

## Case Report

## Acute Myocardial Infarction Following the Combined Use of Cocaine and Alcohol

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**Key words:**

**Acute myocardial infarction, cocaine abuse, ethanol.**

We describe the case of a 37-year-old man who presented with inferior wall myocardial infarction shortly after the concomitant use of cocaine and ethanol. The patient showed prompt ST resolution after thrombolytic therapy. Within two hours from his arrival at the hospital the patient had an episode of ventricular fibrillation, which was successfully treated with electrical cardioversion. Coronary angiography showed normal coronary arteries. The number of patients with acute myocardial infarction after the use of cocaine alone, or in combination with ethanol, is increasing in the USA and other countries; most are young adults. In Greece such cases are still rare, because of the lesser extent of cocaine abuse in the general population and the low sensitivity in recognising cocaine users who present with chest pain in the emergency department.

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Cocaine is an alkaloid produced by the leaves of the *Erythroxylum coca* bush. It may be taken orally, nasally, or intravenously.<sup>1,2</sup> In countries with a high level of cocaine use there have been many reports of patients, mainly young people, who suffered acute myocardial infarction after taking the drug on either an acute or a chronic basis.<sup>3,4</sup> The concomitant use of alcohol (ethanol) increases the risk of sudden death in these patients.<sup>5</sup> The incidence of ventricular arrhythmias in patients who are cocaine users and are hospitalised for myocardial infarction is relatively low (4-17%),<sup>6</sup> despite the fact that cocaine has been found to have an arrhythmogenic action.<sup>7</sup>

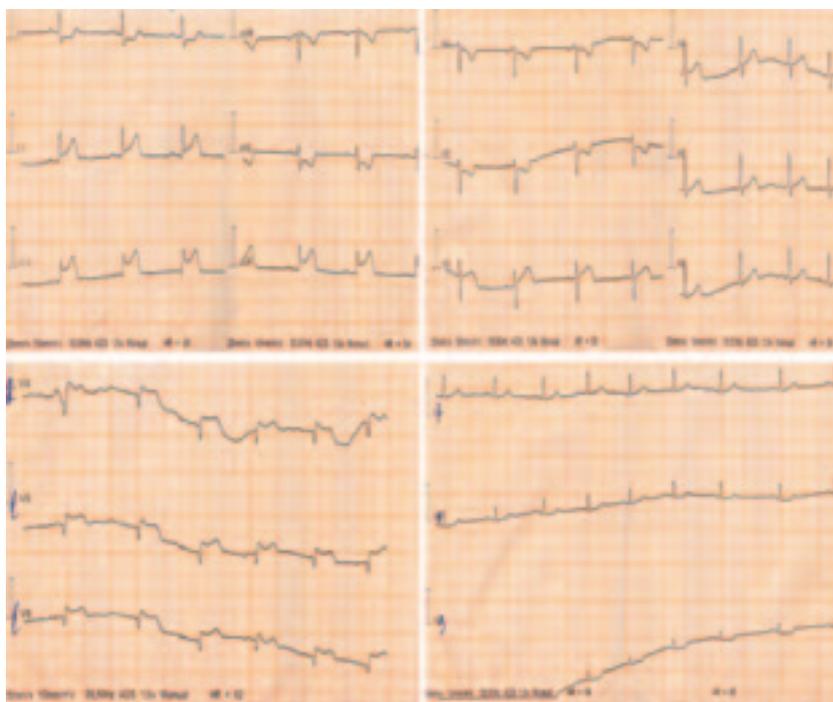
### Case presentation

A man aged 37 years, with a history of smoking and chronic occasional cocaine use, presented to our department complaining of constant retrosternal constrictive pain, reflecting to the left side, that had started 60 min before his arrival at the hospital. The

pain was accompanied by extreme perspiration and nausea. The patient reported sniffing cocaine and drinking a large quantity of alcohol 30 min before the pain started. During the clinical examination he appeared sickly, blood pressure was 120/80 mmHg bilaterally, heart rate was 60/min, and heart sounds were diminished, regular, with an additional fourth sound and without murmurs. The patient's jugular veins showed dilation, while lung examination was normal.

