Case reports

Coronary slow flow phenomenon: description of three cases evaluated with myocardial perfusion scintigraphy

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The coronary slow flow phenomenon (CSFP) is an angiographic finding characterized by delayed opacification of the epicardial coronary arteries in the absence of significant stenosis, spasm, dissection or thrombus. Although this poorly understood phenomenon received little attention, patients with CSFP at coronary angiography often suffer from recurrent episodes of chest pain, sometimes occurring during an acute coronary syndrome.

We describe 3 cases of patients with CSFP who complained of recurrent chest pain; in one of them an episode of chest pain was so severe as to bring the patient to the emergency department. Indeed, in all our 3 cases myocardial ischemia was evaluated on the basis of a positive myocardial scintigraphy result.

In conclusion, it is suggested that CSFP may be an acute and recurrent perturbation of microvascular function with an often severe impairment of quality of life. Myocardial perfusion scintigraphy might help for an accurate assessment of myocardial ischemia in such patients.

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Introduction

The coronary slow flow phenomenon (CSFP) is an angiographic finding characterized by delayed opacification (TIMI 2 flow) of the epicardial coronary arteries in the absence of significant stenosis, spasm, dissection or thrombus[1].

This poorly understood phenomenon has been merely considered an angiographic curiosity and thus received little attention. However, patients with CSFP often have recurrent episodes of chest pain frequently requiring hospitalization[2-4], even if inducible myocardial ischemia cannot always be proven[5]. Although the pathophysiology of this phenomenon is not clearly known, it seems correlated with an anatomic luminal reduction of the small coronary arteries[6,7] as well as with a functional component such as an increased basal coronary microvascular tone[4,5,8,9].

We describe 3 cases of patients with CSFP, who had chest pain and myocardial perfusion defects.

Description of cases

Case 1. The first patient was a 33-year-old man who complained of several episodes of resting and effort chest pain for the last 2 months. He had a family history of coronary artery disease, was a previous smoker, treated for hyperlipidemia with statins and for mild hypertension with angiotensin-converting enzyme inhibitors. The basal electrocardiogram was normal. An echocardiogram showed normal left ventricular function with no evidence of hypertrophy. He underwent an exercise ^{99m}Tc-tetrophosmin myocardial perfusion scintigraphy SPECT which showed a reversible perfusion defect in the medium inferior segment and a partially reversible perfusion defect in the apical anterior segment (Fig. 1). The concomitant exercise testing was maximal (the heart rate achieved was 90% of the maximal heart rate predicted for age and sex), the rate-pressure product at peak exercise was 29 700 mmHg $\times$ b/min and the electrocardiogram was negative. The patient did not experience chest pain during exercise. Coronary angiography showed completely normal coronary arteries and CSFP of the left anterior descending coronary artery and of the right coronary artery (Fig. 2), while the dye run-off was normal into the left circumflex coronary artery.

Case 2. The second patient was a 39-year-old woman who complained of effort chest

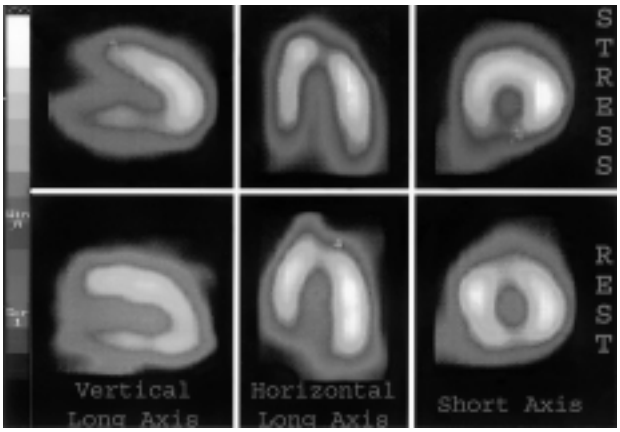

Figure 1. *^{99m}Tc-tetrophosmin myocardial perfusion scintigraphy SPECT at stress and rest showing a reversible perfusion defect in the medium inferior segment and a partially reversible perfusion defect in the apical anterior segment.*

