Case reports

Resolution of myocardial ischemia due to coronary microcirculatory vasoconstriction in a patient with mixed angina

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Key words:
Angina;
Collateral circulation;
Coronary angioplasty;
Ergonovine test.

Vasoconstriction of collateral vessels has been previously reported as a mechanism of spontaneous transient ischemic episodes and after the administration of ergonovine. This case report describes a 47-year-old woman with mixed angina and a right coronary artery occlusion supplied by a collateral system related to the left anterior descending artery. Angina and ECG changes at rest were present for more than 1 year and also provoked by intracoronary ergonovine which induced collateral vasoconstriction. To the best of our knowledge, this report is the first demonstration that the reopening of the right coronary artery and the disappearance of collateral vessels may definitively relieve angina and ECG changes occurring at rest, thus confirming small coronary vessel constriction as the main cause of the disease status.

(Ital Heart J 2002; 3 (9): 525-528)

Received April 19, 2002; revision received July 9, 2002; accepted July 10, 2002.

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Introduction

It is well known that constriction of the distal coronary arteries, collateral vessels or both may cause myocardial ischemia in patients with chronic stable angina[1]. It has also been noted that an alteration of the coronary microcirculation plays an important role in the pathogenesis of myocardial ischemia in the "no-reflow" phenomenon[2] and in syndrome X[3].

We report a case of a woman with mixed angina and a right coronary artery (RCA) occlusion supplied by a collateral system related to the left anterior descending artery (LAD). Angina and ECG changes at rest which were present for more than 1 year and also provoked by intracoronary ergonovine which induced collateral vasoconstriction, were relieved by the reopening of the RCA, thus confirming small coronary vessel constriction as the main cause of the disease status.

Case report

A 47-year-old woman, with a family history of stroke, was admitted in June 1999 to our department for episodes of mixed angina.

She had no history of hypertension or diabetes mellitus, but she had hyperlipidemia. She had taken oral contraceptives and had smoked 20 cigarettes daily for 25 years. She had a transient ischemic attack 8 years previously and a myocardial infarction in November 1998 which was followed by long-lasting episodes of mixed angina.

On admission, her physical examination was normal. The chest X-ray was within normal limits. The ECG showed normal sinus rhythm, pathologic Q waves and negative T waves in the inferior leads (DII, DIII, aVF) (Fig. 1). Two-dimensional echocardiography revealed akinesia in the postero-inferior wall and in the postero-basal segment of the interventricular septum and a global ejection fraction of 56%. Blood analysis revealed hypercholesterolemia (238 mg/dl) and hypertriglyceridemia (231 mg/dl); all other laboratory data, including serum cardiac enzymes, were normal.

The day following admission, she had an episode of ischemic chest pain at rest. ECG recorded during symptoms demonstrated negative T waves in the V_5-V_6 leads and a remarkable inversion of the T waves in the II, III and aVF leads (Fig. 2). There was no rise in the creatine kinase (CK) and CK-MB values. In view of this, the patient was started on intravenous nitroglycerin.

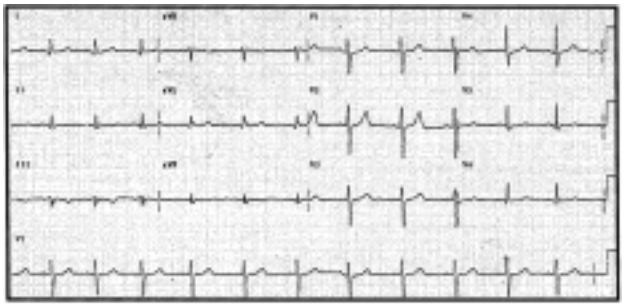


Figure 1. *Basal ECG.*

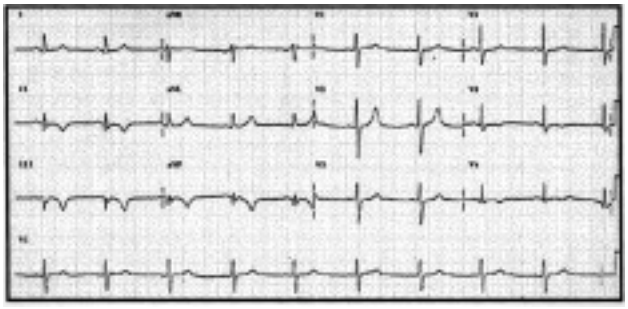


Figure 2. *ECG recorded during symptoms at the time of the patient's first admission.*

