Methamphetamine spasm in the large caliber arteries—the severity is likely underestimated

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ABSTRACT

This report describes two cases of rarely reported, severe large arterial vascular spasms seen on computed tomography images after methamphetamine abuse. Although the effects of methamphetamine on the central nervous system and smaller arteries are relatively well known, its effects on large caliber arteries are rarely discussed. We present two cases of severe large arterial multisegmented vasospasm, captured on contrast-enhanced computed tomography, several hours after methamphetamine abuse. One of the patients was discharged without apparent tissue loss or organ failure. The other developed severe heart failure, liver failure, and toe gangrene. The publication of the de-identified images has been approved by the VA Central California Health Care System's Research and Development Committee and Privacy Officer. Vascular surgeons and, perhaps, acute care physicians, who are usually aware of small arterial vasospastic conditions, should also be aware of this methamphetamine-induced large arterial finding, which can be quite dramatic in appearance on imaging. (J Vasc Surg Cases Innov Tech 2024;10:101376.)

Keywords: Amphetamine; Large arterial vasospasm; Methamphetamine

Sympathomimetic drugs comprise a broad category of natural and ever-evolving synthetic chemicals. When sympathomimetic drugs are ingested, depending on the substance and its dose, a wide variety of presentations can occur, affecting multiple organ systems.[1] Amphetamines, after marihuana and opioids, are the third most popular illicit drugs worldwide.[2] The popular attention appears to be on its effects on the central nervous system; however, its acute and chronic cardiovascular effects are also significant and can be very detrimental or even lethal. Patients can experience headache, abdominal pain, arterial dissection, hemorrhagic and ischemic stroke, Raynaud syndrome, finger and/or toe gangrene, chest tightness, angina, arrhythmia, and myocardial infarction, all of which can represent peripheral artery-related side effects.[3-9] Disturbing side effects can also develop in the central nervous system, such as insomnia, anorexia, and irritability. Sympathomimetic drugs are highly addictive, and, once started, the patient could be reluctant to stop taking them. In a case series that specifically studied the peripheral vascular side effects of amphetamine analogs in patients who received these medications for psychiatric conditions, 75% of the patients continued the medication regardless of the disturbing and detrimental vascular side effects.[10]

Treatment of drug-induced severe arterial vasospasm is not standardized. Case reports suggest that calcium channel blockers, nitroprusside, alprostadil, anticoagulation, and epidural infusion of bupivacaine can be effective. Transluminal balloon dilatation is also described among the efforts to break the spasm.[11] The efficacy of these treatments is unclear, however.

Severe arterial vasospasm is documented in the smaller, peripheral arteries in several studies.[3-9] Involvement of the large diameter aorta and iliac arteries and the severity are much less documented and reported. We present two cases of severe large arterial vasospasm that developed after methamphetamine ingestion to alert vascular surgeons to the unique and potentially drastic presentation. The patients provided written informed consent for the report of their case details and imaging studies. The VA California Health Care System's Research and Development Committee and Privacy Officer reviewed the case report and approved its submission for publication.

CASE REPORT

Patient 1. A 58-year-old white man came to the emergency room with a 1-month history of constant right-sided flank pain that became worse with sitting. The patient denied trauma and any other symptoms. He was afebrile, his vital signs were normal, and he was not clinically intoxicated. On physical examination, the patient's right flank was tender, and the skin was hypersensitive to touch over the area. However, no other significant finding was present. The extremity arteries were weak but palpable bilaterally, and the skin color was normal.

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The patient had a history of hyperlipidemia, hypertension, type 2 diabetes, and methamphetamine abuse. He took atorvastatin, amlodipine, insulin, and hydrochlorothiazide. The laboratory tests showed a normal complete blood count, chemistry panel, and lactate level.

Computed tomography (CT) scans of the abdomen and pelvis with intravenous contrast were obtained (Fig 1). The CT scans showed no atherosclerotic disease, aneurysm, or dissection. Severe stenosis was noted, starting in the supraceliac aorta, which gradually tapered down even further distally. Its maximum was in the infrarenal aorta, proximal to the inferior mesenteric artery. Here, the lumen reached a critical 1-mm level, and the aorta appeared to be near flat. The distal aorta was normal in diameter; however, both common iliac, internal, and external iliac arteries had focal smooth-walled severe stenoses of several centimeters, each measuring ~1 to 2 mm. No other abnormality was found.

