Acute Non-Q Wave Cocaine-related Myocardial Infarction*

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Since our initial report in 1984 of six patients with AMI temporally related to cocaine use, we have observed 19 additional patients in whom ischemic chest pain syndromes occurred shortly after intranasal or IV use of cocaine or after smoking the drug. Seventeen patients (89 percent) developed non-Q wave infarction and two had Q-wave infarction. One patient manifested angina with striking ST-segment elevation. None of the patients had diabetes or hypertension, and all but one were cigarette smokers. The serum cholesterol level was 162 ± 7 mg/dl. Four of the five patients who consented to coronary angiographic studies displayed normal coronary arteries, and one showed proximal stenosis of the right coronary artery. The cold pressor test was performed in seven patients; none had angina or ECG changes induced by cold stimulation. We conclude that T-wave infarction is a common form of an acute cardiac event related to cocaine abuse, and its pathogenesis may involve that of the cocaine-induced coronary vasospasm.

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With the widespread abuse of cocaine, toxicity to the drug has become more apparent.1 Most of the toxicity seen is of the overdose type, in which the cerebral effects of seizures, confusion, and psychosis are associated at highest doses with ventricular arrhythmia and, ultimately, ventricular fibrillation.5 It is likely that most acute overdose deaths resulting from cocaine use are mediated by acute ventricular fibrillation. Cocaine interacts with and potentiates the effect of norepinephrine.3,5 In addition to this acute overdose effect on the heart mediated through catecholamine excess, cocaine also has an effect on the heart that results in myocardial ischemia and myocardial infarction with or without coronary disease.

In 1980, our group began collecting data on patients in whom myocardial infarction occurred immediately after using cocaine or who suffered myocardial infarction at a very young age without risk factors and in the presence of long-term cocaine abuse. In 1982 and early 1984, two single cases were reported from two other institutions in which myocardial infarction occurred immediately after sniffing cocaine.6,7 In one of those cases, a coronary arteriogram was done and was normal. In late 1984, we reported the first series, to our knowledge, of such cocaine-induced infarcts, comprising six cases;6 others have now added more than 30 cases to the original report.8 In this article we add 19 additional cases, 17 of which demonstrated non-Q wave myocardial infarction, accumulated at the Brookdale Hospital Medical Center between 1984 and 1988, to bring our series to 25 cases. We will review these cases and the other published papers and define as fully as we can the clinical characteristics of these patients.

Methods

Patients were selected from those admitted to the coronary care unit between November 1982 and June 1987. Cases were selected on the basis of AMI that had developed within hours of cocaine use. Infarction was defined by either a diagnostic Q-wave or a T-wave (non-Q wave) infarction supported by elevations in the serum CPK level in the appropriate clinical setting. The criteria used to consider a patient as having suffered a non-Q wave infarction are those established previously:9 an acute episode of chest pain without a prior history of myocardial infarction, accompanied by symmetric and deep inversion of the T wave persisting for at least 48 h and elevations of the serum CPK level, but unassociated with abnormalities in the QRS complex. The normal serum CPK level in our institution is up to 90 IU/L for males and up to 50 IU/L for females. In one instance (case 14) infarction was diagnosed by a very strong clinical case, striking ECG abnormalities but without an enzyme elevation. Each patient was invited to have a coronary angiographic study, but only five patients agreed. Seven patients consented to have a cold pressor test performed as previously described,11,12 during which the patient’s right hand was immersed in ice water for one min while the blood pressure and an ECG were monitored.

All results are expressed as means ± SE. The Student t test was used to assess the statistical significance. A value of p<0.05 is considered statistically significant.

Results

The clinical characteristics of the 19 patients (15 male and 4 female) are listed in Table 1. The average age of the patients is 31 ± 2 years, well below the typical age at which patients exhibit clinical coronary artery disease, and the average age of female patients is even lower, 23 ± 4 years. It is evident that T-wave
Table 1 — Clinical Data of 19 Patients with Cocaine-induced Myocardial Infarction

