

# Fatal Postoperative Arrhythmia in a Man with a Remote History of Methamphetamine and Cocaine Use: A Case Report

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## Abstract

*Long-term methamphetamine and cocaine use are associated with significant cardiovascular consequences. Despite these demonstrated associations, adverse effects that persist after cessation of drug use are difficult to establish. Cardiovascular pathology associated with long-term drug use may have subclinical presentations that persist long after cessation of drug use. In asymptomatic persons with a remote history of long-term methamphetamine or cocaine use, it may be prudent to assume existing subclinical cardiovascular pathology with positive methamphetamine or cocaine use history as a cardiac risk factor.*

## Introduction

Methamphetamine and cocaine abuse are associated with significant cardiovascular consequences. These adverse cardiovascular effects include myocardial ischemia and infarction, left ventricular hypertrophy, dysrhythmias, cardiomyopathy, myocarditis, aortic dissection, coronary artery dissection, and aberrant cardiovascular response to physiologic stress.<sup>1-14</sup> Dramatic events such as acute myocardial infarction are well-recognized consequences of acute intoxication.<sup>15</sup> Other adverse cardiovascular effects such as myocarditis, while not strongly linked temporally to drug intake, are associated with long-term drug use.<sup>1,4,5</sup> Despite these demonstrated associations, residual cardiovascular aftereffects of methamphetamine or cocaine have been difficult to establish in large-scale observational studies.<sup>16</sup> Presented below is a fatal case of dysrhythmia that occurred after low risk surgery in a man known to have only minor cardiovascular clinical predictors preoperatively.

## Case report

A 45-year-old male with a history of heavy alcohol, methamphetamine, and cocaine use presented with acute postprandial abdominal pain, bloating, and obstipation without nausea or vomiting. The patient noted recent resumption of heavy alcohol use after three years of abstinence but denied resuming illicit drugs. His medical history was negative for any sur-

gery, gastrointestinal disease, cardiac disease including hypertension, or medications. Notable, however, was a cardiac evaluation done eighteen months prior for new onset exertional dyspnea and orthopnea. A Persantine-thallium stress test and echocardiogram showed mild concentric left ventricular hypertrophy with normal left-ventricular function and no evidence of valvular disease, dilated cardiomyopathy, or coronary artery disease. The patient denied chest pain, palpitations, or syncopal episodes. His temperature was 98.2 °F, blood pressure 147/84 mmHg, heart rate 73 beats/min, and respiratory rate 20 breaths/min. On examination, the patient was of tall stature, moderately obese, and in moderate discomfort. No jaundice or scleral icterus was noted. Neck veins were not distended. The lungs were clear. Heart sounds were normal. The abdomen was moderately distended with minimal bowel sounds. Right upper quadrant tenderness was noted with guarding. No hepatosplenomegaly or masses were noted. The hernia exam was negative.

An abdominal radiograph showed multiple loops of distended small bowel in the mid-abdomen with air-fluid levels and no gas in the large bowel. Ancillary data consisting of an electrocardiogram, complete blood count, serum chemistries including amylase and lipase, cardiac enzymes, and urinalysis were unremarkable except for an AST of 73 and ALT of 139. No blood or urine drug screens were obtained.

The patient was evaluated for a small bowel obstruction and received supportive care. Further testing on the second hospital day suggested a diagnosis of acute cholecystitis. On the third hospital day the patient underwent a diagnostic laparoscopy with an open cholecystectomy. The patient's preoperative hospital course was unremarkable. Intraoperatively, induction of anesthesia, maintenance of anesthesia, and the operative procedure itself were performed without complications. However, following reversal of anesthesia, the patient experienced a rapid episode of bradycardia and desaturation. Administration of atropine resulted in a transient episode of supraventricular tachycardia

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followed by asystole. Despite resuscitation efforts, the patient's status deteriorated with multiple episodes of bradycardia, supraventricular tachycardia, ventricular tachycardia, and asystole. Blood counts and chemistries drawn thirty minutes into the resuscitation effort showed no electrolyte or metabolic derangements and a mild anemia consistent with the operative blood loss of 800 ml with adequate fluid resuscitation. Resuscitation efforts were discontinued seventy minutes after the initial bradycardic episode and the patient expired.

An unlimited postmortem examination was performed with the final pathological diagnoses of status post open cholecystectomy, cardiomegaly, mild atherosclerosis of the coronary arteries and aorta, marked bilateral pulmonary congestion and edema with hemorrhages, and portal inflammation consistent with chronic hepatitis. In particular, postmortem examination of the heart showed borderline enlargement of 600 grams with right and left ventricular wall thicknesses of 0.5 cm and 1.6 cm, respectively. No evidence of an acute or old myocardial infarction was seen on gross or microscopic exam. Further microscopic examination showed myocyte hypertrophy and diffuse contraction band necrosis of the myocardium (Figure 1). Examination of the coronary arteries revealed mild atherosclerosis but no evidence of occlusion via either atherosclerotic plaque or thrombus (Figure 2). Furthermore, no thromboemboli were seen on inspection of the pulmonary arteries, the great vessels, and cut surfaces of the lung. Neither blood nor urine drug tests were performed postmortem.

