

## CLINICAL VIGNETTE

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# Acute Cardiogenic Shock in a Patient with Dilated Cardiomyopathy due to Chronic Methamphetamine Use: A Case Report and Discussion

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Digish Shah, MD, John Ly, MD and Nathan Cox, MD

### *Introduction*

Dilated cardiomyopathy (DCM) is characterized by dilation and impaired contraction of one or both of the ventricles.<sup>1</sup> Patients diagnosed with dilated cardiomyopathy have reduced systolic function and may or may not develop overt congestive heart failure.<sup>2</sup> DCM accounts for approximately 10,000 deaths and 46,000 hospitalizations per year in the United States.<sup>3</sup> Substance abuse accounts for approximately 3% of the causes of DCM in the United States,<sup>4</sup> with methamphetamine cited as a potential etiology. The mechanism of methamphetamine-associated dilated cardiomyopathy is not well understood. According to the 2017 United Nations Drug Report, there are an estimated 37 million regular methamphetamine users with an annual prevalence of approximately 0.77%.<sup>5</sup> Given the prevalence of worldwide methamphetamine use, we should see cases of dilated cardiomyopathy attributed to methamphetamine use. We present a case of acute cardiogenic shock in a patient with dilated cardiomyopathy due to chronic methamphetamine use.

### *Case Report*

A 56-year-old man with known methamphetamine abuse without any other chronic problems presented to the emergency department complaining of generalized abdominal pain. On initial evaluation, the patient was tachycardic with heart rate of 130 bpm. He was afebrile with normal blood pressures, ranging from 110-140 mmHg systolic over 60-90 mmHg diastolic. Oxygen saturation was >95% on room air and he was free of respiratory distress. The patient was confused and somewhat agitated, oriented only to self, but he was easily redirectable, not combative, and able to follow simple commands. Abdominal exam elicited severe, diffuse tenderness without rebound or involuntary guarding. The rest of his physical examination was unremarkable, including grossly normal cardiopulmonary and nonfocal neurologic exams. The patient acknowledged ongoing daily methamphetamine use, with the last use several hours prior to presentation to the emergency department. He denied any other tobacco, alcohol or recreational drug use. He also denied chronic prescription medications or any known pertinent family medical history.

Initial laboratory evaluation was notable for: reduced bicarbonate level (7 mmol/L), elevated creatinine level (2.42 mg/dL), elevated anion gap (45); elevated white blood cell count (11.3 10E3/uL); elevated transaminases (>500 U/L) and total bilirubin

level (3.1 mg/dL). Serum lactate was severely elevated (195 mg/dL). There were no prior baseline laboratories available. Initial serum lipase, troponin and total creatine phosphokinase levels were within normal limits. Initial arterial blood gas was consistent with a pure metabolic acidosis (pH 7.11 and bicarbonate level 5.2 mmol/L, without any significant derangements in the pCO<sub>2</sub> or pO<sub>2</sub> levels). Urine toxicology screen was positive for amphetamine/methamphetamines; the serum toxicology screen was negative for ethanol, acetaminophen and salicylates. Routine urine analysis was unremarkable for pyuria. Initial electrocardiogram revealed sinus tachycardia without signs of acute ischemic disease. Initial chest radiography was free of focal infiltrates or consolidations, but showed cardiomegaly with increased pulmonary vascularity. Computed tomography (CT) scan of the abdomen and pelvis was ordered. Blood and urine cultures were pending. The patient was given sepsis protocol 30 mL/kg/hr intravenous normal saline fluid resuscitation, empiric intravenous vancomycin and piperacillin-tazobactam for broad antimicrobial coverage, and he was admitted to the intensive care unit with a diagnosis of severe septic shock with a presumed intraabdominal source of infection.

Further review of chest radiography raised concern regarding cardiomegaly and increased pulmonary vascularity, in a patient without history of congestive heart failure. A B-type natriuretic peptide (BNP) level returned severely elevated >4,902 pg/mL. Transthoracic echocardiogram revealed global hypokinesis with estimated left ventricular ejection fraction of 21% with four-chamber dilation and elevated pulmonary arterial systolic pressure of 70 mmHg. There was also a well-circumscribed left ventricular apical thrombus measuring 2.3x1.9 cm without significant valvular disease. The CT scan of the abdomen and pelvis ordered from the emergency department revealed global signs of fluid overload (pleural effusions, anasarca, ascites and mesenteric edema). There was no evidence of intraperitoneal free air or air within the bowel walls. There was no intra-abdominal abscess or other foci of infection identified. The patient was felt to have severe cardiogenic shock with evidence of reduced end-organ perfusion and end-organ damage. A Swan-Ganz catheter was inserted for accurate measurement of central/cardiopulmonary pressures and hemodynamics to guide therapy; initial hemodynamic measurements were consistent with a cardiogenic cause of shock. Empiric intravenous fluids and antibiotics were discontinued. The patient was started on titratable intravenous nitroglycerin and milrinone for preload/

afterload reduction and inotropic support, respectively. He was diuresed with twice daily dosing of intravenous furosemide. He was also started on titratable intravenous heparin for his left ventricular apical thrombus. The patient's ischemic work-up was deferred due to clinical instability. The clinical diagnosis was chronic non-ischemic dilated cardiomyopathy due to methamphetamine use and his acute cardiogenic shock was due to ongoing abuse.

