Recurrent Myocardial Infarction Associated With Cocaine Abuse in a Young Man With Normal Coronary Arteries: Evidence for Coronary Artery Spasm Culminating in Thrombosis

FRANKLIN H. ZIMMERMAN, MD,* GREGORY M. GUSTAFSON, MD, HARVEY G. KEMP, Jr., MD, FACC

Myocardial infarction has been reported as a consequence of cocaine abuse (1–9) in patients with and without coronary atherosclerosis. However, the underlying mechanism for myocardial infarction in this setting remains obscure. This report describes a young man suffering from recurrent myocardial infarction associated with cocaine abuse, despite the presence of angiographically normal coronary arteries. Evidence supports coronary artery spasm culminating in coronary thrombosis, as the probable mechanism.

Case Report

Clinical presentation. A 29 year old man noted chest discomfort at rest approximately 5 hours after intranasal administration of an unspecified amount of cocaine. He had been in excellent health, and other than tobacco use had no risk factors for coronary atherosclerosis. His symptoms worsened over the next 7 hours and he presented at the emergency room, where an electrocardiogram revealed ST elevation in leads II, III and aVF, with T-wave inversions in leads III and aVF. Physical examination, chest X-ray film and routine laboratory values were all normal. The patient was admitted to the coronary care unit, where serial electrocardiograms demonstrated evolutionary changes consistent with a non-Q wave inferolateral wall myocardial infarction (Fig. 1). Maximal serum creatinekinase (CK) elevation was 438 IU/liter (normal, 0 to 125) with an MB fraction of 3.2% (normal, 0 to 3).

Course and catheterization findings. Seven days after admission, cardiac catheterization demonstrated angiographically normal coronary arteries and mild inferoapical hypokinesia of the left ventricle. Ergonovine administration failed to induce coronary spasm. The patient was discharged on treatment with sublingual nitroglycerin alone, and he was well until 2 months later when he was awakened from sleep with chest discomfort, again 5 hours after use of an unspecified amount of cocaine. He took two sublingual nitroglycerin tablets with relief of symptoms and presented to the emergency room, where an electrocardiogram was unchanged from that at discharge from his previous hospitalization. He was admitted to the coronary care unit and treated empirically with topical nitrates and diltiazem. Serial electrocardiograms and serum CK failed to show evidence for new myocardial necrosis, and the patient was well except for several brief episodes of chest discomfort. On the third hospital day, he developed severe chest pain at rest with ST elevation in leads V1 to V6 (Fig. 2A). He denied use of cocaine while in the hospital. Sublingual nifedipine and intravenous nitroglycerin were administered with complete resolution of symptoms and ST changes (Fig. 2B). A twodimensional echocardiogram, performed while the patient experienced pain, revealed severe hypokinesia of the inter-
ventricular septum and anterior left ventricular wall with marked improvement in wall motion abnormalities after treatment. The patient did well for 2 hours, when symptoms and electrocardiographic changes that were refractory to medical management recurred.

Emergency cardiac catheterization revealed complete occlusion of the left anterior descending coronary artery at its origin (Fig. 3A). Care was taken to ensure that subselective injection of the left circumflex artery had not occurred and that actual occlusion of the left anterior descending artery was present. After administration of intracoronary nitroglycerin, the left anterior descending artery could be visualized and demonstrated an intraluminal filling defect in the proximal portion of the artery that was consistent with thrombus (Fig. 3B). A total of 120,000 U of intracoronary streptokinase was administered, which partially recanalized the artery and resulted in resolution of symptoms. The procedure was complicated, however, by intimal dissection of the proximal portion of the left anterior descending artery, secondary to placement of the guiding catheter for selective streptokinase infusion. The patient returned from the procedure in good condition and was treated with heparin, nitrates and diltiazem. Serial electrocardiograms demonstrated biphasic T wave changes in leads

Figure 1. Electrocardiogram during patient's first hospitalization demonstrating T wave abnormalities in leads II, III, aVF, V₃ and V₆ and ST elevations in leads I, II, aVL and V₂ to V₆.

Figure 2. A, Electrocardiogram during patient's second hospitalization showing ST elevation in leads V₁ to V₆ consistent with acute anterior transmural ischemia. B, Electrocardiogram after intravenous nitroglycerin and oral nifedipine therapy demonstrating resolution of ST changes.
V_2 to V_4. Peak serum CK was 508 IU/liter with an MB fraction of 5.1%. Repeat coronary arteriography 24 hours later showed near complete resolution of the previous filling defect; however, it also demonstrated a progressive coronary artery dissection involving the left anterior descending artery and intermediate arteries (Fig. 3C).

The patient underwent uneventful coronary bypass surgery with repair of the dissection. At surgery, a small intramural plaque was present at the site of the original left anterior descending artery occlusion. The patient has been well on beta-adrenergic blocker therapy and strict prohibition of the use of cocaine.