## Discussion

This report proposes that a history of methamphetamine and/or cocaine abuse, despite an extended period of abstinence, may contribute to increased cardiovascular complications during physiologic stress or anesthesia. While the history of alcohol abuse and the finding of hypertrophic cardiomyopathy on postmortem examination are acknowledged as contributing risk factors, this report focuses on the cardiovascular consequences of methamphetamine and cocaine abuse.

### *Complications of acute intoxication*

Methamphetamine and cocaine are sympathomimetic drugs and, to a large degree, share common mechanisms of action along with a multitude of common adverse effects.<sup>17</sup> While the exact mechanisms differ, both exert effects centrally and peripherally to increase the levels of epinephrine, norepinephrine, and dopamine systemically and within the synaptic cleft.<sup>1,5</sup> Acutely, intoxication typically increases systemic arterial pressure and heart rate, stimulates cardiac contractility, induces inappropriate coronary vasospasm, and promotes thrombosis formation.<sup>1,3,18-20</sup> These changes favor an ischemic myocardium thereby increasing the risk of acute myocardial infarction or ischemia-induced

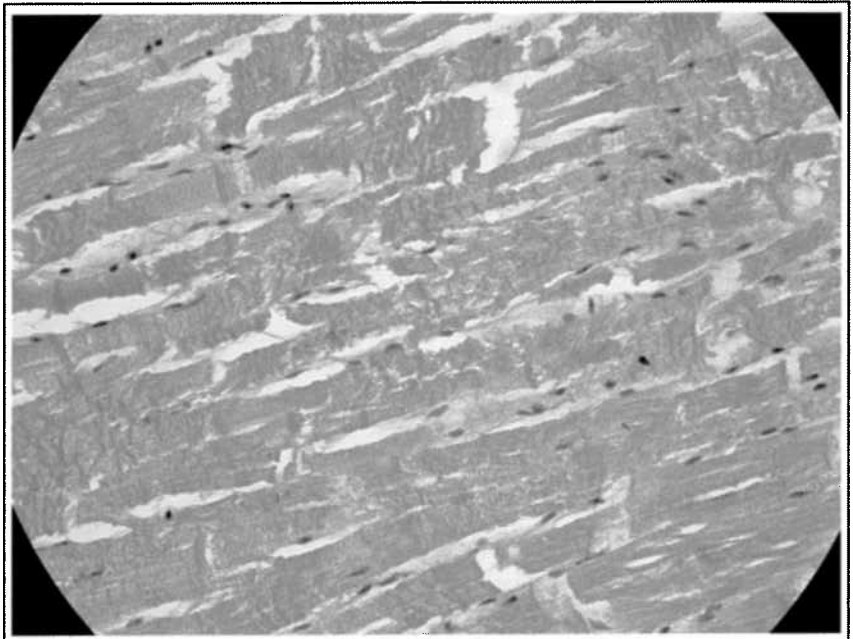


Figure 1.— Photomicrograph of left ventricle obtained on postmortem examination revealing hypertrophic myocytes with diffuse contraction band necrosis (400x).

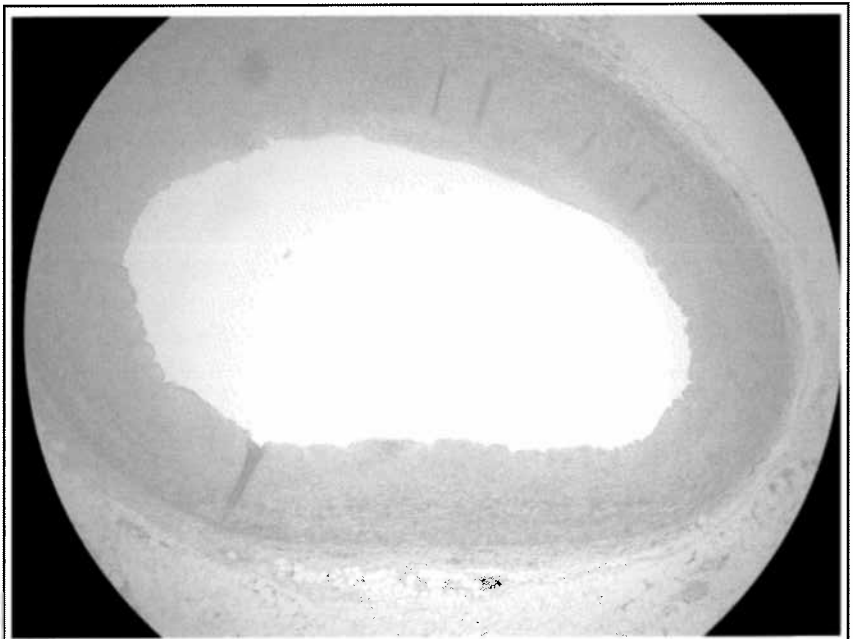


Figure 2.— Photomicrograph of coronary artery cross section obtained on postmortem examination revealing essentially normal architecture without evidence of occluding thrombus or significant coronary artery disease (20x).

