Short Communications

Severe Transmural Myocardial Ischemia after Dipyridamole Administration Implicating Coronary Steal

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Summary: Myocardial perfusion imaging with coronary vasodilators is routinely used for patients with suspected coronary disease who are unable to exercise. Since these agents work by increasing blood flow without significantly changing myocardial oxygen demand, they generally do not produce ischemia. A minority of patients show evidence of ischemia which some investigators suggest is due to a coronary steal phenomenon, but this has been challenged by several investigators. We present the case of a patient who developed severe transmural myocardial ischemia manifested by ST-segment elevation and severe perfusion defects which occurred after dipyridamole administration and which were reversed with aminophylline and nitroglycerin. This case supports the notion that coronary vasodilation with dipyridamole can induce a coronary steal.

Key words: dipyridamole, coronary steal, myocardial perfusion imaging

Introduction

The use of coronary vasodilators in conjunction with myocardial perfusion imaging has become routine for the diagnosis of coronary disease in patients who are unable to exercise adequately. Since these agents increase myocardial blood

flow without significantly increasing myocardial oxygen demand, patients usually do not develop ischemia from them. Between 6 and 21% of patients develop evidence of ischemia as manifested by ST-segment depression on the electrocardiogram (ECG).¹ It has been proposed by some investigators that a myocardial steal phenomenon occurs in these patients, which reduces blood flow below resting levels and thus creates ischemia. The existence of a steal, however, is controversial.^{1,2} We report the case of a patient undergoing dipyridamole stress testing who developed severe ischemia, presumably secondary to coronary steal.

Case Report

A 47-year-old man with a 30-pack-year history (1 pack of cigarettes per day/per year) of smoking but no prior cardiac history was being evaluated prior to total hip replacement for severe osteoarthritis. The patient had several weeks of very atypical chest pain and was noted to have an abnormal baseline ECG. His symptoms typically occurred postprandially and were only relieved by standing and walking. He was referred for dipyridamole perfusion imaging.

Upon completion of the dipyridamole infusion (total dose 0.56 mg/kg), the patient began to complain of dyspnea which was followed by chest pain and ST-segment elevation in the anterior ECG leads (Fig. 1). During infusion, the patient's heart rate increased by 25–30 beats/min and the systolic pressure dropped by 8 mmHg. After the development of chest pain, his heart rate increased another 10–15 beats/min and his blood pressure increased by over 30 mmHg. Thallium was injected, and the patient was immediately given aminophylline. After a total of 250 mg of intravenous aminophylline and three sublingual nitroglycerin, the patient's chest pain and ECG changes resolved. Single-photon emission computed tomography (SPECT) imaging was performed while preparations were being made for the patient's transfer to the coronary care unit. These images revealed severe anteroapical and inferior wall perfusion defects (Fig. 2). He remained pain free and was ruled out for myocardial infarction. Redistribution imaging was not performed.

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FIG. 1 The resting ECG was abnormal and showed poor R-wave progression and biphasic T waves anteriorly. There were no Q waves. After dipyrindamole, the patient developed chest pain and ST-segment elevation. Leads V₃ and V₅ are shown at rest (A) and after dipyrindamole (B).

The following day, the patient underwent cardiac catheterization. This was remarkable for total occlusions of both the right and the left anterior descending coronary arteries (arrows, Fig. 3A and B), as well as an occluded distal circumflex and 60% stenosis of the first oblique marginal (not shown). Both left anterior descending and right coronary arteries could be seen to fill completely by collaterals (Fig. 3C). Ventriculography revealed normal systolic function in both the anterior and inferior walls (Fig. 4). The patient was referred for coronary artery bypass grafting and underwent successful revascularization.

Discussion

This case demonstrates an episode of severe transmural myocardial ischemia after dipyrindamole infusion in a patient with coronary occlusions, good collateral flow, and no evidence of acute or previous infarction. His ischemia resolved after the administration of aminophylline and nitroglycerin.