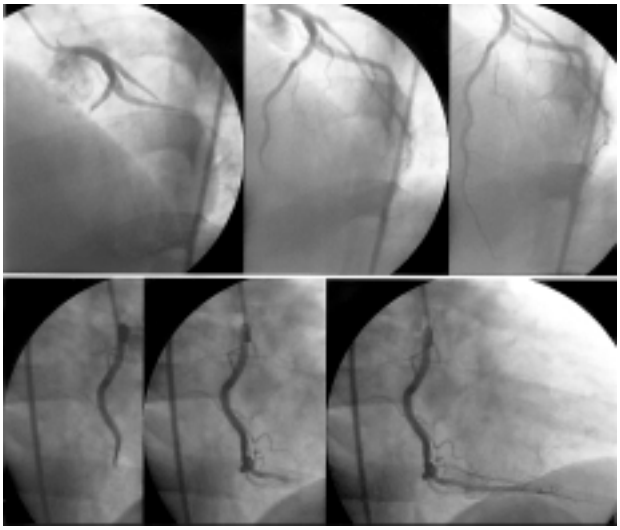

Figure 2. *Coronary angiogram of the left anterior descending coronary artery* (upper panel) *and of the right coronary artery* (lower panel) *showing the opacification in three consecutive beats.*

pain for the last 3 months. She had hyperlipidemia (total cholesterol 300 mg/dl, LDL cholesterol 217 mg/dl, triglyceridemia 291 mg/dl) and was a smoker of 20 cigarettes per day. The basal electrocardiogram was normal. An echocardiogram showed mild hypokinesia of the apex with no evidence of left ventricular hypertrophy. She underwent an exercise ^{99m}Tc-tetrophosmin myocardial perfusion scintigraphy SPECT which showed a partially reversible perfusion defect in the anterior and lateral apical segments (Fig. 3). The concomitant exercise testing was maximal (the heart rate achieved was 88% of the maximal heart rate predicted for age and sex), the rate-pressure product at peak exercise was 27 000 mmHg × b/min and the electrocardiogram was negative. The patient experienced mild, not limiting, chest pain during exercise. Coronary angiography showed completely normal coronary arteries and a CSFP of the left anterior descending coronary artery (Fig. 4). The dye run-off was normal into both the left circumflex coronary artery and the right coronary artery.

Case 3. The third patient was a 53-year-old woman who had suffered 2 years before our observation from a short period of effort chest pain. She had a family history of cerebrovascular disease, moderate ponderal excess and a normofunctional thyroid nodule. At that time she was found to have mild hypertension; the basal electrocardiogram was normal and an echocardiogram showed normal left ventricular function with no evidence of hypertrophy. Thus, she was treated with low-dose beta-blocker, non-dihydropyridinic calcium antagonist and aspirin, and was encouraged to reduce her weight. Since the patient started the antianginal medications she remained asymptomatic for another year. Then, she suddenly complained of a severe rest chest pain that required hospitalization. On admission to the emergency room, the electrocardiogram showed sinus tachycardia (109 b/min) with ST-segment depression of 1 mm in leads V_5 and V_6. The blood pressure was 160/90 mmHg. Blood samples for creatine phosphokinase-MB and troponin at the time of admission in the emergency room (2 hours from symptom onset) were normal. Thereafter, the patient refused admission into the cardiology unit. Ten

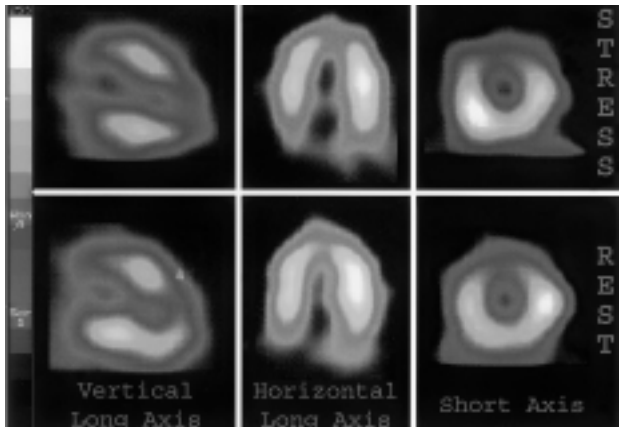

Figure 3. *^{99m}Tc-tetrophosmin myocardial perfusion scintigraphy SPECT at stress and rest showing partially reversible perfusion defects in the anterior and lateral apical segments.*

