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Acute Limb Ischemia Caused by Inadvertent Arterial Drug Self-Injection: A Case Report

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5 Division of Infectious Disease, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA**Corresponding Author:** Sarah Ann Schmalzle, e-mail: sschmalzle@ihv.umaryland.edu
Conflict of interest: None declared**Patient:** Male, 35-year-old
Final Diagnosis: Thrombosis
Symptoms: Pain
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases • Medicine, General and Internal • Psychiatry**Objective:** Unusual clinical course**Background:** A predictable consequence of long-term injection drug use is the destruction of the native venous system; as a consequence, people who inject drugs may eventually move to injection into skin and subcutaneous tissue, wounds, muscles, and arteries. These practices put people who inject drugs at risk for injection-related soft-tissue infection, vascular damage, ischemia, and compartment syndrome, all of which have overlapping presenting symptoms.**Case Report:** A 35-year-old man who injects drugs presented with foot swelling and discoloration initially concerning for necrotizing fasciitis or compartment syndrome. After progression despite appropriate antimicrobial and surgical treatment for soft-tissue infection, he was diagnosed with arterial insufficiency and resultant distal ischemia. This diagnosis was discovered only after obtaining additional history of the patient's drug use practices. Just prior to his symptoms, he had unintentionally injected a formed thrombus into his dorsalis pedis artery.**Conclusions:** Intra-arterial injection of drugs can cause ischemia through a variety of mechanisms, including direct vessel trauma, arterial spasm, toxicity from the drug of abuse or an adulterant, embolism of particulate matter, and as proposed here, direct injection of preformed thrombus. Medical providers should be aware of the steps of injection drug use and their associated risks so that they can ask appropriate questions to focus their differential diagnosis, increase their understanding of common or current local injection practices, and develop rapport with the patient. Patient education on safe injection techniques may also reduce the risk of serious complications.**Keywords:** Harm Reduction • Hyperbaric Oxygenation • Injections, Intra-Arterial • Ischemia • Opioid-Related Disorders • Substance Abuse, Intravenous**Abbreviations:** IDU – injection drug use; OUD – opioid use disorder; PWID – people (person) who inject(s) drugs; SSTI – skin and soft-tissue infection; CK – creatinine kinase; ABI – ankle brachial index; HBOT – hyperbaric oxygen therapy; rtPA – recombinant tissue plasminogen activator; SSP – syringe service program; SCF – safe consumption facility; MUOD – medications for opioid use disorder**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/932903>

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Background

Injection drug use (IDU) is associated with numerous sequelae in addition to addiction and potential overdose death, including infections such as skin and soft-tissue infection (SSTI) and blood-borne infection, and non-infectious complications such as direct vascular and soft-tissue injury [1,2]. The somatic sequelae of IDU in people who inject drugs (PWID) can have overlapping clinical presentations, confounding early efforts at diagnosis. Gaining more detailed knowledge of drug preparation and injection techniques allows health care professionals to elicit potentially crucial details in the patient's history that could guide them toward differentiation between SSTI, vascular injury and ischemia, and direct tissue injury. However, education and clinical guidelines on this topic are often lacking.

Case Report

A 35-year-old man with a 24-year history of IDU and opioid use disorder (OUD) complicated by multiple SSTIs presented to the Emergency Department 3 days after his last injection into the dorsal left foot. He reported recently injecting heroin into his bilateral feet, forearms, and groin. While he did obtain needles from a syringe service program (SSP), he also licked and reused his needles and shared injection equipment, including needles, with a monogamous sexual partner, raising suspicion for infectious complications of IDU.

The dorsal surface of his left foot was erythematous, swollen, and tender, though not warm, and had a patchy dusky purple discoloration (Figure 1A, 1B). The foot pain was described as severe, burning in quality, and non-radiating. Upon examination there was full strength and sensation in the entire limb, except reduced motor activity in the great toe only, and tenderness throughout the foot. Dorsalis pedis and posterior tibial pulses were palpable as well as audible by Doppler ultrasonography.



Figure 1. Left foot on hospital day 1. (A) Dorsal left foot. (B) Plantar left foot; puncture site of the most recent drug injection can be seen in mid-dorsal foot over DP artery.



Figure 2. Left foot on hospital day 10. Despite treatment for SSTI, the patient's foot developed progressive discoloration and pain by hospital day 10. (A) Dorsal left foot. (B) Plantar left foot.

Initial laboratory studies demonstrated a white blood cell count of 10.1 K/mcL, erythrocyte sedimentation rate of 51 mm/hr, C-reactive protein of 8.8 mg/dL, lactate 1.7 mmol/L, and an elevated creatinine kinase (CK) to 1,414 units/L. Urine toxicology was positive for cannabinoids, fentanyl, oxycodone/oxymorphone, and opiates. Fentanyl was likely present in the urine from illicitly manufactured fentanyl, which is commonly “cut” with heroin in Baltimore; oxycodone/oxymorphone was likely from oxycodone he had received in the Emergency Department prior to providing the specimen; and opiates were likely from morphine, a metabolite of heroin.