### Discussion

Historically, methamphetamines were initially synthesized in the early 1900s and were first marketed as bronchodilators,<sup>5</sup> although they became misused as stimulants and appetite suppressants. In 1970, methamphetamine became a schedule II drug and their use decreased until the late 1980s, when they started to reappear in the western United States.

After cannabis, methamphetamines and related compounds have become the second most commonly used illicit drug globally.<sup>6</sup> They can be used in a variety of ways: smoked, injected, ingested, or inhaled. They are sympathomimetic amines that increase intra-synaptic levels of catecholamines (serotonin, norepinephrine, and dopamine) through various mechanisms, including displacement of hormones from cytoplasmic vesicles, and inhibition of reuptake and degradation. The increase in these catecholamines drives methamphetamines' effect on users: euphoria, hallucinations, anorexia, and stimulation.

While methamphetamines can lead to a myriad of neurologic, psychologic, metabolic, and gastrointestinal complications, the effect on the cardiovascular system are often the most serious and can be life-threatening. After direct toxicity and death from overdose, cardiovascular complications are the second leading cause of death among methamphetamine users. Methamphetamine use is associated with hypertension, aortic dissection, acute coronary syndrome, pulmonary arterial hypertension (PAH) and methamphetamine-associated cardiomyopathy.<sup>7</sup> Most of the deleterious cardiac effects of methamphetamines are a result of the hyperadrenergic state induced by increased intra-synaptic catecholamines, such as epinephrine and norepinephrine, which directly cause hypertension and tachycardia. Methamphetamines have also been associated with arrhythmias, coronary vasospasm, and accelerated atherosclerosis. Animal studies have demonstrated that methamphetamine administration in rats leads to hypertension, tachycardia and direct myocardial cell toxicity including cellular death, fibrosis, and contraction band necrosis.<sup>8</sup>

A retrospective review from the University of California at Davis found methamphetamine users had a significantly higher risk of abnormal BNP and heart failure compared to the population of non-methamphetamine users. The study found over a 2-year period, 10.2% (450/4407) of patients presenting to the emergency department with positive urine toxicology screen for amphetamines, had abnormal BNP (>100 pg/mL), versus 6.7% (7263/108,608) of those who had negative toxicology screens for amphetamines or who were not tested.<sup>9</sup>

Different patterns of cardiomyopathy have been associated with methamphetamine use including: dilated, hypertrophic, and stress-induced (Takotsubo's) cardiomyopathy. Of these, dilated cardiomyopathy, as in our case, has been the most commonly reported. Prior case reports have noted reversibility in the cardiac changes seen in methamphetamine-associated dilated cardiomyopathy. One example was a woman who had severe dilated cardiomyopathy with left ventricular ejection fraction of 37%. She had a cardiac magnetic resonance imaging (MRI) done that showed no delayed gadolinium enhancement, suggesting no significant fibrosis. After stopping methamphetamine use and concomitant treatment with an ACE-inhibitor and  $\beta$ -blocker, her left ventricular ejection fraction improved from 37% to 64% in 6 months.<sup>10</sup>

A recent German case series of 30 patients with methamphetamine-associated dilated cardiomyopathy who all had endomyocardial biopsies and echocardiograms were followed prospectively to determine their clinical outcomes.<sup>11</sup> Similar to our case, all patients who had a BNP checked had an abnormal BNP (mean value of 5,553 pg/mL), 33% (10/33) had a left ventricular or right ventricular thrombus, and all had severely depressed heart function with mean left ventricular ejection fraction of 19%. The extent of fibrosis seen on endomyocardial biopsy was related to the length of methamphetamine use, with more fibrosis seen in those who had used longer. Of these 30 patients, 23 subsequently stopped using methamphetamines, while 7 continued using. Discontinuation of methamphetamines was associated with improvement in heart failure symptoms and cardiac function. However, the level of fibrosis seen at baseline endomyocardial biopsy was an independent predictor of left ventricular ejection fraction during follow-up, indicating that the extent of damage from prior methamphetamine use likely limits the extent to which heart function can improve.

### Conclusion

As seen in the case presented, cardiac side-effects and complications must be considered in all patients who use/abuse methamphetamines. BNP can be a useful screening tool in those who have clinical signs and symptoms of heart failure with echocardiograms used to formally evaluate for cardiac function and possible intracardiac thrombi. Cardiac MRI can be helpful in determining the extent of fibrosis and helping to guide expectations for recovery. Ultimately, treatment and prognosis rests on cessation of methamphetamine use as well as the usual treatment for advanced cardiomyopathy: ACE-inhibitors,  $\beta$ -blockers, anticoagulation, and AEDs on a case-by-case basis.

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