Fatal Small Intestinal Ischemia Due to Methamphetamine Intoxication: Report of a Case With Autopsy Results

Hamid Attaran

Legal Medicine Research Center, Legal Medicine Organization, Mashhad, Iran

Received: 8 Apr. 2016; Accepted: 21 Oct. 2016

Abstract- Methamphetamine is one of the most common abused drugs, so its various effects on different body organs should be familiar to all physicians. Regarding its gastrointestinal sequels, there are few reports of ischemic colitis induced by its vasoconstrictive effects. This is the first report of isolated small intestinal infarction resulting in death following methamphetamine toxicity. A 40-year-old woman with a past history of medical treatment for obesity referred to hospital with severe chest and back pain, perspiration, nausea, agitation, high blood pressure, bradycardia and subsequent lethargy and vasomotor instability. Cardiac evaluations were normal, and a toxicologic urinalysis revealed methamphetamine. Later, abdominal pain predominated, and ultrasonography revealed signs of bowel infarction. She did not consent to surgery and succumbed afterward. At autopsy gangrene and perforation of distal ileum were found. The cause of death was determined as intestinal gangrene following methamphetamine toxicity. Methamphetamine has anorectic effects and so is used in some "diet pills"; Consumers may not even know they are using methamphetamine. Hence in cases of either known MA abuse or those using unknown weight reduction drugs presenting with gastrointestinal complaints or abdominal pain, intestinal ischemia should be kept in mind and if plausible, intervened promptly.

Acta Med Iran 2017;55(5):344-347.

Keywords: Methamphetamine; Intestinal ischemia; Drug abuse; Diet pills

Introduction

Methamphetamine (MA) abuse is Increasing all over the world and combined with amphetamine, the prevalence of its abuse is second only to cannabis (1,2). Since its introduction during the early years of 20th century, amphetamines have been used for the treatment of obesity, enuresis, depression, parkinsonism, attention deficit hyperactivity disorder (ADHD), coma and even alcoholism (3); but currently, their use are limited to few indications including ADHD, narcolepsy, and short-term weight reduction (2,3). Unlike most other drugs of abuse, MA is almost equally used by women and men, and women are suggested to be more attracted to MA for weight-loss and controlling symptoms of depression (1). MA increases the release of dopamine, norepinephrine, and serotonin from presynaptic neurons, producing euphoric and reinforcing effects. The peripheral effects are induced by release of norepinephrine, and the central effects are caused mainly by dopamine (4). So it causes excessive sympathetic nervous system activity and vasoconstriction, and thus produces cardiovascular effects including tachycardia and cardiac arrhythmias (2). Coronary artery thrombosis in crystal MA abuser also has been reported (5). Amphetamine and MA can induce progressive necrotizing vasculitis in different organs, including CNS, cardiovascular, renal, and gastrointestinal systems.

There are few case reports of intestinal ischemia or infarction associated with MA abuse, which is suggested to be caused mainly by vasoconstriction and vasculitis (6). There is no previous report of isolated small intestinal infarction resulting in death following MA use as described here.

Case Report

A 40-year-old obese white woman presented to the emergency department of a general hospital at 1 AM complaining of severe chest pain radiating to her back and lumbar area with perspiration, nausea and agitation

Corresponding Author: H. Attaran
Legal Medicine Research Center, Legal Medicine Organization, Mashhad, Iran
Tel: +98 915 1164863, Fax: +98 38452100, E-mail address: hmdattaran.ha@gmail.com

started two hours before admission. Except for depression she had no previous history of any significant disease including ischemic heart disease, hypertension, hyperlipidemia, and diabetes. She was working as a driving instructor and had a sedentary lifestyle. Her drug history included metformin, orlistat, and fluoxetine which were prescribed to her eleven months earlier by a nutritionist in a weight-reduction program, but only used for almost two months and then discontinued.

Her weight was 86 kg, height 158 cm, and BMI 34.4. On arrival at ED, her GCS was 15, temperature 37^{o}; blood pressure, $^{170}/_{60}$ mmHg; pulse, 52 beats/min; respiration, 16 breaths/min; and SPO_2, 96%. With a primary suspicion of acute inferior myocardial infarction, she was admitted to CCU for further evaluation and treatment. Her chest pain subsided with the administration of 75 mg Meperidine, and her initial electrocardiogram revealed no significant finding except sinus bradycardia.

Other prescribed drugs were normal saline, aspirin, alprazolam, ranitidine, heparin, and nitroglycerin which were ordered by emergency physician, but later discontinued by cardiologist at CCU after completion of cardiac evaluations. Her cardiac enzymes were normal, and her transthoracic echocardiography revealed no abnormality, with an ejection fraction of 65%.

