Beta-blockers were withheld in view of the documented coronary vasospasm. After discharge he remained symptom-free and when last seen as an outpatient he had discontinued smoking and was asymptomatic on therapy. The 12-lead ECG remained unchanged.

Discussion

The detection of Prinzmetal's variant angina,[1] now universally accepted as being due to coronary vasospasm (often superimposed on an underlying atherosclerotic lesion),[2] has often proved most difficult.[3] This fact led to the introduction of the ergometrine maleate provocation test,[4] a procedure ideally carried out in the cardiac catheterization laboratory but applied on an outpatient
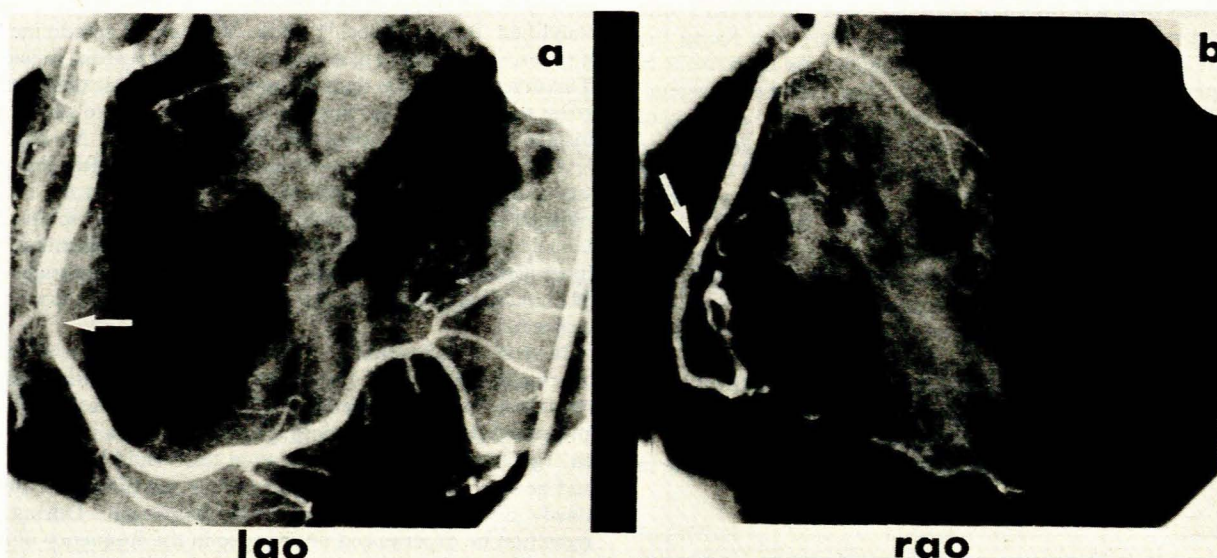