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Type of Infarction</th>
<th>Peak CPK Value</th>
<th>Administration-to-Symptom Interval</th>
<th>Route of Cocaine Use</th>
<th>Concomitant Drug Use</th>
<th>Serum Cholesterol</th>
<th>Diabetes</th>
<th>History of Smoking</th>
<th>Hypertension</th>
<th>Angiography</th>
<th>Additional Data</th>
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</thead>
<tbody>
<tr>
<td>1, 30, M</td>
<td>T wave infarction</td>
<td>747 5 min Nasal &amp; “Crack”</td>
<td>0</td>
<td>146</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Normal coronaries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2, 22, M</td>
<td>T wave infarction</td>
<td>382 30 min “Crack”</td>
<td>0</td>
<td>202</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Normal coronaries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3, 18, F</td>
<td>T wave infarction</td>
<td>112 8 h “Crack” &amp; free basing</td>
<td>0</td>
<td>137</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4, 36, F</td>
<td>T wave infarction</td>
<td>900 Uncertain IV</td>
<td>0</td>
<td>160</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5, 46, M</td>
<td>T wave infarction</td>
<td>440 1-2 h “Crack” Marijuana</td>
<td>0</td>
<td>185</td>
<td>0</td>
<td>Yes</td>
<td>+</td>
<td>Not done</td>
<td></td>
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<tr>
<td>6, 22, M</td>
<td>T wave infarction</td>
<td>531 Uncertain IV</td>
<td>0</td>
<td>192</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
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<tr>
<td>7, 27, M</td>
<td>T wave infarction</td>
<td>147 1-2 h Nasal</td>
<td>0</td>
<td>157</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Normal coronaries</td>
<td></td>
<td></td>
<td>Initial marked ST elevation during chest pain</td>
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<tr>
<td>8, 25, F</td>
<td>T wave infarction</td>
<td>284 6 h “Crack”</td>
<td>0</td>
<td>143</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9, 20, M</td>
<td>T wave infarction</td>
<td>378 Immediate “Crack”</td>
<td>0</td>
<td>143</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
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<tr>
<td>10, 25, M</td>
<td>T wave infarction</td>
<td>301 20 min “Crack”</td>
<td>0</td>
<td>Not done</td>
<td>0</td>
<td>Not done</td>
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<tr>
<td>11, 30, M</td>
<td>T wave infarction</td>
<td>358 2 h Nasal Alcohol</td>
<td>162</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
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<td></td>
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<tr>
<td>12, 49, M</td>
<td>Q wave inferior infarction</td>
<td>582 A few min Nasal Marijuana</td>
<td>211</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Proximal occlusion of RCA</td>
<td></td>
<td></td>
<td></td>
<td>90% proximal LAD stenosis 11 months later</td>
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<tr>
<td>13, 30, M</td>
<td>T wave infarction</td>
<td>145 Immediate “Crack”</td>
<td>0</td>
<td>131</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
<td></td>
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<tr>
<td>14, 20, F</td>
<td>T wave infarction</td>
<td>48 4 h “Crack” Methadone</td>
<td>0</td>
<td>Not done</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
<td></td>
<td>Infarction associated with ventricular tachycardia</td>
</tr>
<tr>
<td>15, 30, M</td>
<td>T wave infarction</td>
<td>271 Within min Nasal and IV</td>
<td>0</td>
<td>208</td>
<td>0</td>
<td>0</td>
<td>Normal coronaries</td>
<td></td>
<td></td>
<td>Negative cold pressor test during coronary angiography</td>
<td></td>
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<tr>
<td>16, 35, M</td>
<td>Q wave anterior infarction</td>
<td>330 30 min “Crack” and IV</td>
<td>178</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17, 19, M</td>
<td>T wave infarction</td>
<td>147 Within min “Crack”</td>
<td>0</td>
<td>Not done</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
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<tr>
<td>18, 52, M</td>
<td>T wave infarction</td>
<td>141 Uncertain IV</td>
<td>0</td>
<td>141</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
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<tr>
<td>19, 19, F</td>
<td>T wave infarction</td>
<td>117 2-3 h Nasal</td>
<td>0</td>
<td>136</td>
<td>0</td>
<td>Yes</td>
<td>0</td>
<td>Not done</td>
<td></td>
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</tr>
</tbody>
</table>

*CPK and serum cholesterol levels measured in IU/L and mg/dL, respectively. RCA, right coronary artery; LAD, left anterior descending coronary artery.