The admission ECG, with simultaneous recording of right and posterior leads, showed ST elevation >1 mm in leads II, III, aVF, and V<sub>4</sub>R, as well as ST depression in leads I, aVL, V<sub>1</sub> and V<sub>2</sub> (Figure 1).

The patient was admitted to the coronary care unit. Since the ST elevations persisted for >15 min, he was given tenecteplase, as well as aspirin, intravenous heparin, pethidine for the pain, diazepam, atorvastatin and lisinopril. Nitrates were avoided in the initial phase because of the right ventricular involvement, while in view of the recent history of cocaine use beta-blockers were not given. The patient's pain



**Figure 1.** The patient's 12-lead ECG on admission, with simultaneous recording of right and posterior leads. ST elevation can be seen on the inferior and right leads.

receded rapidly and the ST elevations on the ECG decreased. Within 30 min of the initiation of thrombolysis the patient suffered an episode of ventricular fibrillation, which was cardioverted with a non-synchronised 360 J shock from a monophasic defibrillator. Subsequently, the patient remained free of symptoms. His electrocardiographic (appearance of q waves in leads II, III, aVF, Figure 2) and biochemical (peak total CK 1116 IU/L, CK-MB 155.2 IU/L, troponin T 2.17 ng/ml) findings were typical of an inferior wall infarction. The two-dimensional echocardiogram prior to the patient's

discharge showed hypokinesia of the basal and middle sections of the inferior wall.

In view of the reported cocaine use, a urine sample was taken during the first 24 hours of hospitalisation so that it could be sent for toxicological analysis in the forensics laboratory of the Aristotelian University of Thessaloniki. Ethical considerations required the patient's permission for this analysis; since he refused, the sample was not sent.

Coronary angiography, performed 8 days after the initial event in "Cianus Stavros", a private institu-



**Figure 2.** The patient's ECG before discharge from the hospital, showing q waves on the inferior leads.

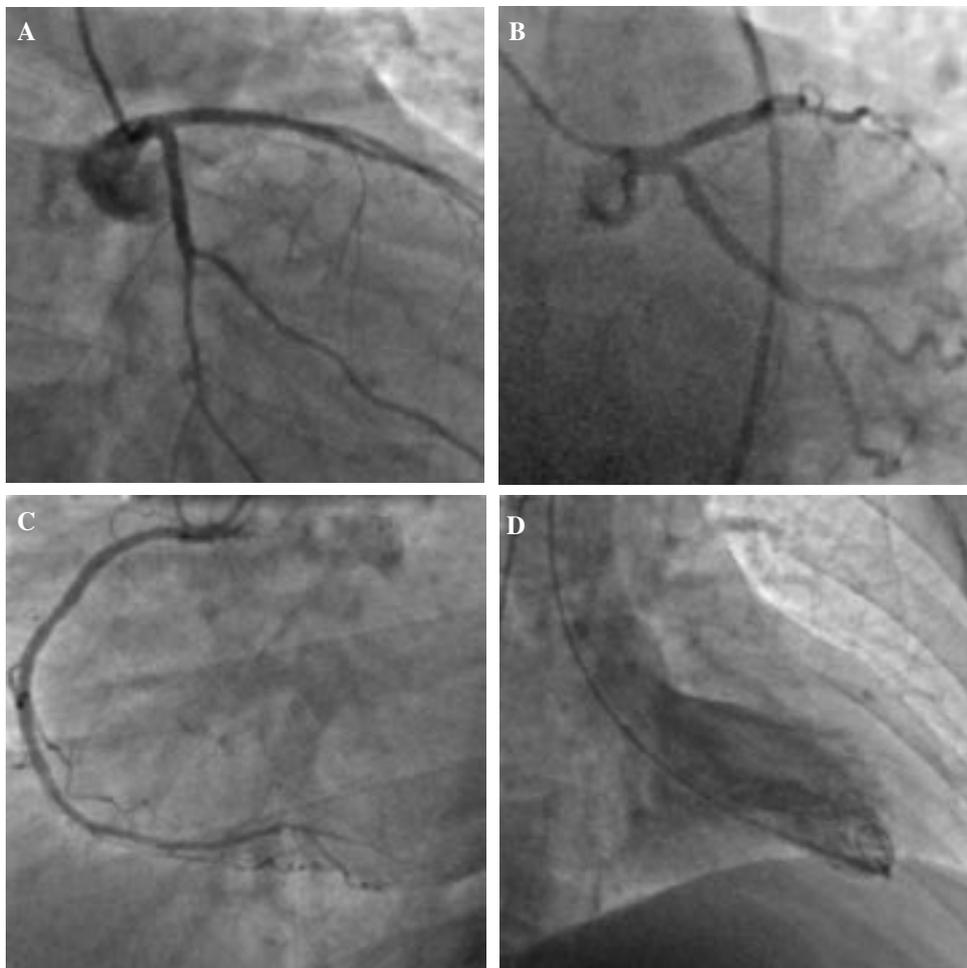
tion in Thessaloniki, showed normal coronary arteries (Figure 3). The patient was advised to stop smoking and to refrain from using cocaine and alcohol. He was put on a discharge regimen of aspirin, statin and sublingual isosorbide dinitrate to be taken in the case of angina.