Fig. 1. Right coronary cine angiograms in the (a) left anterior oblique (LAO) and (b) right anterior oblique (RAO) views. The vessel is dominant and there is a 40% atherosclerotic lesion (arrowed) in its second part. The remainder of the vessel appears free of obstructive disease.
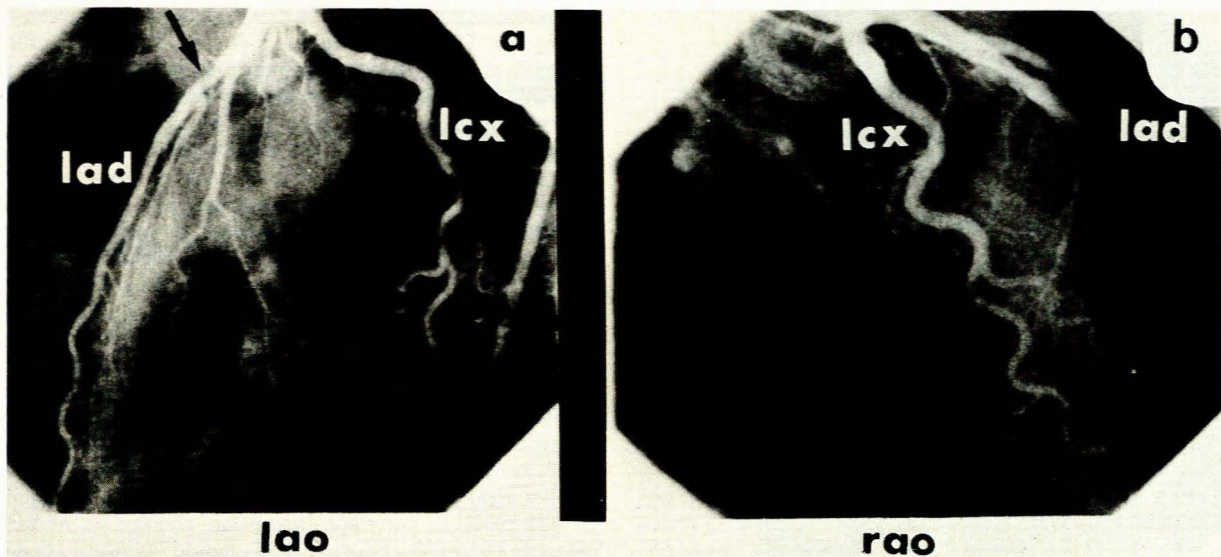
Fig. 2. Left coronary cine angiograms in the (a) LAO and (b) RAO views demonstrating a 20% obstructive lesion (arrowed) in the left anterior descending branch just distal to the origin of the first diagonal branch. The left circumflex branch is non-dominant and displays no atrioventricular groove branch, an area which is supplied by the very dominant right coronary artery. No further obstructive lesions are visible in the left coronary artery (lad = left anterior descending branch; lcx = left circumflex branch).
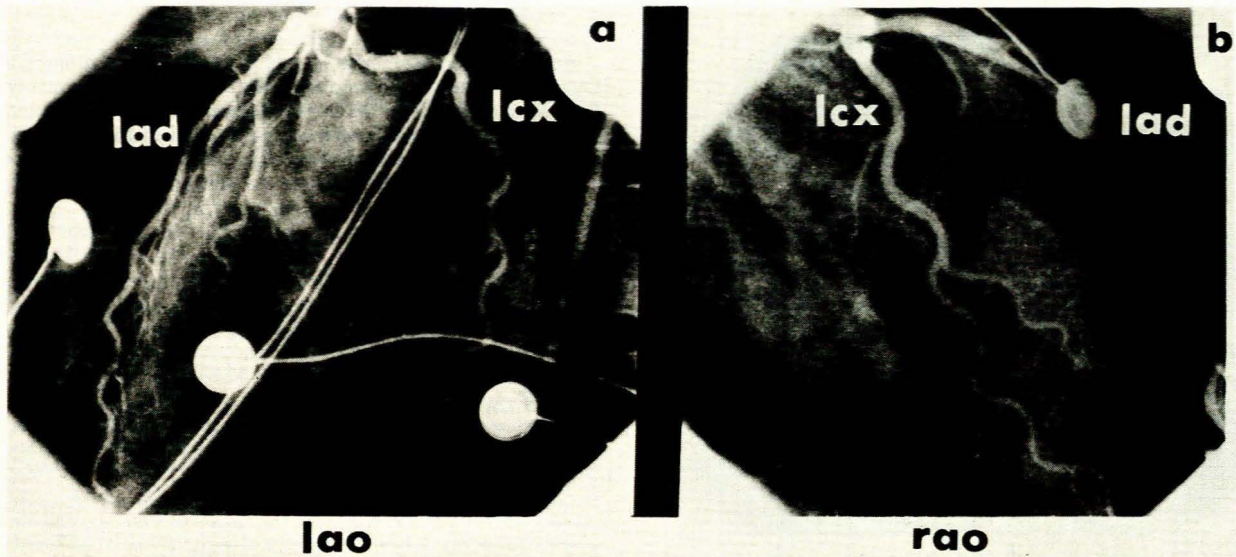

Fig. 3. Left coronary cine angiograms in the (a) LAO and (b) RAO views immediately after a total dose of ergometrine maleate of 0,40 mg. Generalized narrowing of the vessels is seen without any significant localized coronary vasospasm (lad = left anterior descending branch; lcx = left circumflex branch).

basis with precautions.[5] This has caused much discussion, especially since this test is not without complications since acute MI as well as death have been reported by some workers.[6] Furthermore, it has been demonstrated that some types of provoked coronary vasospasm are unresponsive to both sublingual and intravenous nitrates, whereas intracoronary nitroglycerin is effective.[7] Naturally this can only be used at the time of cardiac catheterization. The establishment of a vasospastic mechanism as the cause of symptoms is not only of academic interest but provides for a more rational form of medication in that the long-acting nitrates and calcium antagonists are physiologically more applicable in this clinical setting.[8,9] This is all the more important when it is realized that coronary vasospasm can result in acute MI[10] as well as potentially life-threatening arrhythmias such as atypical ventricular tachycardia ('torsade de pointes').[11,12] Sudden death has also been documented as a complication of coronary artery spasm.[13]

The ergometrine maleate provocation test has been shown to correlate well with spontaneous coronary vasospasm in patients suffering from Prinzmetal's variant angina,[14] despite the fact that the exact mechanism of drug action is only speculative. The normal 'physiological' response to ergometrine maleate provocation is an insignificant diffuse coronary artery constriction which does not result in either chest pain or ECG features of myocardial ischaemia.[4] This type of response is classically seen in those patients with 'normal coronary arteries' and the 'atypical anginal syndrome', in whom prognosis is very good. Rich et al.[15] have documented two very different types of response to ergometrine maleate provocation: (i) dose-dependent diffuse coronary vasoconstriction responding favourably to nitrates but not to nifedipine; and (ii) significant focal coronary vasospasm reversed by nifedipine but not always by nitrates.