On questioning, the patient reported that he used methamphetamine 4 days prior. The urine drug screen obtained was positive for amphetamines. Severe large arterial vasospasm was suspected; however, no diagnosis was secured behind the patient's right flank pain. He was admitted for observation and received heparin to prevent arterial thrombosis caused by the severe arterial narrowing. Calcium channel blocking medication was considered but not given. The patient received cyclobenzaprine and gabapentin for pain control of his right flank. By the next day, the patient's flank pain had improved significantly. He underwent another CT scan with intravenous contrast that included his chest, abdomen, and pelvis to evaluate for the extent of the narrowing in the large arteries. This CT scan showed complete resolution of all previous findings (Fig 1). The aorta measurement had improved to 21 mm at the celiac artery, 15 mm at the renal artery and bifurcation, and 9 mm at the external iliac arteries. The heparin anticoagulation was stopped after ruling out embolism as the cause of the patient's symptoms. Because no resultant organ damage had occurred, the patient was discharged from the hospital with instructions.

Patient 2. A 60-year-old homeless white man came to the emergency room with bilateral severe foot pain. On inquiry, the patient reported that he had been exposed to cold weather and rain in the past several weeks while he was mainly barefoot. He also reported that he was an active inhaled methamphetamine user with recurrent chest tightness at almost every use. Although he had used the drug about 12 hours prior, he did not appear intoxicated. The patient had no medical history, used a nicotine patch to aid his smoking cessation effort, and took hydrocodone/acetaminophen for foot pain. On examination, his vital signs were normal. His bilateral distal feet were pale, with several superficial and deep ulcerations. Around the ulcers some erythema was present, but there was no purulence, malodor, or crepitus. The pedal arteries were weakly palpable. His laboratory test results were normal, except for the liver function test, with both aspartate aminotransferase and alanine aminotransferase significantly elevated. The urine drug screen was positive for amphetamines and oxycodone. The electrocardiogram showed atrial flutter. The echocardiogram showed a severely reduced left ventricular ejection fraction (20%-25%) and a significantly dilated right ventricle. These findings were new compared with a previous echocardiogram. The patient was diagnosed with acute biventricular heart failure and atrial flutter secondary to methamphetamine use, acute liver injury secondary to congestion or acetaminophen toxicity, and extensive soft tissue injury on the distal feet from frostbite or methamphetamine use, or both.

The patient also underwent a CT scan of the abdomen and pelvis with intravenous contrast to further assess his liver (Fig 2). The CT scan showed no atherosclerotic disease, aneurysm, or dissection and no narrowing in the paravisceral aorta. Smooth-walled stenosis was present, starting in the common iliac arteries and measuring ~2 to 3 mm, which gradually tapered down further distally. Its maximum size was in the femoral arteries, where the lumen reached 3 mm in diameter. This had resolved on repeat CT scans (iliac vessel, 10-11 mm; common femoral artery, 8-9 mm; Fig 2). No other pathology was found. Diuresis, N-acetyl cysteine, and wound care were started, to which the patient responded well. His feet returned to a normal color, except for some of his toe tips, which developed gangrenous changes.

DISCUSSION

Amphetamines are a subclass of sympathomimetic drugs that contain various compounds. Cathinone is one of the naturally occurring amphetamines consumed for hundreds of years by humans for its stimulative, euphoric, and hallucinogenic effects. Cocaine is also quite well known for these effects. Amphetamine, the drug, was synthesized in Germany in 1887. Its more potent version, methamphetamine, was also synthesized, but in Japan in 1893. Both drugs were used by the Axis and Allied forces during the Second World War to extend wakefulness in combat situations.[1,2]

The amphetamines' main mechanism of action is increasing the dopamine, noradrenaline, and serotonin neurotransmitter levels at the synapses. This is achieved by releasing these substances from their cytosolic storage vesicles, depleting their reserve at the same time. Methamphetamine also inhibits its reuptake into the presynaptic terminals and blocks the monoamine oxidase enzyme, both of which result in slower clearance of the neurotransmitter.[1,3] The substance also has a direct agonistic effect on the dopamine, noradrenaline, and serotonin receptors themselves.[3,4,13]

Depending on the ingested dose, individuals with acute intoxication often present with agitation, which can reach a hazardous level for self-injury. Hallucination, paranoia, hyperthermia, hyperreflexia, and seizure can also be present. The strong euphoric effect, which is desired by drug addicts, is thought to be related to dopamine release in the mesolimbic system. Rhabdomyolysis, severe hypertension, ischemic and hemorrhagic stroke,

