Methylene 3, 4 Dioxymethamphetamine–Induced Acute Myocardial Infarction

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Methylene 3, 4 dioxymethamphetamine (MDMA) has been gaining popularity as a recreational drug over the past few decades around the globe. Although once thought to be safer than its mother compound, amphetamine, several life-threatening adverse reactions have been reported. Among the cardiovascular toxicities documented, MDMA commonly causes various forms of arrhythmia and heart failure. However, MDMA-induced acute myocardial infarction is rarely reported. We report a case of acute myocardial infarction in a young man shortly after taking MDMA. Massive thrombosis over the right coronary artery was demonstrated by means of emergency angiography. After treatment with intravenous glycoprotien IIb/IIIa inhibitor and intracoronary urokinase infusion, the coronary artery was shown to be patent without any apparent stenotic lesions. The mechanism of MDMA-induced acute myocardial infarction was discussed.

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INTRODUCTION

The abuse of amphetamine and its derivatives has been increasing in modern society, especially among the younger generation.[1,2] Methylene 3, 4 dioxymethamphetamine (MDMA) is a derivative of amphetamine. The drug was made synthetically as an appetite inhibitor in 1912. In 1985, the derivatives of the amphetamines were placed in Schedule 1 of the restricted drug list in the United States, Canada, and the United Kingdom.[3] Although law prohibited the use of the drug, it is commonly used at rave parties and among college students. Physicians in the emergency department (ED) should become more familiar with this drug because of the emerging trend toward its use. Although it was once thought that the drug does not cause dependency and adverse side effects, this belief has been overturned by many reports of side effects in recent literature. To date, there is only one case report demonstrating acute myocardial infarction as a result of MDMA use.[4] Herein, we report a case of inferior wall acute myocardial infarction in a young man that occurred 3 hours after oral use of MDMA.

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CASE REPORT

A 27-year-old man arrived at the ED of a community hospital complaining of chest discomfort and tightness persistent for 3 hours. Before the onset of chest tightness, he

had been partying and had drunk one bottle of whisky at a club. With it, he claimed to have taken one half of a pill of MDMA. Three hours after taking the drug, he felt a persistent discomfort in his anterior chest area. His chest became tight, and he began to experience nausea, vomiting, and dizziness. There was neither radiating pain nor cold sweating. The patient reported that he had no prior history of chest pain, allergies, or heart disease. He denied that he was a habitual abuser of the drug and claimed to have only taken the drug 4 random times in his lifetime. Each time, he only used the maximum dose of one pill. He had only taken the drug orally. He denied habitual use of any other kind of amphetamines. Other habits included smoking 2 packs of cigarettes per day for 2 years and club hopping on a regular weekly basis, during which he drank various amounts of liquor. His mother had a history of hyperlipidemia, but no heart disease was noted in other family members. He did not have hypertension or diabetes.

On appearing at the ED of a community hospital, he looked to be agitated, diaphoretic, and in severe pain. He complained of severe nausea and epigastric discomfort. ECG showed ectopic atrial rhythm with ST elevation, Q wave, and T inversion over leads II, III, and aVF. He had a total creatine kinase level of 606 U/L, a creatine kinase–MB level of 43 U/L, and a troponin I level of 1.1 ng/mL about 3 hours after the onset of chest pain. Under the impression of acute myocardial infarction, he was given morphine, aspirin, and intravenous nitroglycerin. He was transferred to our hospital. On arrival to our hospital, 6 hours after the initial onset of chest pain, his blood pressure was 105/49 mm Hg, and his pulse rate was 73 beats/min. Physical examination was unremarkable except for the presence of grades II/VI systolic murmur at the lower left sternal border and apex. No venipucture marks were noted. Findings on respiratory and abdominal examinations were normal. Toxicology screening of urine revealed the presence of methylenedioxyamphetamine, MDMA, morphine, and lidocaine metabolites (lidocaine was used because of central venous catheter insertion at the community hospital). The urine MDMA level was 96,800 ng/mL, and the methylene dioxyamphetamine level was 13,900 ng/mL. The plasma MDMA level was 1,100 ng/mL, and methylene dioxyamphetamine was not detectable. A right-sided ECG showed a V4R ST elevation. The follow-up level of cardiac enzymes at our hospital 6 hours after the initial onset of chest pain showed an increase, with a creatine kinase level of 857 U/L, a creatine kinase–MB level of 85.6 U/L, and a troponin I level of 18.8 ng/ml. His cholesterol level was 189 mg/dL, and his triglyceride level was 36 mg/dL. Bedside ultrasonography showed left ventricular hypokinesia, especially over the inferior and posterior wall of the heart.