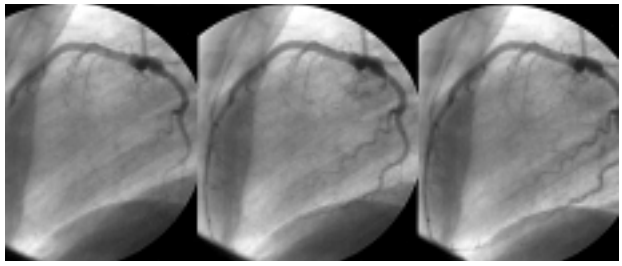

Figure 4. *Coronary angiogram of the left anterior descending coronary artery showing the opacification in three consecutive beats.*

days later she underwent an exercise testing who was maximal (the heart rate achieved was 85% of the maximal heart rate predicted for age and sex), the rate-pressure product at peak exercise was 25 000 mmHg × b/min and the electrocardiogram was negative. At peak exercise the patient experienced chest pain and a short episode of atrial fibrillation which spontaneously disappeared during the recovery phase. Thus, it was decided to perform a dipyridamole ^{99m}Tc-tetrophosmin myocardial perfusion scintigraphy SPECT which showed a reversible perfusion defect in the apical and medium anterior segments, in the basal and medium anteroseptal segments and in the basal inferolateral segment (Fig. 5). The concomitant dipyridamole electrocardiogram was negative. Coronary angiography showed completely normal coronary arteries and a CSFP of the left anterior descending coronary artery and of the right coronary artery (Fig. 6), while the dye run-off into the left circumflex coronary artery was normal.

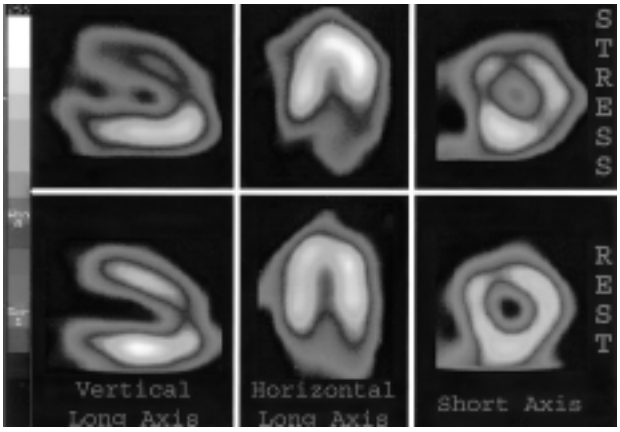

Figure 5. *Dipyridamole ^{99m}Tc-tetrophosmin myocardial perfusion scintigraphy SPECT showing reversible perfusion defects in the apical and medium anterior segments, in the basal and medium anteroseptal segments and in the basal inferolateral segment.*

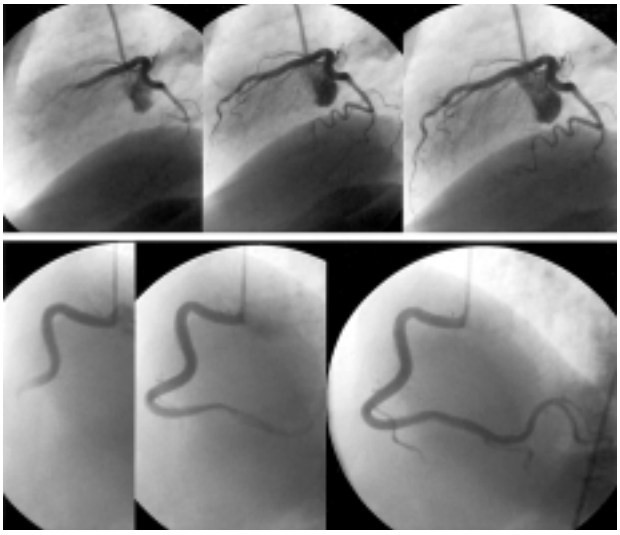

Figure 6. *Coronary angiogram of the left anterior descending coronary artery* (upper panel) *and of the right coronary artery* (lower panel) *showing the opacification in three consecutive beats.*