Other laboratory findings were as follows: hematocrit, 40.5%; white blood cell count, 17600/micl with 82% neutrophils; platelet, 245000/micl; serum urea, 39 mg/dl; creatinine, 1 mg/dl; fasting blood sugar, 184 mg/dl; cholesterol, 172 mg/dl; triglycerides, 113 mg/dl; Na, 144 meq/L; K, 5.2 meq/L; INR,1; aPTT, 31 sec. urinalysis showed a PH of 5, 3 plus of sugar, and negative ketones.

During subsequent hours heart rate and blood pressure returned to normal, but she became lethargic, and then signs of vasomotor instability including orthostatic hypotension and syncope in sitting position developed.

A neurology consultation was done which revealed no focal neurologic signs, and a brain CT scan was performed with normal results.

Toxicologic urinalysis was positive for methamphetamine, morphine, and benzodiazepines and negative for amphetamine, cocaine, marijuana, methadone, and methylenedioxymethamphetamine. Thus, after 14 hours of inpatient workup with a final diagnosis of MA intoxication, she was referred to the toxicology emergency department of a university hospital, where she admitted in a confused state with blood pressure, 130/60; heart rate, 102/min; respiratory rate, 26/min; and temperature, 36.5° C.

Because of complaining of abdominal pain, a surgical consultation was requested and chest radiography and abdominal ultrasonography performed. CXR was normal, but ultrasonography revealed large amount of abdominal free fluid, mild distension of intestinal loops, gas in intrahepatic branches of the portal vein, and intestinal intramural gas.

Laboratory findings were as followed: hematocrit, 25%; white blood cell count, 37500/micl with 86% neutrophils; platelet, 357/micl; blood sugar, 449 mg/dl; urea, 51 mg/dl; creatinine, 2.2 mg/dl; Na, 135 mg/dl; K, 4.4 mg/dl; venous blood gas, PH=7, HCO_3=12 mEq/L, Po_2=22 mmHg, PCO_2=49 mmHg.

With a preoperative diagnosis of intestinal ischemia an emergent laparotomy was planned but she refused to consent (which was clearly documented in hospital records) and left the clinic just to refer to a nearby private hospital, where after arrival and before any supportive or interventional measures could be done, a cardiopulmonary arrest happened and did not respond to resuscitation.

Her body was referred to legal medicine center for a postmortem forensic examination. Positive findings at autopsy were as followed: Pale lividity, Facial pallor and edema, distended abdomen, pulmonary edema, no emboli in pulmonary arteries, a normal heart, 900 ml of serosanguinous intraperitoneal fluid, distension of small intestinal loops with frank gangrene of 80 cm of ileum that was perforated at the distal part, from which bloody fluid was draining into the peritoneal cavity (Figure 1).

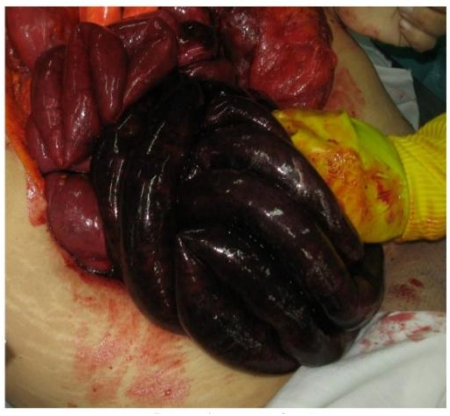

Figure 1. Small intestinal gangrene as found at autopsy

There was no skip area, and colon had no signs of ischemia. Liver, spleen, kidneys, Adrenals, and pancreas were normal. No obvious obstructive pathology was found at the base of mesenteric arteries. Brain was normal, and there was no intracranial hemorrhage.

A toxicologic analysis of viscera with GC-Mass revealed MA.

The cause of death was determined as intestinal gangrene and perforation following MA toxicity.

Discussion

One of the few pharmaceutic uses of MA that is mostly appealing for women is for weight reduction, with recommended daily doses up to 15 mg. But at usual doses, tolerance to its anorectic effects develops after several months, and weight will regain after the development of tolerance or stopping of drug administration (2).

Considering its anorectic properties, MA may be used in manufacturing some illicit and out of pharmacopeia "diet pills" that is offered by unauthorized sources to those seeking weight reduction remedies. Since their ingredients are often unknown, consumers of these illicit drugs may even not know that they are using a MA containing product, as in this case with no confirmed history of drug abuse, but positive clinical and laboratory results.