Interpretation of the response of the coronary circulation to ergometrine provocation can sometimes be made more difficult by the occurrence of 'catheter-induced coronary vasospasm'.[16] This form of coronary artery spasm has always been considered
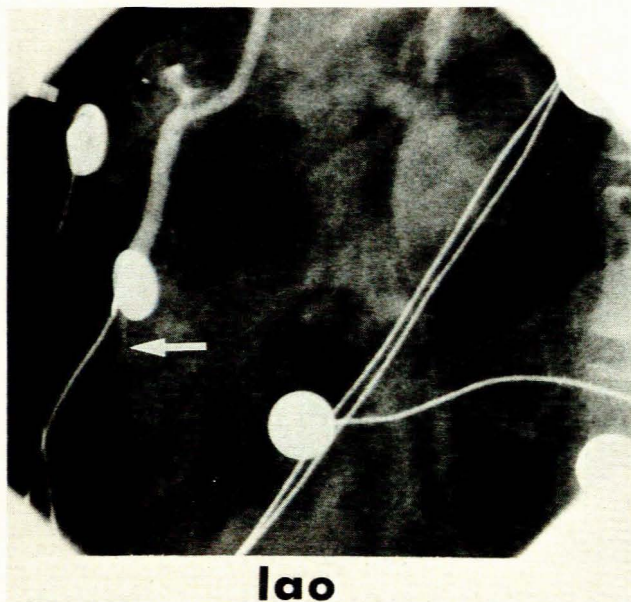
lao

Fig. 4. Right coronary cine angiogram in the LAO projection after provocation with ergometrine maleate in a total dose of 0,40 mg. Total occlusion (arrowed) of the vessel is visualized at the site of the previously demonstrated 40% lesion.
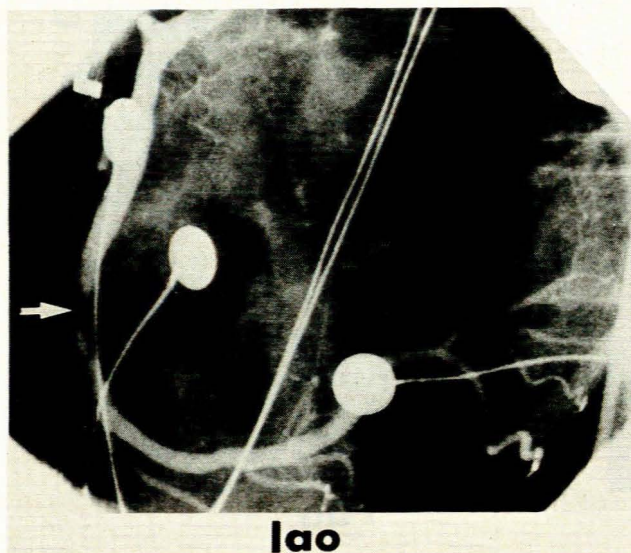

lao

Fig. 5. Right coronary cine angiogram in the LAO view after administration of intracoronary nitroglycerin 200 μg. The previously demonstrated total occlusion has now been relieved, leaving a 50% obstructive lesion at the initial site of obstruction in the vessel (arrowed). The rest of the artery is markedly dilated due to the nitroglycerin.

to be benign and is said to occur in some 1 - 3% of all coronary cine angiograms.[16] Catheter-induced spasm is most frequent in the right coronary artery and is usually localized to the coronary artery segment just distal to the tip of the catheter.[4] It does not give rise to angina pectoris, ECG signs of myocardial ischaemia or hypotension, and also does not correlate with the frequency of spontaneous coronary vasospasm in patients with Prinzmetal's angina,[17] or with ergometrine-provoked coronary vasospasm.

It is postulated that our patient sustained his acute transmural inferoposterior MI as a direct result of severe coronary vasospasm superimposed upon the insignificant atheromatous obstructive lesion in the very dominant right coronary artery.[18] The coronary vasospasm visualized in this same segment at the time of cardiac catheterization is believed not to have been catheter-induced but to have occurred as a direct result of ergometrine maleate

provocation since there was a direct relationship between those two events. The most intriguing aspect, and the reason for this report, is the fact that the ensuing total occlusion of the right coronary artery failed to cause angina pectoris or ECG evidence of myocardial ischaemia. This may have been a result of the absence of any myocardium 'at risk' supplied by the dominant right coronary artery since that segment of myocardium had already been affected by the previous MI. His chest pain episodes subsequent to the MI therefore cannot be attributed to right coronary artery spasm or to possible vasospasm of the left coronary artery since the latter failed to respond to the ergometrine maleate test.

These findings raise several important issues. Firstly, recurring severe vasospasm of a coronary artery supplying an infarcted area of myocardium may well be of no functional or prognostic significance if the infarction is 'complete'. Secondly, is it possible for significant angiographic coronary artery spasm to occur without any clinical or ECG evidence of myocardial ischaemia in a viable segment of myocardium? Could this mean that there are various types of coronary vasospasm giving rise to varying pathophysiological sequelae, and should all these types be treated with equal enthusiasm? Furthermore, are those workers who advocate early intracoronary thrombolysis after acute MI really reducing MI size? It seems quite clear that much further research is needed in order to find answers to these various questions.

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