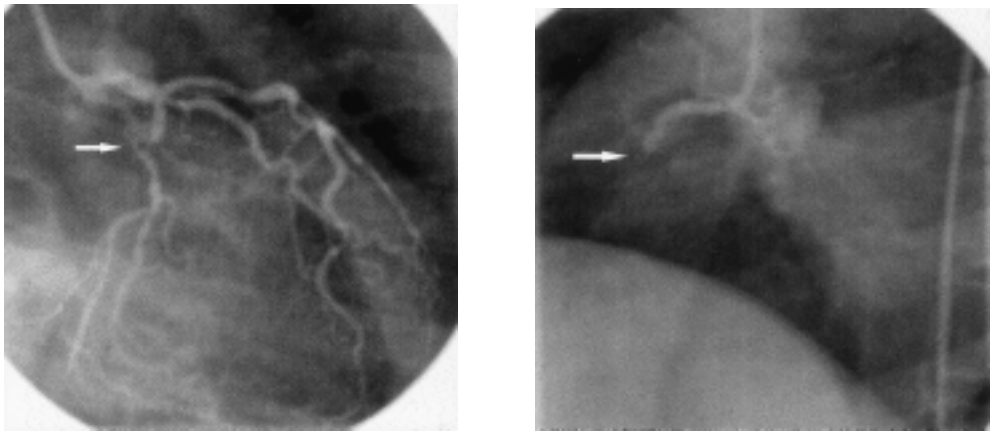
Her symptoms rapidly resolved. At this stage, she also underwent coronary artery angiography which showed subocclusion of the proximal circumflex artery; the main RCA was totally occluded in its proximal segment; the posterior descending coronary artery was revealed through a collateral vessel system which was supplied by the LAD (Fig. 3). Therefore, it was decided to perform coronary angioplasty of the proximal circumflex artery and a 18 mm stent was implanted. The outcome was excellent and a control angiogram revealed a TIMI 3 flow through the stent. The patient remained asymptomatic after the procedure and was thus discharged on medical therapy including nitrates, calcium antagonists, ticlopidine, aspirin, and statins.

In December 1999, the patient presented with recurrent episodes of chest pain both at rest and on exertion. She was submitted to exercise 99m-Tc-tetrofosmin SPECT scintigraphy which showed a fixed uptake defect in the infero-basal wall, a partially reversible uptake defect in the basal segment of the infero-lateral wall and a completely reversible uptake defect in the mid segment of the infero-lateral wall. At peak exercise she developed angina, but not significant ST-segment changes. Hence, she was stabilized on medical therapy and beta-blockers were added to the previous regimen.

In August 2000, she was readmitted because of recurrent mixed angina. Her physical examination was unremarkable and her ECG showed no ST-T changes in comparison to the admission ECG. She reported ischemic ST-T episodes not preceded by an increase in heart rate during 24-hour Holter monitoring. At the time of admission, she had an episode of typical anginal pain at rest. ECG, recorded during symptoms, showed positive T waves in the III and aVF leads and negative T waves in the V_2-V_4 leads (Fig. 4). The patient was then submitted to coronary angiography which confirmed TIMI 3 flow through the circumflex artery and a well-developed LAD-related collateral system (Fig. 5).

In this setting, as epicardial coronary artery vasospasm was hypothesized, the ergonovine test was performed in order to identify the mechanism responsible for recurrent angina.

Ergonovine maleate was infused into the LAD at incremental doses of 25, 50, 100, 200 and 300 μg at intervals of 5 min. The patient's blood pressure and 12-lead ECG were continuously monitored throughout the infusion. Following the administration of 200 μg of ergonovine, the patient developed her habitual anginal chest pain ST-T changes. Coronary angiography performed at this time revealed obliteration of the collater-



A **B**

Figure 3. A: *basal coronary angiography, left coronary artery in the 30° right anterior oblique and 20° caudal projections. The* arrow *indicates the site of stenosis of the proximal left circumflex artery.* B: *basal coronary angiography, right coronary artery in the 45° left anterior oblique projection. The* arrow *indicates the site of occlusion of the proximal right coronary artery.*

