Case reports

Mechanisms of myocardial ischemia in a patient with left main coronary artery atresia

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This report describes the different clinical and instrumental manifestations of coronary ischemia in a patient with left main coronary artery atresia. Exercise test and thallium-201 perfusion scintigraphy during isometric exercise test were negative for angina and electrocardiographic changes. Conversely, dipyridamole infusion caused severe angina, marked ST-segment changes and diffuse thallium-201 uptake abnormalities. This peculiar anatomical condition offers the opportunity of highlighting the role played by the microcirculation in determining myocardial ischemia.

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Among all cases of anomalous origin and distribution of the coronary arteries, isolated congenital atresia of the left main coronary artery is extremely rare and seldom reported[1]. Besides those cases due to atherosclerotic disease, the findings of acquired lesions as in Kawasaki disease, polyarteritis nodosa, Takayasu disease, or embolic episodes are more common[2]. The natural history of this disease invariably leads to premature ischemic heart disease and often the diagnosis is made at autopsy. Surgical therapy significantly modifies the prognosis of these patients.

From a pathophysiological point of view this rare anatomical abnormality offers the unique opportunity to investigate the *in vivo* mechanisms of myocardial ischemia in the presence of a single left coronary artery supplying flow retrogradely to the myocardial system. Indeed, in this anatomical setting, the pathogenesis of myocardial ischemia and particularly the nature of compensatory antiischemic mechanisms are still uncertain mainly because of the lack of information during different stress tests. We describe the case of a patient with congenital atresia of the left main coronary artery and attempt to characterize the mechanisms of myocardial ischemia in this peculiar anatomical condition.

Case report

A 27-year-old man was referred to us for frequent episodes of angina mainly at rest. Anginal symptoms had started at the age of 7. During the first two decades of life, because of inconsistency and variability of symptoms, their brief duration and the normal appearance of rest ECG tracing, further tests were withheld. At the age of 25 the patient started to complain of a worsening in the frequency and intensity of symptoms. At that time a maximal treadmill exercise test was negative for symptoms and ischemic ECG changes; a 24-hour Holter monitoring was negative for arrhythmias and ischemic ECG changes and an echocardiographic study showed normal cardiac structure and function. Eventually, minor ischemic-like ST-segment changes during an episode of rest angina prompted further diagnostic evaluation. Thallium-201 perfusion scintigraphy during isometric exercise test revealed a small reversible defect in the apical wall in the absence of pain and ECG changes (Fig. 1). During isometric exercise, brachial blood pressure rose from 120/80 to 140/85 mmHg and heart rate from 68 to 91 b/min. By contrast, thallium-201 perfusion scintigraphy during dipyridamole infusion caused severe angina, marked ischemic ST-segment changes in all precordial leads and diffuse uptake abnormalities (Fig. 1). During dipyridamole infusion, brachial blood pressure went from 120/80 to 115/75 mmHg and heart rate from 72 to 81 b/min. Echocardiographic examination during dipyridamole infusion showed a marked hypokinesia of the

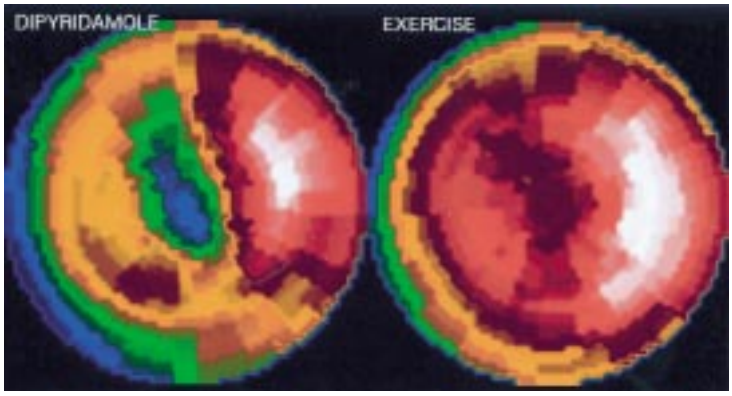

Figure 1. *Bull's eye view of thallium-201 scintigraphy after dipyridamole infusion showing large perfusion defects in the septal, apical, and anterior wall of the left ventricle* (left). *The same view after a maximal exercise stress test did not show any significant decrease in myocardial perfusion in the left ventricle* (right).

left ventricular septum and antero-lateral wall. In both cases, aminophylline infusion promptly reversed angina, ischemic ST-segment changes and functional abnormalities. At coronary angiography the left coronary ostium could not be found. A dominant right coronary artery provided collaterals to the left descending coronary artery through the interventricular septum and to the circumflex artery via the postero-lateral vessels. At surgery, the left internal mammary artery was anastomosed to the left anterior descending coronary artery. The postoperative course was uneventful. Angiography performed 1 week after surgery demonstrated patency of the internal mammary artery graft with disappearance of the collateral vessels (Fig. 2). Nine months after surgery, dipyridamole thallium-201 myocardial scintigraphy showed normal perfusion of the left ventricle.