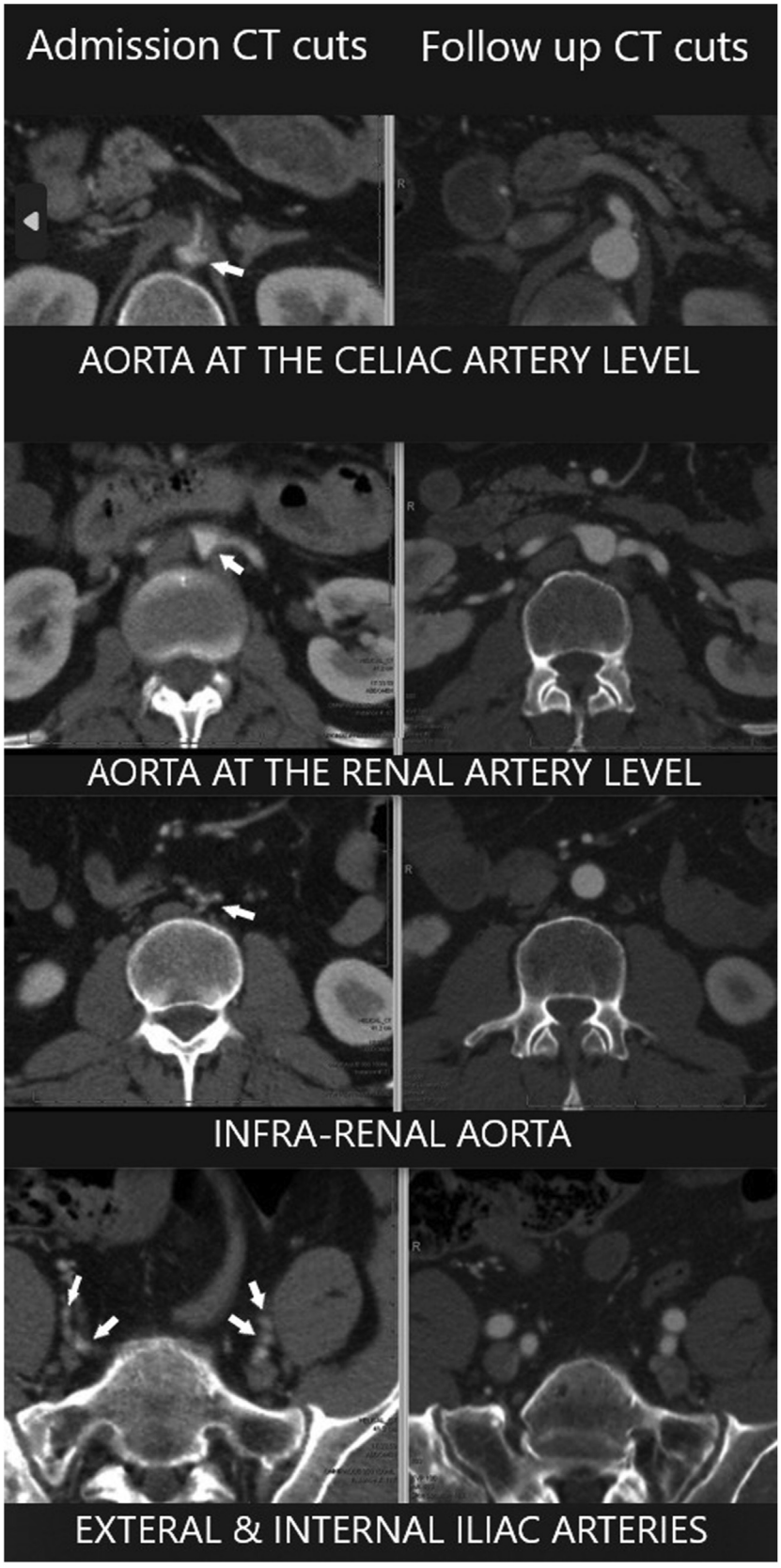

Fig 1. Initial and follow-up computed tomography (CT) scans of patient 1.