### Discussion

Cocaine, as stated above, is an alkaloid produced by the leaves of the *Erythroxylum coca* bush. It is available in two forms, as a hydrochloric salt and as free base. It may be taken orally, nasally, or intravenously, but it is well-absorbed by all the body's mucous membranes.<sup>1</sup> Its half life ranges from 45 to 90 min and for this reason it is detectable in the user's blood for only a few hours after it is taken. Its metabolites, however, can be detected

in the blood and urine for 24-36 hours, allowing a larger time window for identifying users.<sup>2</sup> In developed countries such as the USA and Australia, an increase in cocaine use has been observed in the general population during the last decade.<sup>8,9</sup> This has led to an increase in the number of patients who are treated for cardiac complications related to cocaine use.

In Greece, according to data from the National Centre for the Study of the Use of Drugs and Alcohol, 8.6% of the population in the 12-64 year age bracket report using an illegal substance, such as cocaine, one or more times in their lives. In 2003, 20% of school students aged 17 years reported using an illegal substance, mainly cannabis. The rate of cocaine use in this group of young people was just 1.5%. In 2004, 256 narcotics-related deaths were confirmed by the Coroner's department. Of those deaths, 98.7% were related with heroin



**Figure 3.** Coronary angiography. A: Right anterior oblique projection, showing the anterior descending and circumflex arteries (branches of the left coronary artery) without critical lesions. B: Left anterior oblique projection, showing normal main coronary trunk. C: Right coronary arteries without critical lesions, in lateral projection. D: Left ventriculography without wall hypokinesis.

use and only 1.3% with the use of other substances.<sup>10</sup> Unfortunately, there are no official data specifically for cocaine. In European countries the number of cocaine users is increasing.<sup>11</sup>

The most common cardiovascular complication related to the use of cocaine is acute myocardial infarction.<sup>3,4,12,13</sup> These patients are usually young men, and the only risk factor they have for coronary artery disease is smoking, features that also applied to the patient presented here. Cocaine appears to cause acute myocardial infarction in patients with or without pre-existing coronary artery disease. Approximately 33-50% of patients with an infarction caused by cocaine have normal vessels on angiography.<sup>10,14,15</sup> The risk of acute myocardial infarction increases by 24-31 times during the first 60 min after cocaine use.<sup>16</sup> More rarely, symptoms appear several hours after the drug use, when the cocaine concentrations are very low, probably because of an increase in its main metabolites in the blood. The long-term risk of infarction throughout the life of cocaine users is 6% greater than in non-users.<sup>13</sup>