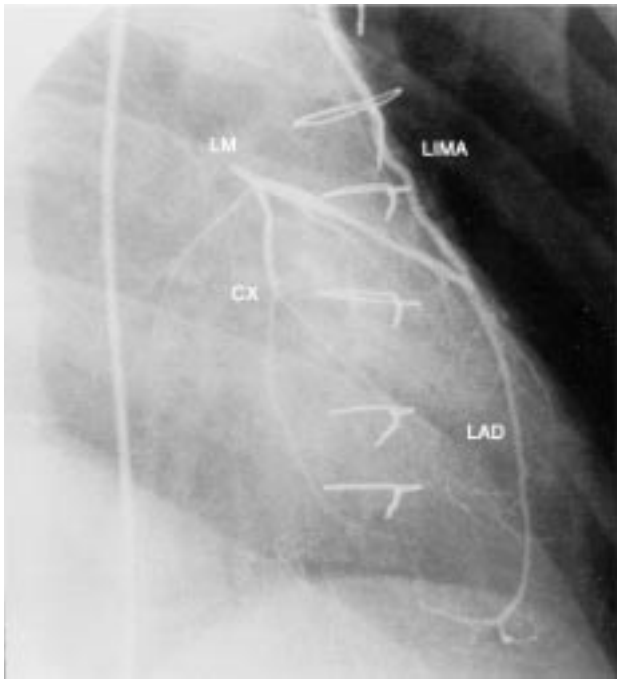

Figure 2. *Coronary angiography after coronary bypass grafting. The left internal mammary artery provides flow anterogradely to the left coronary system. Collateral vessels with the right coronary system are no longer present. CX = circumflex coronary artery; LAD = left anterior descending coronary artery; LIMA = left internal mammary artery; LM = left main coronary artery.*

Discussion

Congenital malformations of the left main coronary artery are rare and their etiopathogenesis can be ascribed to embryogenic defect or inflammatory process occurring during fetal or neonatal life. Similarly to the single right coronary artery, the entire coronary circulation depends upon the right coronary artery. However, in the former condition the anomaly is not responsible for ischemia since the coronary flow is always antegrade, while in the case of left main coronary atresia, the flow is retrograde and the left coronary system is totally dependent upon the collaterals present between the right and left coronary bedding. This peculiar anatomical situation provides the opportunity of investigating the mechanisms of myocardial ischemia under different pathophysiological conditions.

The observations that our patient experienced chest pain mainly at rest and that maximal exercise test was negative for symptoms and ischemic ECG changes suggest that an increase in myocardial oxygen demand was unlikely to be the mechanism responsible for myocardial ischemia; conversely, it indicates that the episodes of myocardial ischemia were more likely caused by vasoconstriction of collateral or distal coronary vessels resulting in a primary reduction in coronary blood flow. Indeed, this pathogenetic mechanism of transient myocardial ischemia has been documented in a previous study in patients with stable angina, total occlusion of a single coronary artery that was supplied by collateral vessels, normal ventricular function, no evidence of coronary artery spasm, and no other coronary stenoses[3].

The absence of ischemic ECG changes during exercise might be due to the combination of two mechanisms: 1) an increase in perfusion pressure in collater-

al giving coronary artery branches resulting in an increase of perfusion pressure at the outlet of the collateral circulation; 2) the activation of sympathetic-mediated vasoconstriction of the subepicardial coronary microcirculation in the territory of the left anterior descending coronary artery adequate to prevent subendocardial underperfusion[4]. The absence of any significant thallium-201 perfusion defects during isometric exercise, which promotes sympathetic-mediated vasoconstriction, supports this mechanism.

Conversely, the infusion of dipyridamole, a potent non-selective vasodilator of coronary microcirculation, caused diffuse regional myocardial underperfusion, as demonstrated by thallium-201 uptake abnormalities, severe enough to cause objective and subjective signs of myocardial ischemia. The regional underperfusion during dipyridamole infusion might have been caused by two possible mechanisms: 1) a reduction of perfusion pressure in collateral giving coronary artery branches; 2) enhanced subepicardial dilation in the territory of the left anterior descending coronary artery resulting in transmural steal and subendocardial underperfusion in the presence of a suboptimal perfusion pressure at the outlet of the collateral circulation (due to the pressure drop through the collateral circulation itself)[5]. As the reduction in aortic pressure during dipyridamole was negligible, transmural redistribution of myocardial perfusion was probably the prevailing mechanism of ischemia. The administration of aminophylline promptly reversed subendocardial ischemia. Of note, aminophylline, a potent non-selective antagonist of adenosine receptors, improves ischemic threshold by counteracting transmural coronary blood flow steal in patients with both epicardial coronary stenoses and microvascular angina[5-8]. Aminophylline increases epicardial coronary vascular resistance probably by promoting the release of catecholamines from perivascular nerve endings thus favoring subendocardial perfusion[9].

In conclusion, this rare case report provides further evidence for the crucial role played by the coronary microcirculation in determining both spontaneous and induced myocardial ischemia.

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