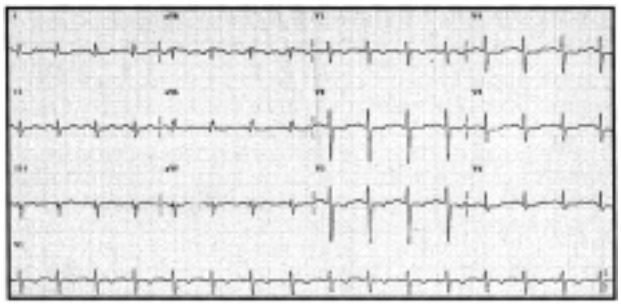


Figure 4. *ECG recorded during symptoms at the time of the patient's readmission.*

al vessels in the absence of detectable spasm of the epicardial coronary arteries (Fig. 6). Symptoms and signs of ischemia were promptly relieved by the administration of 2 mg of isosorbide dinitrate and repeat angiography confirmed the refilling of the collaterals (Fig. 7).

Thereby, as myocardial scintigraphy demonstrated myocardial ischemia in the infero-lateral wall and since coronary angiography showed spasm of the collateral vessels up to the occluded RCA, it was hypothesized that reopening of the RCA would have improved patient's clinical status.

Thus, it was decided to perform coronary angioplasty of the RCA. An 18 mm stent was implanted in the proximal part of the RCA and a TIMI 3 flow was revealed at the end of the procedure (Fig. 8). A control angiogram demonstrated that there no longer was any blood flow through the collaterals.

The patient's symptoms had completely resolved and she was discharged on medical therapy including oral nitrates, ticlopidine, aspirin, calcium antagonists, and statins. At a follow-up of 12 months the patient was still symptom free.

Discussion

Vasoconstriction of collateral vessels has been previously reported as a mechanism of spontaneous transient ischemic episodes and after the administration of ergonovine. Yamakado et al.[4] reported the disappearance of ergonovine-induced filling of the collaterals associated with symptoms and ECG changes during ischemic episodes at rest, without epicardial coronary artery spasm. Biagini et al.[5] reported the complete reduction of a well-developed collateral system associated with asymptomatic and transient ST-T changes in patients with unstable angina. More recently, a similar mechanism has been shown to be responsible for vasoconstriction of the distal coronary vessels. In patients with chronic stable angina, ischemic episodes may be caused by an excessive increase in myocardial oxygen consumption, by a transient impairment of the myocardial blood flow or by a combination of a subliminal transient reduction in coronary blood flow and an in-

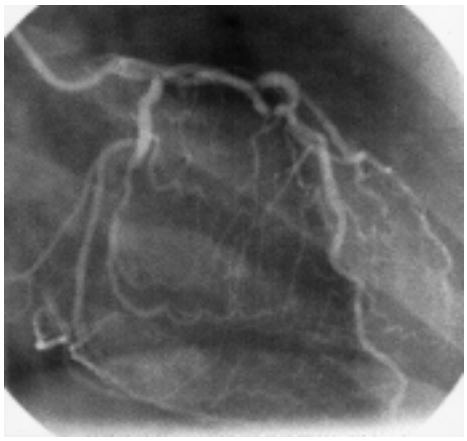


Figure 5. *Left coronary artery in the 30° right anterior oblique and 20° caudal projections: TIMI 3 flow throughout the circumflex artery after angioplasty and stenting of the proximal segment.*

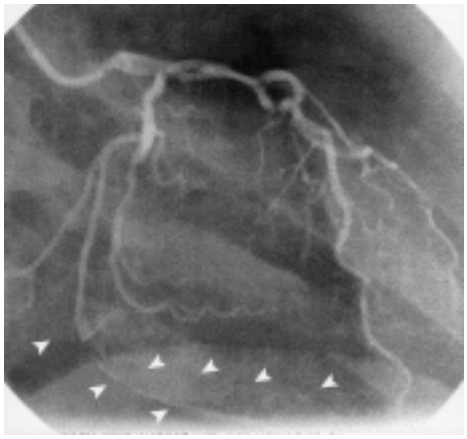


Figure 6. *Left coronary artery in the 30° right anterior oblique and 20° caudal projections: coronary angiography during ergonovine administration. The* arrows *indicate a significantly reduced filling of the collaterals up to the right coronary artery in the absence of detectable spasm of the epicardial coronary arteries.*

