

## Case Report

# Methamphetamine Associated Cardiovascular Complications

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### Abstract

Cardiovascular complications are the second most common cause of death in methamphetamine use following accidental overdose. Methamphetamine use remains at an alarmingly high rate in the United States. With approximately 51 million users between the ages of 15 to 64 years, cardiovascular dysfunction secondary to methamphetamine will soon become more prevalent in our emergency departments.

We present the case of a 28-year-old male who presented to the emergency department with shortness of breath, cough and intermittent diarrhea. Patient was initially thought to have and treated for severe sepsis. However, as his clinical course in the hospital progressed, it was clear that patient had developed severe heart failure due to his substance use history. He developed multiple cardiovascular complications including severe biventricular failure requiring acute mechanical circulatory support.

This case highlights cardiovascular complications associated with methamphetamine use. It has become increasingly important for research to focus on understanding the pathogenesis of methamphetamine induced cardiovascular disease at a molecular and pathological level. Physician awareness will lead to early diagnosis and treatment of cardiovascular disease due to methamphetamine use. With so much attention on the opioid crisis, the consequences or sequela of methamphetamine use are at risk of being overshadowed.

### Keywords

Methamphetamine, Overdose, Cardiovascular, Pathogenesis, Complication

### 1. Introduction

Methamphetamine is a highly potent synthetic amine stimulant that is structurally similar to amphetamine [1]. Methamphetamines produce significant effects on physical, behavioral, cognitive, and psychiatric wellbeing. Methamphetamine use has become an epidemic in this country and worldwide. The intense euphoria the drug produces is the reason behind its widespread misuse [2]. Epidemiological studies have reported that amphetamine-type stimulants are the most used illicit drug in the world after cannabis, with approximately 51 million users between the ages of 15 to 64 years [2, 3].

According to the National Institute on Drug Abuse in the United States, approximately 10 million people have tried methamphetamine at least once in their lifetime [4]. According to a National Survey on Drug Use and Health, in 2017 approximately 1.6 million people admitted to using methamphetamine in the past year. Methamphetamine toxicity is a common cause of visit to the emergency department. Patients typically present with diaphoresis, agitation, hypertension, tachycardia, psychosis, and seizures. Severe cardiac complications may include cardiomyopathy, myocardial infarction, arrhythmias, and dissecting aneurysms. The effects that methamphetamine has on the cardiovascular system are not as extensively studied in comparison with those of cocaine. Both stimulants, cocaine and methamphetamine, can cause hypertension and tachycardia which will increase myocardial oxygen demand and this can lead to myocardial ischemia [4]. A study by Sun and colleagues, analyzed methamphetamine use in rat cardiomyocytes it found an association between methamphetamine use and the cardiac mechano-transducer protein [5]. Melusin plays an important role in maintaining normal heart function. While several studies have shown an association with acute coronary syndrome, dilated cardiomyopathy, ventricular dysrhythmias, and increased rates of early atherosclerosis, there exists need for more research examining the association between methamphetamine use and adverse cardiovascular outcomes [1-3]. Here we present a case of methamphetamine-associated cardiovascular complications.

### 2. Case Description

A 28- year-old male presented to the emergency room (ER) with complaints of shortness of breath, cough, and intermittent diarrhea for 10 days. He had a past medical history of tobacco and methamphetamine use. He did

not have any prior cardiac history and he reported no chronic medical conditions. He did not take any chronic medications. He had no reported surgical history. He had no pertinent family history of cardiac disease. Patient reported using about 1 gram of methamphetamine daily or whenever obtainable for the past 5 years. He reported smoking 1-2 gms of methamphetamine daily for the past two weeks prior to presentation in ER. Upon physical exam, it was noted that the patient had a height of 165 cm and weight of 98kg. His vitals showed that he was tachycardic and tachypneic. He appeared agitated, anxious, anicteric, and found to be in mild respiratory distress. Lung examination revealed equal, bilateral air entry and clear breath sounds. Cardiac exam showed elevated rate and regular rhythm. Abdominal exam revealed generalized tenderness. He was found to have bilateral lower extremity pitting edema as well. Otherwise, physical exam had no pertinent findings. Significant laboratory results in the ER were elevated transaminases (alkaline phosphatase: 145, aspartate aminotransferase (AST)/alanine aminotransferase (ALT): 1179/1143), brain natriuretic peptide (BNP): 1397, Lactic acid: 4.43, and D-Dimer: 3.4. Streptococcus screening rapid test was positive. Urine drug screen was positive for methamphetamines and cannabinoids. Electrocardiogram (EKG) demonstrated sinus tachycardia. Computed Tomography (CT) Chest Angiography Non-coronary demonstrated no pulmonary embolus, thoracic aortic aneurysm, or aortic dissection but it did show borderline to mild cardiomegaly and small ground glass infiltrate in the medial left upper lobe. CT abdomen/pelvis demonstrated gallbladder wall thickening, trace perihepatic free fluid, and right upper quadrant edema and stranding. Patient was started on empiric broad spectrum antibiotics for severe sepsis, secondary to possible pneumonia or hepatobiliary source. Patient then developed acute hypoxemic respiratory failure requiring rapid sequence intubation. Then, transthoracic echocardiogram (TTE) demonstrated ejection fraction (EF) of 5-10% and mild to moderate mitral regurgitation. He was evaluated by general surgery for a hepatobiliary cause of sepsis and transaminitis, it was unlikely that his presentation was due to cholecystitis and more likely due to hepatic congestion from congestive heart failure. Patient was becoming hypotensive since his admission. Patient was placed on vasopressor support to maintain adequate mean arterial pressure most likely secondary to cardiogenic shock. Patient had developed ischemic hepatopathy and acute kidney injury due to his severe left ventricular dysfunction causing decreased cardiac output. His transaminases improved with vasopressor support, indicative that his hepatic dysfunction was most likely secondary to decreased cardiac output. Patient received aggressive diuresis during the hospitalization while maintaining central venous pressure <12 mm hg to reduce afterload. Patient underwent a hepatobiliary iminodiacetic acid (HIDA) scan which was negative for cholecystitis. He required a right thoracentesis to