There are many mechanisms that have been postulated to play a part in the occurrence of ischaemia and infarction in patients who use cocaine. First of all, cocaine appears to contribute to platelet activation; it increases the accumulation of platelets and enhances their thromboxane production.<sup>17,18</sup> These actions, in combination with an observed increase in plasminogen activator inhibitor,<sup>19</sup> probably contribute to thrombus formation in the coronary arteries. This possibility is supported by the finding of platelet-rich thrombi in *post mortem* studies of patients whose cause of death was acute myocardial infarction after cocaine use.<sup>20</sup> In addition, there are *in vitro* studies showing that cocaine accelerates the development of atheromatosis by causing structural anomalies in the vascular endothelium. These lesions increase the endothelium's permeability to low density lipoproteins and lead to the expression of adhesion molecules and the migration of leukocytes into the endothelium, all of which are associated with the process of atheromatosis.<sup>21,22</sup>

Another factor that appears to play an important role in ischaemia is the disturbance of the myocardial oxygen supply/demand relationship that is caused by cocaine use. Cocaine increases heart rate, left ventricular contractility and systemic blood pressure, resulting in an increase in myocardial oxygen demand. This happens because of cocaine's powerful sympathomimetic action via changes in stimulus transmission

at the presynaptic level. Cocaine inhibits the reabsorption of norepinephrine and dopamine by the presynaptic neuron, producing an excess of these neurotransmitters at the site of the postsynaptic receptor.<sup>1,2</sup> In patients with a substrate of coronary artery disease, this increase in oxygen demand can lead to myocardial ischaemia. At the same time as increasing oxygen demand, cocaine reduces oxygen supply to the myocardium by causing paradoxical vasoconstriction in the epicardial coronary arteries.<sup>2,12</sup> So far, we know of two mechanisms that cause this vasoconstriction: first, the stimulation of the alpha-adrenergic receptors,<sup>12</sup> and second, the increased production of endothelin (which has a vasoconstrictive effect) by the endothelium.<sup>23</sup>

It is important to note that the combined use of cocaine and ethanol increases the probability of sudden death in comparison with each substance separately, probably because of an additive or synergistic effect of ethanol on the occurrence of cardiovascular complications from cocaine use.<sup>5</sup> A possible explanation of this is the production of a specific metabolite by the liver during the combined use of the two substances, the so-called cocaethylene. This metabolite, like cocaine, inhibits the reabsorption of dopamine by the presynaptic neuron and consequently boosts the toxic effect of cocaine on the cardiovascular system.<sup>24</sup> Indeed, animal studies suggest that cocaethylene is more lethal than cocaine itself.<sup>25</sup>

There is little evidence available concerning the arrhythmogenic effect of cocaine. Theoretically, cocaine could have arrhythmogenic properties via multiple mechanisms. More specifically, because of its sympathomimetic properties, it could increase myocardial excitability and lower the threshold for the occurrence of ventricular fibrillation.<sup>7,26</sup> In addition, because of its ability to block Na<sup>+</sup> channels at a cellular level, it could inhibit stimulus production and transmission, resulting in a prolongation of the QRS and QT intervals (similarly to the action of class I antiarrhythmic drugs).<sup>27</sup> This arrhythmogenic action of cocaine may arise from or be enhanced in pathological conditions such as myocardial ischaemia.<sup>28</sup> It is not clear whether or not the occurrence of lethal arrhythmias following cocaine use definitely requires the existence of a pathological myocardial substrate. Experimental studies in animals have shown that cocaine causes ventricular arrhythmias only in the presence of myocardial ischaemia.<sup>7</sup> In humans, the majority of lethal arrhythmias and sudden deaths associated with cocaine use have been observed in patients

with myocardial ischaemia or other pathological structural heart disease. On the other hand, the long-term use of cocaine is associated with an increase in left ventricular mass, which could form a suitable substrate for the development of arrhythmias.<sup>29</sup> In patients who are hospitalised for infarction following cocaine use, ventricular arrhythmias occur in a relatively small percentage that ranges from 4-17%. The young age of these patients probably acts as a buffer against severe arrhythmias.<sup>2</sup>