Emergency cardiac catherization was performed 8 hours after the initial onset of chest pain. There was much thrombus noted in the right coronary artery (Figure A). The patient received tirofiban with an initial dose of 1.6 mg per 30 minutes and 0.4 mg/h thereafter. Other therapies prescribed were 630 U/h of heparin sodium, 1 mg/h of nitroglycerin, oxygen, and aspirin.

The patient was admitted to the cardiac ICU for observation. A series of cardiac enzyme measurements was subsequently performed. ST-segment elevation returned to normal, and the patient was free of symptoms by the second day after the attack.

Repeat coronary angiography was performed 5 days after the attack. The result showed thrombus in the proximal part of the right coronary artery. The patient then received an intracoronary injection of 300,000 units of urokinase and continued with heparinization.

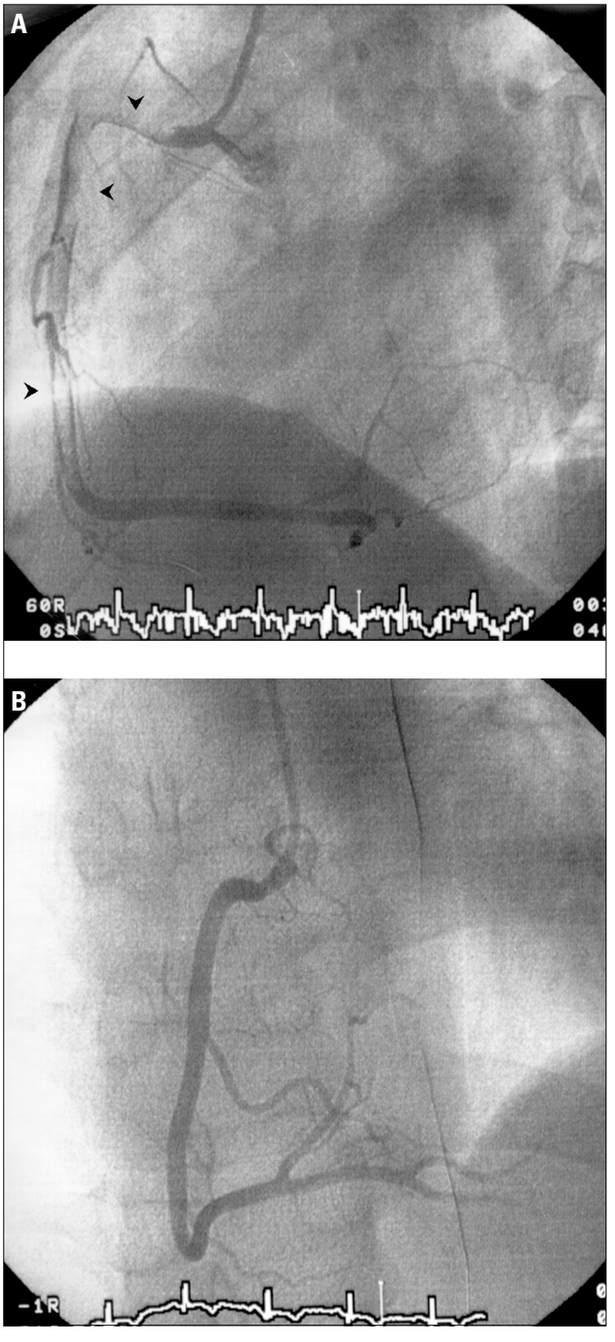
Right coronary angiography was performed again to reevaluate the condition of the right coronary artery 10 days after the initial attack. The right coronary artery was patent, and no residual thrombus was noted (Figure B). The patient was discharged in stable condition and has been without symptoms since that time.

DISCUSSION

MDMA has many street names, such as "ecstasy," "E," "XTC," and "Adam." It can be sniffed, smoked, and injected. The most common form of use is oral intake. The effect of MDMA is believed to result from the increase in serotonin, dopamine, and epinephrine levels in the brain. Users are attracted to the drug as a result of the effect of euphoria, a feeling of affection, and heightened feelings of empathy, emotional warmth, and self-acceptance.[1] Thus, it gains other nicknames, such as "hug drug" and "love drug."

MDMA is a synthetic drug that is derived from methamphetamine and has a similar structure as a hallucinogen, mescaline. Because of this, its effect is a combination of both drugs. Its amphetamine-like characteristics produce effects such as tachycardia, hyperthermia, and sweating. With this similarity to hallu-

Figure.
A, *Angiography of the right coronary artery was performed 8 hours after the onset of chest pain. There were many filling defects in the vessel (arrowheads).* ***B,*** *Right coronary angiography was performed 10 days after the onset of chest pain. The vessel became patent after treatment.*



cinogens, it produces the effects of euphoria and a sense of "high."