improve his respiratory status prior to being extubated. A total of 500cc of pleural fluid was drained and pleural fluid studies demonstrated transudate effusion, secondary to congestive heart failure. Blood cultures grew gram positive clusters (staph non-aureus), and he completed intravenous (IV) vancomycin for 5 days and IV meropenem for 7 days therapy. Patient continued to have high fevers and chest x-ray was suspicious for left lower lobe consolidation/density with pulmonary edema. He underwent a bronchoscopy and moderate thick secretions in the left lung were washed and suctioned. Repeat TTE demonstrated EF of 12%, dilated left ventricular, mild to moderate right ventricular systolic dysfunction, and mild pericardial effusion without tamponade. Patient's high fever without leukocytosis was more suggestive of a noninfectious cause of fever, suspect drug induced or atelectasis. Patient was weaned off of mechanical ventilation after failing multiple awakening and breathing trials. Following extubation, his EKG demonstrated narrow complex tachycardia and after administering 6mg of adenosine followed by 12 mg of adenosine his cardiac monitoring revealed atrial flutter with rapid ventricular rate. Patient underwent emergent electrical synchronized cardioversion and he converted to normal sinus rhythm. He developed Cheyne-Stokes respiration due to his congestive heart failure. Patient was required to have positive inotrope support to maintain systolic blood pressure and was started on intravenous dobutamine and digoxin. He underwent right heart catheterization which showed severe biventricular failure. Patient required acute mechanical circulatory support with two microaxial flow impella catheters for biventricular support (BiPella). He was transferred to a tertiary care facility for further management.

### 3. Discussion

Methamphetamine use is growing worldwide regardless of wealth, location, and culture. Cardiovascular disease is the second leading cause of death in methamphetamine users following only accidental overdose [2]. Cardiovascular manifestations can range from hypertension and tachycardia to more severe complications such as myocardial infarction, lethal arrhythmias, cardiomyopathy, dissecting aneurysm, and sudden cardiac death [3]. Our patient developed severe dilated cardiomyopathy with cardiogenic shock and atrial flutter with rapid ventricular rate. It was theorized that methamphetamine users have a 3.7 times increased risk of developing cardiomyopathy compared to individuals without amphetamine use [3]. Methamphetamine is a sympathomimetic agent, which can cause cardiovascular complications through catecholamine toxicity or through direct effects on cardiac or vascular tissue [2]. The mechanism of cardiovascular disease in methamphetamine users remains largely unknown, however several studies have postulated the pathogenesis of various complications [1-3]. Methamphetamine use is associated with coronary

arteries or microvasculature vasospasm, resulting in decreased blood flow to the cardiac tissue, causing acute angina. Myocardial infarction is often observed in young patients with a history of methamphetamine use [2]. Previous studies from Australia showed increased risk of coronary artery disease in methamphetamine users, with 54% of patients with coronary artery disease and <10% with severe coronary artery disease compared to control cohorts. The pathogenesis of atherosclerotic plaque formation in methamphetamine use is due to enhanced inflammation from endothelial activation and increased T cell and macrophage driven proinflammatory signaling. Methamphetamine causes structural (fibrosis, inflammation) and electrical remodeling of cardiac tissue leading to arrhythmias (prolonged QT) and heart failure [2]. The only study to evaluate acute effects of methamphetamines on cardiac rhythm was conducted in animals, and it showed increased atrial and ventricular ectopic beats and sinus tachycardia 30 minutes after administering methamphetamine [6]. Methamphetamine commonly causes dilated cardiomyopathy and diminished contractility resulting in severe systolic dysfunction [2]. The molecular mechanisms of cardiomyopathy are multifactorial, potential mechanisms are oxidative stress, accelerated apoptosis, increased p53 activity, necrosis, perfusion defects, fatty acid toxicity, altered cardiac gene expression, abnormal cardiac protein synthesis and function, and defects in intracellular calcium hemostasis [1]. Previous studies have shown that methamphetamine exposure causes cellular damage and hypertrophy in cardiomyocytes regardless of the duration of exposure, supporting the theory of catecholamine-independent direct cardiotoxicity [2]. Clinical and autopsy reports from methamphetamine users has revealed findings such as necrosis, fibrosis, hypertrophy, and enlargement of the heart, all consistent with cardiomyopathy. The degree of fibrosis is a good prognostic factor of recovery following cessation of methamphetamines. Patients who continued to use methamphetamine showed no improvement in their cardiac function. A retrospective analysis of US National Inpatient Sample database consisting of more than 35 million individuals and over 180,000 methamphetamine users showed that users have a 27% increased risk of sudden cardiac death [2].

#### 4. Conclusion

The opiate epidemic has received significant media attention and financial resources to help alleviate the issue,

but methamphetamine use is increasing worldwide and is developing into its own epidemic. If the trend continues, methamphetamine-induced cardiovascular dysfunction will become a more common presentation in emergency departments across the US. It is therefore essential that future research seek to better understand the pathogenesis of methamphetamine-induced cardiovascular disease at a molecular and pathological level. This will assist in providing physicians with the information needed to hopefully prevent and treat methamphetamine-associated cardiovascular disease.

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#### 6. Consent

The patient provided informed consent.

#### 7. Disclaimer

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