**Figure 3.** Left coronary angiograms in the left anterior oblique view. A, Demonstrating complete occlusion of the left anterior descending artery (LAD) at its origin (arrow). B, After intracoronary nitroglycerin demonstrating a filling defect in the proximal portion of the left anterior descending artery (arrow). C, 24 hours after intracoronary streptokinase therapy demonstrating improved flow and partial lysis of the previous filling defect (arrow). Cx = circumflex artery; Im = intermediate artery.
Discussion

Pathogenesis of infarction. Myocardial infarction is being recognized more frequently as a complication of the use of cocaine. In patients with fixed coronary stenosis, cocaine may result in ischemia by virtue of its action on catecholamine release, thereby elevating heart rate, blood pressure and, hence, myocardial oxygen consumption. Some patients suffering from myocardial infarction associated with cocaine abuse do not have significant coronary atherosclerosis, and the cause of infarction in these patients remains obscure (1,2,4,6,8). The present case provides the first evidence that cocaine may induce coronary artery spasm and subsequent thrombosis in persons with minimal coronary artery disease.

The syndrome of myocardial infarction with angiographically normal coronary arteries was first described in 1970 (10). The prevalence of normal or near normal coronary arteries in patients with myocardial infarction is now recognized to be between 1 and 3% (11,12). The pathogenesis of this syndrome has yet to be defined; however, coronary artery spasm culminating in coronary thrombosis is an attractive hypothesis. The patient described herein provides documentation of such a sequence and suggests that it may be precipitated specifically by the use of cocaine.

The diagnosis of coronary spasm in this patient is supported by the demonstration of chest pain, ST elevation and wall motion abnormalities that were initiated at rest and subsequently resolved after nitrate and calcium channel blocker therapy. Alternative concepts of either coronary embolization or in situ thrombosis with rapid clot lysis would be extremely unlikely in an individual with widely patent coronary arteries who has no predisposing factors for thromboembolism (13,14). Furthermore, the demonstration of improved flow in an occluded artery after intracoronary administration of nitroglycerin has been considered highly supportive of coronary spasm (15). The negative response to ergonovine testing in this patient does not preclude the diagnosis of isolated coronary spasm, but it does eliminate the syndrome of variant angina. Ergonovine testing was performed in four previously reported patients with normal coronary arteries who sustained a myocardial infarction associated with cocaine abuse, and in all the results were negative (1,6,8). This agrees with data indicating that a positive response to ergonovine is seen in the setting of myocardial infarction with normal coronary arteries only in those patients who have the syndrome of variant angina (16).

Cocaine and coronary vasoconstriction. The effect of cocaine on the coronary circulation has not been well studied. Cocaine is a powerful sympathomimetic amine with local vasoconstrictor properties and it sensitizes peripheral organs to the effects of endogenous catecholamines (17). Recent data (18) demonstrated a direct vasoconstrictor effect of cocaine on the coronary circulation. It is unknown whether additional factors mediate this response. For example, it has yet to be determined why a patient who repeatedly uses the drug would develop coronary spasm at one time and not another. Recurrent myocardial ischemia secondary to cocaine use has been alluded to in previous reports (3,4,6,9), but in only one other instance has it been documented in a patient with normal coronary arteries (6). Furthermore, some reports (4-6) note the development of symptoms shortly after the inhalation of cocaine, whereas others (1,2) describe the onset of symptoms only after several hours. This discrepancy may be caused by significant individual variability in the absorption of cocaine following intranasal administration (19).

Coronary artery spasm and myocardial necrosis. Our patient had unequivocal evidence of two separate episodes of myocardial necrosis that were temporally related to the use of cocaine. A prodrome consistent with coronary artery spasm was documented to have preceded the second episode and may be hypothesized to have preceded the first. Each episode produced different electrocardiographic manifestations, but it is not possible to conclude that spasm occurred at separate sites (20). It is also unclear why this patient developed one episode of severe coronary spasm after 2 days in the hospital, long after plasma levels of cocaine would have been expected to decline. A plausible explanation is that the initiating episode of cocaine-induced spasm resulted in endothelial disruption at the site of an atherosclerotic plaque, thereby initiating a cycle of platelet aggregation (21). The necessity for surgery in this patient provided confirmation that an atherosclerotic plaque was present at the site of spasm, despite the absence of angiographically normal coronary arteries. Vasoactive prostanoids released by platelets at this site may, in turn, have eventually stimulated further vasoconstriction (22,23). Such a sequence may have been active, but not recognized as such because of modification due to antianginal therapy. It may be further concluded that this cycle eventually produced severe coronary spasm that became unresponsive to conventional vasodilating agents when it culminated in coronary thrombosis.

Conclusion. The use of cocaine has increased dramatically in all age groups in recent years with a concomitant rise in cocaine-related deaths (24). It has been demonstrated that persons who use cocaine are at risk for myocardial infarction, which may be caused by coronary artery spasm. Whether or not all cocaine-related cases of myocardial infarction involve coronary artery spasm is unknown. Nevertheless, a careful inquiry concerning cocaine use should be obtained in all patients presenting with symptoms of myocardial ischemia and, if present, therapeutic measures should particularly include means to alleviate coronary artery spasm.

We express our appreciation to Esther Yulfo and Jeanne Hurd for careful preparation of the manuscript.
References