Although the sense of euphoria is what attracts users to this drug, many undesired effects could occur. Side effects include dizziness, vertigo, muscle tension, trismus, bruxism, nausea, blurred vision, rapid eye movement, shills, sweating, and faintness.[5] After the sense of a high wears off, many users often experience severe anxiety, paranoia, sleep problems, and vivid nightmares for days. Users also exhibit features of dependency, such as tolerance, mood disturbances, and the desire to continue taking the drug to avoid a withdrawal state or to elevate mood.[5] Serious and potentially life-threatening reactions to the drug can be divided into 4 principal types[3]: hepatic, cardiovascular, cerebral, and hyperpyretic. Hepatic toxicity causes the liver to be large and tender, similar to the effect of acute hepatitis.[6] Cerebral toxicity includes seizures and consciousness changes. Hyperthermia is the most dangerous form of toxicity. It can cause further side effects, such as rhabdomyolysis, myoglobinuria, renal failure, liver damage, and disseminated intravascular coagulopathy. Most cases of mortality are often the result of this effect.[3] Adverse effects of the drug on the cardiovascular system, predominantly related to activation of the sympathetic nervous system by increased catecholamine, include various types of arrhythmias, asytole, and cardiovascular collapse.[7] Arrhythmias are caused by its stimulation of release of noradrenalin, dopamine, and serotonin from the central and autonomic nervous systems. Myocardial infarction is not an uncommon adverse effect in amphetamine users; however, this side effect rarely occurs in MDMA users.[4]

The role of MDMA on coronary vessels is not well documented. In vitro studies have suggested that cocaine produces a procoagulant effect by decreasing concentrations of protein C and antithrombin III, activating platelets, and potentiating thromboxane production, thereby facilitating thrombotic coronary occlusion.[8] Speculation is based on the similar effect of cocaine and amphetamine: the drug produced vasospasm on the coronary arteries and thus resulted in chest pain, ischemic ST-segment and T-wave changes on ECG, and even myocardial injuries.[9,10] There have been early reports of acute myocardial infarction caused by thrombus-filled coronary vessels after the use of amphetamine.[10,11] Compared with the previous case report by Qasim et al,[4] our case clearly documented the

existence of thrombus in the coronary arteries during emergency coronary angiography. The contribution of thrombus formation associated with MDMA has not been reported. However, speculations can be made that the pathogenesis of MDMA-related acute myocardial infarction is similar to that caused by amphetamine.

The typical dose of MDMA varies from 50 to 150 mg, but the amount per tablet can vary 70-fold or more.[3] The serum concentration 6 hours after ingestion of 125 mg of MDMA is around 150 ng/mL.[12] Our patient had a much higher concentration (1,100 ng/mL) 6 hours after ingestion. It is possible that the dose of MDMA ingested might be higher than reported by the patient. Although there are no data available documenting the toxic MDMA level, most of the cases of serious toxicity or fatality have involved blood levels ranging from 500 to 10,000 ng/mL.[3]

Medical treatment for drug-induced myocardial infarction, such as cocaine and amphetamine, deviates from the standard treatment in certain aspects. Initially, oxygen, aspirin, and benzodiazepines can be given in amphetamine-related chest pain. If chest pain continues, coronary vasodilators, such as nitrates, might be necessary to reverse residual coronary spasm.[8] €Blockers were avoided because of the concern of unopposed/ activation, which could result in severe hypertension.[4] Emergency coronary angiography provides evidence of thrombotic occlusion in the coronary artery and provides an opportunity for the use of intracoronary infusion of thrombolytic agent directed to the occluded vessel. Our patient had much thrombus inside an apparent normal coronary tree. Because the postthrombotic coronary blood flow was adequate and for fear of MDMA-associated intracranial hemorrhage, thrombolytic therapy was not prescribed initially. We chose pharmacologic treatment with intravenous glycoprotein IIb/IIIa inhibitor to prevent progression of thrombus. However, the subsequent angiogram 5 days later confirmed that thrombi were still present, and therefore, intracoronary thrombolytic therapy was given to resolve the remaining coronary thrombi.

In conclusion, MDMA use is emerging as an important drug abuse problem. This case demonstrates that, in young patients without apparent risk factors who present with acute coronary syndromes, high suspicions of drug abuse should be considered.

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