In the case of our patient, the pain started within an hour from cocaine use, at which time the levels of the substance are at their highest and the risk of acute myocardial infarction is greatly elevated. Given the non-pathological angiographic findings, the mechanisms most likely to have led to the occurrence of ischaemia and infarction were vasoconstriction, the thrombogenic properties of cocaine, and the high levels of cocaethylene due to the concomitant alcohol consumption. The patient's ventricular fibrillation was attributed in this case to an increase in myocardial excitability resulting from the cocaine use, which, in combination with the myocardial ischaemia, created suitable conditions for the arrhythmia to occur.

As regards the therapeutic approach to a patient with myocardial infarction after cocaine use, it must be stressed that beta-blockers, such as propranolol, should be avoided, because of the risk of exacerbating the cocaine-induced vasoconstriction related to alpha-receptor stimulation.<sup>30</sup> This vasoconstrictive action of cocaine may be countered by the administration of an alpha-adrenergic receptor antagonist such as phentolamine.<sup>31</sup> The use of medications that block both alpha and beta receptors, such as labetalol, seems to be effective in treating the hypertensive response associated with cocaine use, although they do not have a significant effect on coronary artery vasoconstriction.<sup>32</sup> In its latest guidelines (2005) for the treatment of patients with acute coronary syndromes after cocaine use, the American Heart Association suggests as first-line medications nitrates, since in cardiac catheterisation studies they reversed cocaine-related vasoconstriction, and benzodiazepines, since they reduce heart rate and blood pressure in these patients. Phentolamine follows as second-line treatment.<sup>30</sup> Regarding thrombolysis in this category of patients, it seems to entail an increased complication rate, especially when there is severe hypertension. For this reason, it should be employed carefully and cardiac catheterisation with intracoronary administration of thrombolytic or vasodilator medication should

be preferred whenever possible.<sup>30</sup> Finally, as far as the treatment of ventricular tachycardia or fibrillation caused by cocaine use is concerned, the suggested treatment depends on the patient's haemodynamic condition. Thus, in haemodynamic instability the treatment of choice is electrical cardioversion according to standard protocols, whereas if the patient is haemodynamically stable lidocaine or sodium bicarbonate should be given.<sup>28,30,33</sup>

In our case we avoided beta-blockers for the reasons mentioned above. Nitrates, although absolutely indicated in patients with acute myocardial infarction following cocaine use, were not given to our patient because of the right ventricular involvement. The persistence of ST elevations for >15 min after the administration of pethidine, aspirin and diazepam led us to the decision to give thrombolytic medication through a peripheral vein, since the patient had been normotensive since his admission and it would have taken >90 min to transfer him to a hospital with a catheterisation laboratory. The patient's ventricular fibrillation was treated successfully with electrical cardioversion. Although there are no clear guidelines for the long-term treatment of these patients after an acute coronary syndrome, we decided on aspirin, statin, and sublingual nitrates when needed. In spite of the known beneficial effects of beta-blockers after acute myocardial infarction, none was given since we could not be sure that the patient would not use cocaine again, in which case the consequences could have been catastrophic.

## Conclusions

In patients with an acute coronary syndrome or chest pain, cocaine use should be investigated rigorously, especially by cardiologists, when the patient is young and does not have multiple risk factors for coronary artery disease. The identification of these patients is of significance not only for statistical and epidemiological purposes, but also because their treatment differs in specific ways from the treatment of major coronary events in the general population. The physician should be aware of this in order to avoid undesirable consequences for the patient.

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