Infarction predominates in our current series (17 of 19 patients, or 89 percent), which represents all of the patients seen by us in the study period. The serial ECGs in a typical patient (case 13) are illustrated in Figure 1. An initial ECG showed upright T-waves in leads 2, 3, aVL, and V₁. Approximately 21 h later, inversion of T-waves developed in these leads, and deep, symmetric T-wave inversion eventually evolved. It should be noted that in most cases the ischemic episode was clearly associated with the use of cocaine and that all common routes of administration (intranasal, IV, and smoking in the form of "crack" cigarettes) were used. All patients were alert and fully oriented, and in none was seizure activity noted. None of the patients had diabetes mellitus or hypertension, and all but one were cigarette smokers. The serum cholesterol level was 162 ± 7 mg/dL. No death occurred in the present series. Four of the five patients who consented to coronary angiographic studies displayed normal coronary arteries, and one showed proximal stenosis of the right coronary artery; in none was spasm induced by ergonovine administered during the cardiac catheterization study.

Angina with marked ST-segment elevations developed in one patient (case 7). This 27-year-old man experienced severe substernal chest pain after snorting cocaine. An ECG taken 2 h later, when he arrived at the hospital emergency room, displayed marked ST-segment elevation in leads V₅,6 and less prominent elevation in leads 1, aVL, 2, 3, and aVF (Fig 2). The ECG reverted to nearly normal in 1 h (Fig 3), associated with cessation of the chest pain. No arrhythmia, atrioventricular block, or hypotension occurred. A coronary arteriography study performed on the fourth hospital day revealed normal coronary arteries, and an ergonovine challenge failed to provoke coronary artery spasm. A repeated ECG taken one month later showed only the normal variant of early repolarization (Fig 4).

In seven patients who underwent the cold pressor test, cold stimulation caused a significant increase in the brachial systolic blood pressure (from 108 ± 4 to 127 ± 1 mm Hg; p<0.01). However, in none did angina or ECG changes result from cold stimulation. In case 15, normal coronary arteries were seen during the arteriographic study, and cold pressor stimulation did not provoke coronary artery spasm.

**DISCUSSION**

The patients with AMI after cocaine abuse in our present series shared many clinical features of the patients in our previous report, including youth;
absence of hypertension, diabetes mellitus and hyperlipidemia; and close temporal relationship between the myocardial ischemic episodes and cocaine use. A widespread occurrence of non-Q wave infarction, evident in the present series (17 of 19 patients or 89 percent), was not described in our previous report.8

In our initial report,5 five of the six cases had Q-wave infarction, which was observed in only two of the 19 patients in the current series. It is unlikely that the syndrome has changed since our original 1980-1982 collection. In our initial series we did not include what we then thought of as marginal cases in order to establish the validity of the syndrome. Now that the syndrome is well accepted, we have broadened its

FIGURE 2. Electrocardiogram in case 7 taken during an episode of chest pain after cocaine snorting, demonstrating ST-segment elevation in leads 1, 2, 3, aVL, aVF, and V1.

FIGURE 3. ECG in the same patient taken 1 h later, when the chest pain subsided, demonstrating reversion of the ST-segment.
clinical spectrum in the current series and included as myocardial infarction cases that show deep symmetric T inversions persisting more than 48 h and associated with CPK elevation. One patient (14) was accepted as infarction without documented CPK elevation, but the ECG changes were striking, and ventricular tachycardia was associated.

It is clear that the use of cocaine by any of the available routes can produce myocardial ischemia and myocardial infarction. In many of the patients this occurs in the absence of significant underlying coronary disease. In such patients, it has been a reasonable clinical assumption that cocaine has somehow precipitated spasm of the coronary arteries, leading to ischemia and infarction. In some patients, the cocaine-induced ischemia is superimposed on underlying coronary disease, sometimes of minor and sometimes of considerable degree. In a few cases, thrombi in normal or nearly normal arteries seem to have resulted from cocaine abuse and led to myocardial infarction. One might postulate that such thrombi could result from prolonged spasm and intimal damage, but this has not been established. The patients found to have preexisting coronary disease generally were young, and the majority were not hyperlipidemic, diabetic, or hypertensive, although most were cigarette smokers. Finding atherosclerosis in such patients at these young ages is suspicious but not conclusive of a contributory effect on the acceleration of atherosclerosis by cocaine. If such an effect is indeed present, the series so far collected has not established it. There are, however, no data available to exclude the possibility that atherosclerosis may be accelerated by intimal damage due to spasm triggered by cocaine. Alternatively, some of these patients may have developed direct endothelial injury in the coronary artery associated with cocaine abuse. Several years ago, Furchgott and Zawadzki observed that an intact endothelium is critical for acetylcholine to exert its vasodilator effect on arteries. It has been established that a large body of endogenous humoral substances relax blood vessels indirectly by stimulating the release of endothelium-derived relaxing factor(s). In cardiac transplant patients in whom the endothelium of the coronary artery is injured, the release of endothelium-derived relaxing factor is lost, and the normal vasodilator response to acetylcholine is replaced by paradoxical vasoconstriction. It is thus conceivable that in some patients with myocardial infarction associated with cocaine abuse, damage of endothelium occurs, leading to a loss of vasodilator function and, on exposure to cocaine, hypercontractility of coronary arteries ensues.