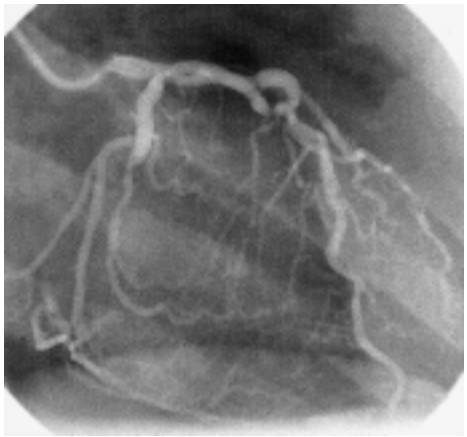


Figure 7. *Left coronary artery in the 30° right anterior oblique and 20° caudal projections after 2 mg intracoronary nitroglycerin administration. The reappearance of significant filling of the collaterals up to the right coronary artery is noteworthy.*

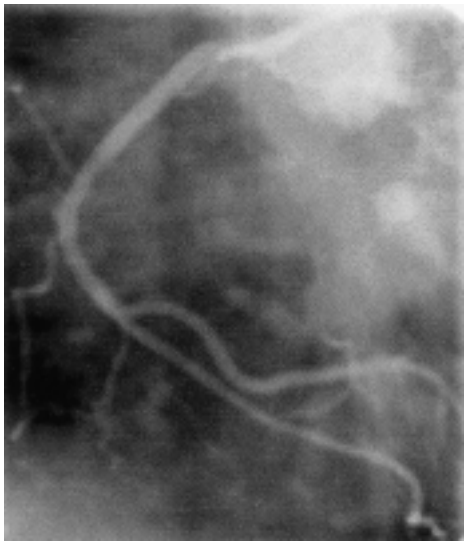


Figure 8. *Right coronary artery in the 45° left anterior oblique projection. Successful reopening and angioplasty with stenting of the proximal right coronary artery occlusion with TIMI 3 flow throughout the vessel.*

crease in myocardial oxygen consumption. An increase in oxygen consumption may be either due to a primary increase in heart rate such as that occurring during exercise or to primary changes in left ventricular preload or afterload such as those occurring in case of a rise in blood pressure. With regard to the present case report, we presume that the excessive increase in myocardial oxygen consumption may have been the prevailing mechanism of myocardial ischemia during myocardial scintigraphy, while a decrease in oxygen supply seems to have characterized the chest pain and ECG changes with which the patient presented during chest pain. However, we cannot exclude the possibility that both mechanisms were present and not simultaneously documented. Furthermore, constriction of the distal or collateral vessels or both may represent an additional precipitating mechanism of myocardial ischemia[1].

An endothelial dysfunction, a primary smooth muscle hyperreactivity[6], an enhanced sympathetic stimulation by neuropeptide Y[7], a raised concentration of blood constrictors such as endothelin[8] and serotonin[9] or a combination of all these factors may all concur to the genesis of such vasoconstriction. Although smooth muscle vessel hyperreactivity similarly constricts distal and proximal vessels, it has been found that neuropeptide Y, endothelin and serotonin constrict distal vessels more than the epicardial coronary arteries and may play a role in the transient reduction of myocardial blood flow[9,10]. The collateral vasoconstriction in the absence of epicardial coronary artery spasm could be related to the anatomic differences between distal and proximal coronary vessels and thus to a different response to endogenous substances. However, as collateral vessels and the coronary microcirculation have similar anatomic and biochemical characteristics, similar mechanisms such as those responsible for small vessel vasoconstriction, could play a role in vasoconstriction of the collaterals. Indeed, "mature" collateral vessels have the anatomic constituents necessary for vasomotion and besides, coronary blood flow may also be modulated by changes in vasomotor tone mediated by α_2 receptor stimulation[2,11-14].

To the best of our knowledge, this report is the first demonstration that the reopening of the RCA and the disappearance up to this vessel of the LAD-related collaterals may result in the definite relief of angina and of the ECG changes occurring at rest. In our patient, the angiographic evidence of a well-developed LAD-related collateral system up to the RCA and the positive result of the ergonovine test were the factors which led to the indication for the reopening of the RCA. The clinical outcome of this procedure which was successfully performed was excellent and long-lasting.

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