Discussion

An evident slow flow in the epicardial coronary arteries requiring ≥ 3 beats to opacify the distal vasculature in the absence of significant stenosis, spasm, dissection or thrombus is not an infrequent finding during routine coronary angiography. The exact incidence of this phenomenon is not known, probably because it has largely been considered a curiosity and thus received little attention.

Usually, patients with CSFP are referred to coronary angiography for chest pain, sometimes during an acute coronary syndrome. Indeed, all our patients complained of recurrent chest pain during daily life, and in the third case an episode of chest pain was so severe as to bring the patient to the emergency department. In the study of Goel et al.[2] 82% (40/49 patients) of the patients with CSFP had typical angina and 71% had a positive exercise test. Beltrame et al.[3], who followed up 64 patients with CSFP for a median time of 21 months, observed in these patients an 84% of recurrent chest pain with almost two thirds requiring urgent admission to the coronary care unit; the same authors in a different work involving 12 patients with CSFP, documented that 10 of these patients had unstable angina and 2 recurrent chest pain during the follow-up[4]. Interestingly, it has been shown that the symptoms of these patients are episodic and variable over time as it occurs in CSFP[4], thus suggesting that during periods of chest pain a microvascular impediment may result in a worsening of symptoms or sometimes in an acute coronary syndrome presentation.

Some studies reported the histopathological examination of the left[6] and right[7] ventricular endomyocardial biopsies of patients with CSFP, that showed thickening of the small coronary artery walls with a luminal size reduction; this histopathological abnormality could contribute to determine coronary microvascular dysfunction. Interestingly, normal and pathological zones often coexisted in the same specimen. However, behind of the suggested "fixed" anatomic luminal reduction of the small coronary arteries, a functional "dynamic" component may also be implicated, as shown by the great variability in clinical and angiographic studies. Indeed, Beltrame et al.[4] showed a reduced coronary sinus oxygen saturation in 12 patients with CSFP compared with control subject (23 ± 4 vs 31 ± 4%, $p < 0.01$), which may well reflect in this subset of patients a chronically increased basal coronary microvascular tone. In other small studies the administration of dipyridamole[6], nitroglycerin[8] and the calcium T-channel blocker mibefradil[9] seems to normalize the dye run-off in these patients. Although the disappearance of

CSFP by intracoronary vasodilator injection may suggest a microspastic pathogenesis, we could not detect this pathogenetic effect since intracoronary vasodilator injection was performed in none of our patients.

To the best of our knowledge, the only prospective study which deals with patients with CSFP and myocardial scintigraphy is that of Yaymaci et al.[5] who divided 34 patients with CSFP into two groups according to their metabolic responses to atrial pacing on the basis of differences of lactate production and arterio-venous oxygen content. Five of the 6 (83%) patients with proven metabolic ischemia and only 1 of the 28 (4%) patients without metabolic ischemia had myocardial perfusion defects. On the basis of these results, the authors suggested that CSFP might be used as a marker of myocardial ischemia, if associated with myocardial scintigraphic defects. Indeed, in all our 3 cases myocardial ischemia could be postulated on the basis of a positive myocardial scintigraphy result.

In conclusion, based on the observation of these 3 case reports and other previous studies, it is suggested that CSFP could be an acute and recurrent perturbation of microvascular function with an often severe impairment of quality of life, consequent substantial cost burden to the healthcare system and not merely an angiographic curiosity. Myocardial perfusion scintigraphy might help for an accurate assessment of myocardial ischemia in such patients.

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