Sadly, the widening use of cocaine, particularly by children, may resolve the issue of acceleration of atherosclerosis and cocaine-induced infarction; the inference may be established without controlled studies. At present, however, this can only be a suspicion.

Our previous animal study, in which a significant and sustained increase in coronary vascular resistance occurred after cocaine injection in dogs, suggests that cocaine use induces coronary arterial vasoconstriction. The ability of cocaine to augment the contractile response of vascular smooth muscle has been thought to result from inhibition of neuronal uptake of norepinephrine by the adrenergic nerve endings, thereby providing the effectors with increased concentrations of norepinephrine for action. Recent studies in isolated blood vessel preparations have documented, however, that the cocaine also evokes release of norepinephrine from adrenergic nerve terminals and may directly activate the effecter cells. There is also evidence to suggest that IV administration of cocaine stimulates the CNS, resulting in an increase in the release of endogenous catecholamines from the sympathoadrenal medullary system. In view of the existence of α-adrenergic receptors in the coronary vasculature, the coronary vasoconstrictive response to cocaine observed in our study may be explained, in part, by the ability of cocaine to stimulate the neurogenic activity of coronary arteries. It should be noted that all of the dogs responded with increased coronary resistance and, therefore, increased vasoconstriction.

Ischemia and infarction are certainly uncommon complications of cocaine use in view of the large number of persons now abusing this agent. It is not clear whether the patients who get this reaction have an enhanced sensitivity to catecholamine-mediated vasoconstriction. We therefore performed the cold pressor test on these patients, a provocative test known to activate the adrenergic nervous system.

It is well established that the human coronary artery

Figure 4. ECG in the same patient taken one month later, displaying the normal variant of early repolarization.
is capable of rapidly altering vascular resistance during cold pressor stimulation. In a previous study of patients with obstructive coronary artery disease documented angiographically, coronary vascular resistance increased by 27 percent after 1-min of cold stimulation; it also precipitated angina in four of the 12 patients. In a similar study of 35 patients examined angiographically, cold stimulation provoked coronary artery spasm in seven patients, all had an atheromatous plaque at the site of spasm, one had chest pain, and two had ischemic changes on their ECG.

In none of the seven patients who underwent the cold pressor test was angina precipitated or were acute changes observed on the ECG. Cold stimulation activates the adrenergic nervous system but fails to elicit angina or ischemic manifestations. It thus seems unlikely that patients with cocaine-induced myocardial infarction are particularly vulnerable to neurally mediated coronary spasm and myocardial ischemia. Other factors will have to be examined.

It is clear that cocaine use can produce ischemia and myocardial infarction in human subjects with or without preexisting coronary disease. The occurrence of cocaine-induced non-Q wave infarction may be much more prevalent than has been appreciated. The mechanism may involve coronary spasm precipitated by cocaine-induced augmentation of adrenergic nervous activity or coronary endothelium injury, but this remains to be clarified.

REFERENCES

4 Verbeuren TJ, Vanhoutte PM. Cocaine and neuronal uptake in the canine saphenous vein. Naunyn Schmiedebergs Arch Pharmacol 1982; 321:207-12
6 Cregler LL, Mark H. Relation of acute myocardial infarction to cocaine abuse. Am J Cardiol 1985; 56:794
7 Weiss RJ. Recurrent myocardial infarction caused by cocaine abuse. Am Heart J 1986; 111:793
13 Pasternack FF, Colvin SB, Baumann FG. Cocaine-induced angina pectoris and acute myocardial infarction in patients younger than 40 years. Am J Cardiol 1985; 55:847
15 Furchgott RF, Zawadzki JV. The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. Nature 1980; 288:373-76
18 Kossowsky WA, Lyon AF, Chou SY. Cocaine and ischemic heart disease. Practical Cardiol 1986; 12:164-67
20 Chiuve EE, Kopin IJ. Centrally mediated release of cocaine of endogenous epinephrine and norepinephrine from the sympa-thoadrenal medullary system of unanesthetized rats. J Pharmacol Exp Ther 1978; 205:148-54