Chronic use of MA may lead to cardiovascular, pulmonary, neurologic, and dental diseases (1). Therapeutic doses of amphetamines raise blood pressure and initially slow heart rate, but high doses will cause tachycardia, palpitation, and dysrhythmias. Although chest pain frequently happens after the use of amphetamines, electrocardiographic signs of myocardial ischemia are uncommon (2). Regarding splanchnic vasoconstriction that is induced by MA, gastrointestinal incidents including bowel ischemia may happen; however, there are few confirming case reports (4,6,7,8,9,10). In previous few reported cases of intestinal ischemia following MA use, the ischemia was either confined to the colon (Ischemic colitis) (7,8,9) or parts of small bowel and colon (4,6,10) ,but in this case, an isolated 80 cm part of distal ileum was ischemic without the involvement of colon. Regarding no findings of acute thrombotic occlusion at the origin of SMA and no source for arterial emboli, the most probable mechanism of isolated small bowel ischemia could be a nonocclusive vasospastic process.

Although chest pain, hemodynamic instability and lack of a clear history of drug abuse made ischemic heart disease the initial diagnosis, subsequent abdominal symptoms and imaging and laboratory findings made the diagnosis more obvious, even though the fulminant course of the disease together with refusal to consent for surgery lead the patient to death.

Postmortem findings were nonspecific, and toxicologic analysis revealed MA as the most probable initiating factor. Though it should be noted that the interpretation of the significance of postmortem MA needs careful evaluation of the circumstances surrounding the death, clinical pattern of death, the autopsy findings, drug history of the deceased, anatomic site of postmortem sample collection, and the reliability of the sample integrity. So the postmortem MA concentration should not be used alone to determine the cause of death (2).

In the presented case, consistency of clinical history and signs, symptoms, laboratory and postmortem findings with the diagnosis of MA contribution to death, lead to the final determination cause of death as intestinal gangrene and perforation following MA toxicity.

MA abuse is rapidly increasing worldwide, and its toxicity may have miscellaneous and nonspecific presentations. Except for trauma and cardiopulmonary complaints, the most common presenting emergency department complaint of patients with acute MA use is gastrointestinal and genitourinary (11). By the other hand in special groups such as women using anorectic drugs, its consumption may not be as obvious. So MA intoxication must be on the differential diagnosis list of such patients referring to emergency departments. Its ischemia producing effect on bowels needs to be kept in mind when any MA abuser refers with abdominal pain or gastrointestinal complaints, which requires prompt evaluation and treatment.

References

1. Radfar SR, Rawson RA. Current Research on Methamphetamine: Epidemiology, Medical and Psychiatric Effects, Treatment, and Harm Reduction Efforts. Addict Health 2014;6:146-54.
2. Barceloux, Donald G. Medical Toxicology of Drug Abuse Synthesized Chemicals and Psychoactive Plants. 1st ed. N.J: John Wiley & Sons,2012:3-56.
3. Nelson L, Goldfrank LR. Goldfrank's Toxicological Emergencies. 9th ed. New York: McGraw-Hill Medical,2011:1078-90.
4. Brannan TA, Soundararajan S, Houghton BL. Methamphetamine associated shock with intestinal infarction. MedGenMed 2004;6:6.
5. Khaheshi I, Mahjoob MP1, Esmaeeli S2, Eslami V1, Haybar H. Simultaneous Thrombosis of the Left Anterior Descending Artery and the Right Coronary Artery in 34-Year-Old Crystal Methamphetamine Abuser. Korean Circ

J 2015;45:158-60.

6. Parsa C, Orlando R, Felman I, Duarte DA, Jacoby B. Multiple-organ failure due to abuse of methamphetamine - A case of Methamphetamine-associated intestinal infarction presenting with altered mental status, abdominal pain, and laboratory findings reminiscent of diabetic ketoacidosis. J South California Clin 2012;6:25-8.
7. Holubar SD, Hassinger JP, Dozois EJ, Masuoka HC. Methamphetamine colitis: a rare case of ischemic colitis in a young patient. Arch Surg 2009;144:780-2.
8. Johnson TD, Berenson MM. Berenson. Methamphetamine-Induced Ischemic Colitis. J Clin Gastroenterol 1991;13:687-89.
9. Herr RD, Caravati EM. Acute Transient Ischemic Colitis after Oral Methamphetamine Ingestion. Am J Emerg Med 1991;9:406-9.
10. Prendergast C, Hassanein AH, Bansal V, Kobayashi L. Shock with Intestinal Ischemia: A Rare Complication of Methamphetamine Use. Am Surg 2014;80:101-2.
11. Diercks DB, Boghos E, Offerman S, Lee A, Weber JE. Presenting Emergency Department Complaints in Patients with Acute Methamphetamine and Cocaine Use. Ann Emerg Med 2005;46:51.