The safety of dipyrindamole infusion for diagnostic use has been well established. A recent review of over 73,000 patients reported 0.95 deaths and 1.76 nonfatal infarctions per 10,000 patients.³ Its safety is partly due to the fact that it produces hyperemia without significantly increasing myocardial oxygen demand.^{4,5}

Fam and McGregor were the first to suggest that dipyrindamole may, in fact, cause a myocardial steal.⁶ This is thought to occur when a segment of myocardium is dependent upon collaterals for perfusion. Dipyrindamole-induced vasodilatation results in decreased perfusion pressure across the collaterals and a reduction in flow below baseline and thus produces ischemia. Marshall and Parratt demonstrated an absolute reduction in coronary blood flow in five of six dogs with acute ligation of the left anterior descending artery (LAD), which were given dipyrindamole.⁷ In a series of experiments, Becker suggested that a steal would only occur if the vessel supplying collaterals had a significant stenosis itself.^{8,9} The exist-

FIG. 2 The initial thallium images revealed severe anterapical and inferior wall defects. Redistribution imaging was not performed. ASA = apical short axis, MSA = mid short axis, BSA = basal short axis, VLA = vertical long axis, HLA = horizontal long axis.

ence of a coronary steal, however, is controversial.^{1,2} Marchant *et al.* measured great cardiac vein blood flows at rest and after dipyrindamole in 15 patients with LAD stenoses and in 10 normals.² They found similar increases in flow both in patients with CAD and normals and concluded that dipyrindamole did not produce a coronary steal. However, since none of their patients in their study developed ST-segment changes after dipyrindamole, it could be argued that they simply studied a group of patients who happened not to develop a steal. Also, the validity of using great cardiac vein flow as a marker of flow to the LAD could be questioned since there was no significant difference in resting flow between the normals and nine of the patients who had had myocardial infarction and were found to have a totally occluded LAD at catheterization (data from their Table I).

The overwhelming majority of patients who develop electrocardiographic changes with dipyrindamole will have ST-segment depression; ST-segment elevation is extremely rare. There are reports of ST-segment elevation in the literature, but the mechanism causing it in these cases cannot be stated with certainty. Lewen *et al.* reported a patient who initially developed chest pain and ST depression after dipyrindamole, which were reversed by aminophylline and nitroglycerin.¹⁰ Thirty min later she developed chest pain and persistent ST-segment elevation which was refractory to medical therapy and required emergency angioplasty. Picano *et al.* reported the results of dipyrindamole echocardiography in 14 patients without a history of myocardial infarction who had ST-segment elevation with exercise.¹¹ Seven of these patients also developed ST-segment elevation after dipyrindamole infusion. Most of these patients, however, were also noted to have had spontaneous chest pain associated with ST-segment elevation. It seems, therefore, that most of these patients had significant vasoreactivity and clinical instability.

Although we were unable to obtain redistribution images, the normal resting wall motion on ventriculography demon-

FIG. 3 Cardiac catheterization revealed 100% occlusions of the (A) left anterior descending (LAD), and (B) right coronary arteries (RCA). (C) Both the LAD and RCA could be seen filling by collaterals (right anterior oblique view).

FIG. 4 Ventriculography showed normal global systolic function and normal wall motion in the anterior and inferior walls.

strates that most, if not all, of the myocardium in the anterior and inferior walls was still viable. This, in the presence of occluded vessels and visible collaterals, makes it clear that this patient had a large amount of myocardium totally dependent upon collateral circulation. The fact that the vessels were occluded excludes spasm and transient thrombosis in the LAD or right coronary arteries as mechanisms of ischemia. Although transient spasm in the circumflex cannot be completely excluded, this seems unlikely since spasm in the circumflex in a patient with total occlusions of both the LAD and RCA would eliminate all coronary blood flow and quickly lead to cardiovascular collapse. Although the patient's heart rate response to dipyridamole was above average, his initial blood pressure response was within the average range and did not drop sufficiently to implicate hypotension as the cause of the ischemia. There was a strong sympathetic response, but only after the development of chest pain and ECG changes. The exclusion of infarction, low likelihood of spasm, as well as the rapid reversal with intravenous aminophylline suggest strongly that the underlying mechanism of this severe ischemia was a coronary steal and support the notion that dipyridamole can induce ischemia by creating a coronary steal in patients with coronary artery disease.

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