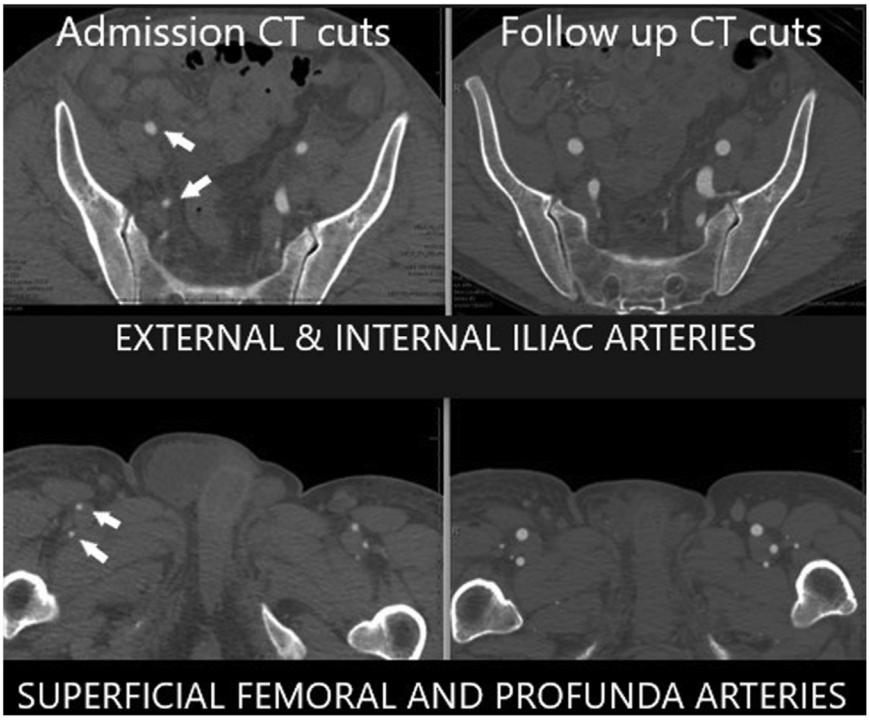

Fig 2. Initial and follow-up computed tomography (CT) scans of patient 2.

liver and kidney failure, acute coronary syndrome with infarction, severe cardiomyopathy, lethal arrhythmia, bowel infarction with resultant perforation, and/or ischemic colitis can also develop. These latter complications are not central nervous system related and are largely attributed to severe and prolonged arterial vasospasm. A similar mechanism is suspected, at least partially, behind these drugs' teratogenic effect. Among the resultant chronic problems, congestive heart failure, cognitive decline, and Parkinson syndrome are common.[5-9] It is useful to know that as a medication, amphetamine and its derivatives or analogs are commonly used in the treatment of attention deficit/hyperactivity disorder, narcolepsy, and other psychiatric diseases. These medications are also used as an appetite suppressor.

The effect of this degree of drug-induced critical stenosis on the end organs and extremities can be dramatic as the arterial flow decreases. The severe contraction of the muscles in the artery wall can also cause sheer injury between the layers, which can result in arterial dissection.[14] Both phenomena can lead to prolonged ischemia, dysfunction, and necrosis and can affect almost any of the organ systems.

Most of the evidence in the literature has demonstrated the impact of amphetamines on smaller blood vessels, including causing stroke due to intracerebral vessel narrowing, myocardial infarction due to coronary vascular narrowing, bowel ischemia due to mesenteric vasoconstriction resulting in nonobstructive mesenteric ischemia, and affecting the vascular system of the extremities.[10,11,14,15] To the best of our knowledge, ours is the first case series to describe and discuss the effects of amphetamines on large blood vessels. It is unclear whether the mode of drug consumption, type (pure or mixture), dose of ingestion, and duration of ingestion affect patients' presentation and/or the degree of vasospasm. In our series, the perivisceral aorta was affected in one patient, and in the other patient, the perivisceral aorta was spared and the iliac and common femoral vessels were affected. Given the paucity of literature on this topic, further investigation is warranted to better understand amphetamine-induced vasospasm.

The imaging studies of our patients demonstrate the severity of methamphetamine-induced arterial spasms in the large caliber arteries. Because their detection was accidental, the complete duration of the spasms could not be determined. One of the patients had received heparin, but the other had not received specific therapy for the arterial finding. Heparin was initially started on evaluation of the patient in the emergency department, pending the imaging and evaluation findings, because embolism was thought to be the initial cause of the patient's presentation. After the imaging and laboratory studies were completed, the cause was thought to be an arterial spasm. Thus, the intravenous heparin was stopped, and conservative management was completed. Ultimately, the spasms resolved in both patients spontaneously within 24 to 48 hours, and both patients survived, although one had developed

toe gangrene. The latter was likely the result of combined cold exposure injury predominantly and some contribution from the severe methamphetamine-induced arterial vasospasm.

CONCLUSIONS

Amphetamines are the third most popular illicit drug worldwide. In addition to its central nervous system and small arterial vasospastic effects, methamphetamine can induce severe segmental spasms, not only in the small, but also in the large arteries. The diagnosis can be secured by the typical presentation on imaging studies and the presence of amphetamines in the urine drug screen test. The arterial spasm can have a relatively benign course, and the symptoms can improve spontaneously, depending on the severity and duration of the reduced perfusion to the different organs, limbs, and fetus and can cause debilitating problems.

DISCLOSURES

None.

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