dysrhythmias during intoxication.<sup>1,15,21,22</sup> Additionally, the increased systemic arterial pressure and vascular wall shear stresses are factors favoring the development of aortic dissection and coronary artery dissection.<sup>1,9-12</sup> Correspondingly, as the drug and its active metabolites are cleared from the circulation and the catecholamine excess resolves, so to does the risk of developing these complications.<sup>1,15</sup>

### ***Complications of long-term abuse***

Cardiovascular complications associated with long-term methamphetamine and cocaine exposure include myocarditis, dilated and hypertrophic cardiomyopathy, accelerated atherosclerosis, dysrhythmias, and aberrant cardiovascular response to physiologic stress.<sup>1-6,8,23-26</sup> Early evidence suggests that the injury is mediated by repeated catecholamines excess and the subsequent ischemia and/or calcium overload, direct drug toxicity, and free radical damage.<sup>3,19,23</sup> In particular, contraction band necrosis (CBN) of the myocardium is a histopathologic finding associated with methamphetamine and cocaine intoxication.<sup>27-32</sup> The occurrence of CBN is non-specific as it is also observed in excess catecholamine states or classically, as a consequence of calcium influx via reperfusion following ischemic injury.<sup>33,34</sup> Pathologic findings of drug-induced CBN are similar to those found in pheochromocytoma, suggesting a plausible link where the myocarditis and the subsequent dilated cardiomyopathy are secondary reactions to CBN.<sup>3</sup>

Ventricular hypertrophy and hypertrophic cardiomyopathy are also associated with long-term methamphetamine and cocaine abuse.<sup>6,25,26</sup> Ventricular hypertrophy is a known risk factor in developing ventricular arrhythmias and diastolic dysfunction.<sup>6,35,36</sup> Additionally, hypertrophy may facilitate the development of myocardial ischemia through increased tissue mass. Limited case reports and animal models indicate that the hypertrophy may resolve with the cessation of drug use.<sup>25,26</sup>

Accelerated atherosclerotic lesions, as demonstrated through animal studies and human autopsies, are associated with long-term cocaine abuse.<sup>3,18</sup> Interestingly, atherosclerotic lesions amplify the vasoconstrictive response to catecholamines in diseased segments.<sup>3,18,19</sup> This interrelation suggests that long-term drug abuse increases the risk of acute myocardial infarction by inducing its own vasospastic coronary lesions during acute intoxication.

Aberrant physiologic stress responses may occur with long-term methamphetamine or cocaine abuse. Bradycardia in the face of hemorrhage is an abnormal response observed in a high percentage of trauma patients reporting cocaine use.<sup>37</sup> Animal studies in rats and pigs chronically exposed to cocaine reproduce this paradoxical bradycardic response to hemorrhage.<sup>13,37</sup> A contrasting but equally peculiar observation is an

increased pressor response to successive binge administrations of methamphetamine in rats.<sup>38</sup> Interestingly, binge administration produces an impaired vasodilatory response ten days after the last binge dose. These responses, however, were not observed with binge cocaine administrations.<sup>39</sup> Molecular studies in rats have identified a cocaine and amphetamine regulated transcript (CART) peptide localized in brain tissue, adrenal glands, sympathetic ganglia, and parasympathetic nuclei that may play a role in modulating autonomic cardiovascular function.<sup>40,41</sup> CART has already demonstrated a physiologic ability to attenuate the baroreflex response.<sup>42</sup> Taken together, these data suggest that long-term methamphetamine and cocaine use can modulate cardiovascular autonomic regulation mediated through lasting cellular changes. Moreover, there appears to be differences between the physiologic responses for cocaine and methamphetamine with methamphetamine exhibiting a sensitizing-like effect.

Physiologically, each complication above is capable of profoundly affecting cardiovascular function: accelerated atherosclerosis may lead to ischemic cardiomyopathy, myocarditis may result in ventricular dysfunction and provide an arrhythmogenic substrate, cardiomyopathy may cause systolic or diastolic dysfunction and provide an arrhythmogenic substrate, dysrhythmias may impair cardiac output, and aberrant cardiovascular response may result in hemodynamic instability.<sup>3,35,43</sup> Integratively, each complication can potentially interact with the others to further alter cardiac function.

### ***Residual cardiovascular effects after cessation***

It is likely that many of the complications of long-term methamphetamine and cocaine use persist even with the cessation of drug use. Atherosclerotic lesions, capable of regressing with intense reduction of risk factors and medical treatment, are unlikely to recede with cessation of drug-use alone.<sup>44</sup> Drug-induced myocarditis may resolve once the toxic effects of drug, catecholamine excess, or stimulus to a hypersensitivity reaction is removed. The sequelae of myocyte necrosis and scarring are, however, permanent and can impair ventricular function and increase the risk of ventricular arrhythmias.<sup>3,35,36</sup> Dilated and hypertrophic cardiomyopathy, while potentially reversible, can persist even with cessation of drug use.<sup>6,25,26</sup> As mentioned above, the functional impairments of unresolved or interim resolution of the cardiomyopathy include systolic and/or diastolic dysfunction and an increased risk of ventricular arrhythmias. Lastly, aberrant cardiovascular responses have been observed with continuing methamphetamine or cocaine use or for the period shortly thereafter. However, evidence in support of a residual effect after an extended period of abstinence has not been established.

A factor common among many of these residual effects is the increased risk of dysrhythmias. Worsening ischemia due to natural progression of coronary artery disease, focal and/or diffuse scarring from myocarditis, and increased and abnormal substrate in the cardiomyopathies contribute to increase the risk of dysrhythmias. While speculative, dysrhythmias may be a focal end manifestation of the multiple pathologies of long-term methamphetamine and cocaine abuse.

### **Integration of case-specific findings**

Residual cardiovascular pathology from amphetamine and cocaine use, as described above, predisposes the patient to increased cardiovascular risk during surgery. The physiologic stress of surgery and anesthesia and the usual changes in fluid and electrolyte balance are capable of exacerbating existing clinical or subclinical disease. An additional case-pertinent stressor to consider is acute alcohol withdrawal. However, for this particular case, the relatively short duration from resumption of alcohol use and an inpatient observation for more than 60 hours without signs or complaints consistent of acute alcohol withdrawal argues against it in this particular case.

Perioperative dysrhythmias are a common occurrence, particularly in the immediate postoperative period.<sup>45</sup> Typically, postoperative dysrhythmia is a manifestation of abnormal cardiac substrate acted upon by electrolyte or acid-base abnormalities, infection, blood loss, or large fluid shifts.<sup>46</sup> Indeed, development of a postoperative dysrhythmia may be the first manifestation of underlying cardiac disease. In extreme examples, dysrhythmia may be an indicator of acute myocardial ischemia or injury, pulmonary embolus, or drug toxicity. In acknowledging the case relevant history of heavy alcohol use, it is recognized that alcoholics have a five-fold increase in postoperative cardiovascular complications that includes heart failure and arrhythmias.<sup>47</sup>

To address the findings of the case, the postmortem examination revealed cardiomegaly with myocyte hypertrophy and contraction band necrosis but little additional significant cardiac pathology. The etiology of his hypertrophy is unknown but plausible origins, as related to this patient's history, are cardiomegaly secondary to a history of methamphetamine and cocaine abuse and heavy alcohol abuse. The presence of contraction band necrosis is a peculiar finding confounded by the patient's history of methamphetamine use and the prolonged resuscitation effort. As described above, binge use of methamphetamine results in progressive increases in pressor response through an undetermined mechanism. One hypothesis for the presence of CBN in this patient is a residual methamphetamine-induced sensitivity to increased

endogenous catecholamines, as would occur during the stress of the surgery. Alternatively, the CBN may be a result of occult methamphetamine or cocaine use several hours prior to surgery. Lastly, the CBN may be a result of the prolonged resuscitation.<sup>29,33,34</sup> If the cardiac insult occurred preoperatively, as would occur with occult drug-use, it would further increase the risk of arrhythmias. Nevertheless, it is plausible that the cardiomegaly, secondary to heavy methamphetamine, cocaine, and alcohol abuse, provided the abnormal cardiac substrate on which the dysrhythmia developed and persisted.

### **Conclusion**

Methamphetamine and cocaine abuse are associated with significant cardiovascular consequences that present acutely, chronically, or subclinically. Continued use is associated with an increased risk of developing additional complications. Even with cessation of drug use, these complications may persist long after drug use has ceased. In persons with a history of current or remote methamphetamine or cocaine use without signs, symptoms, or history of cardiac disease, it may be prudent to assume underlying subclinical pathology. Physiologic stressors such as anesthesia or surgery may unmask subclinical disease and as such, these individuals should be considered to have existing cardiac risk factors despite a negative history and physical.

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