At this time in his disease course, the diagnosis was unclear; the initial differential for his presentation included compartment syndrome, ischemia, SSTI with or without abscess, and necrotizing fasciitis. Given his history of recurrent SSTIs and his physical presentation accompanied by elevated inflammatory markers, he was presumptively diagnosed with a skin and soft-tissue infection and started on empiric vancomycin. Orthopedic and soft-tissue surgeons evaluated the patient and

ultimately suspected necrotizing soft-tissue infection. The patient went to the operating room immediately for intervention. Two incisions were made along the dorsum of the foot and unexpectedly revealed edematous but otherwise healthy tissue. This finding excluded necrotizing SSTI and compartment syndrome. The wound was left open for delayed primary closure and the patient was admitted to the internal medicine service for further evaluation and management.

He underwent successful closure of his surgical wound but continued to report severe pain, uncontrolled with increasing doses of opioids that were prescribed both for opioid replacement therapy and for pain management. There was no evidence of a surgical site infection; the persistent pain was initially suspected to be secondary to opioid tolerance from long-term injection drug use. However, subsequent examinations revealed a progressively darkening great toe (Figure 2). Ankle brachial indices (ABIs) obtained to assess for vascular insufficiency revealed a left-sided ratio of 1.23 and a right-sided ratio



Figure 3. Left foot with progressive ischemic changes 4 weeks after initial presentation. (A) Dorsal left foot. (B) Plantar left foot.

of 1.28 (normal 1.10-1.30). Peak pressure was 0 mmHg in the left great toe, compared to 167 mm Hg in the right great toe.

Further details regarding the patient's IDU immediately prior to his presentation were elicited. The patient revealed that during his last drug use, he made several unsuccessful attempts to locate a site with good blood return, before ultimately injecting into his left foot. With the earlier attempts, a small amount of blood had collected in the syringe and had clotted. He then injected the entire contents of the syringe, including both the drugs and the small thrombus, into what he thought was a vein on the top of his left foot. The injection site, still visible and clearly identified by the patient, was directly overlying the dorsalis pedis artery. He was surprised to learn he had injected into an artery and reported that he did not know how to differentiate between the arteries and veins, or that this was an important distinction.

He was treated with intravenous heparin and vascular surgery was consulted, but no surgical intervention was warranted. A multimodal treatment plan included aggressive hyperbaric oxygen therapy (HBOT), therapeutic anticoagulation, management of opioid withdrawal and pain with methadone, and outpatient follow-up with podiatry and for opioid replacement therapy.

Following discharge, the patient attended his methadone clinic regularly. His left toes were allowed to demarcate (Figure 3), and 2 months after his index admission he underwent amputation with debridement of the tissue beyond the metatarsal phalangeal joints (Figure 4). The patient continued to follow up with podiatry, pain management, and his methadone clinic,



Figure 4. Left foot status after transmetatarsal amputation 12 weeks after initial presentation.

and developed an equinovarus deformity from inconsistent controlled ankle motion boot use approximately 5 months after his presentation. He was to be scheduled for an Achilles tendon lengthening procedure to address his foot deformity but was lost to follow-up.

Discussion

Limb or digit ischemia from intra-arterial thrombus is an unusual complication of IDU. The true epidemiology of IDU-related limb ischemia is unknown, as there are few reports in the literature of limb or digit ischemia after IDU. Treatment of this complication is therefore based on limited case report studies and attempts at reversal of the underlying physiologic process. There are multiple proposed etiologies for vascular damage and ischemia from intra-arterial injection of therapeutic drugs: adulterants causing a local toxic vasculitis, intimal trauma, arterial spasm, recrystallization of drug, high-osmolarity solutions, embolism of particulate matter from crushed pills, thrombus formation from microcrystalline cellulose (a common pill filler), and norepinephrine-mediated vasoconstriction. An association between vascular damage and highly lipid-soluble medications such as benzodiazepines has also been identified, but the mechanism of this association is not clearly understood [3-5].

The mechanism of ischemia in this patient was likely intra-arterial injection of a preformed thrombus that resulted from the patient's method of drawing back on his syringe prior to injecting. This is based largely on the patient's description of his most recent drug use. His extensive experience injecting lends credence to his recollection of injecting a thrombus, but other mechanisms may explain the vascular injury.

Most cases of intra-arterial injection of drugs present with non-palpable pulses, loss of sensation, immobility of the affected limb, and immediate discomfort, occasionally referred to as "hand trip", following injection into an upper extremity [6]; presentation typically occurs within hours of injection. When ischemia is suspected, Doppler ultrasonography, ABI, or an arteriogram can confirm poor blood flow to the affected limb, as was the case here. If this diagnosis is suspected, urgent vascular surgery consultation would be prudent.

Our patient was treated with systemic anticoagulation and HBOT, although there is no established protocol for management of ischemia after intra-arterial drug injection. Low-molecular-weight dextran, heparin, and prostacyclin analogs have been suggested to mitigate the thrombosis and vasospasm thought to be the root cause or major contributing factor of the limb ischemia [7]. Catheter-directed recombinant tissue plasminogen activator (rtPA) demonstrated moderate

success in restoration of flow in a small cohort of patients, but patients who presented with extensive large-vessel thrombosis had worse outcomes than those who presented with small-vessel injury [8], such as the patient in our case. A study of 16 patients who presented after accidental intra-arterial injection utilized a combination of heparin, local rtPA with prostaglandin, cefuroxime, and mechanical interventions, with encouraging results [9].

HBOT may be considered as an adjunct to thrombolytic therapies, as case reports indicate it can assist in restoring circulation to damaged areas, although evidence and experience for its use in limb ischemia is lacking [10]. Furthermore, HBOT has been shown to increase oxygen at low-tension sites, such as diabetic foot ulcers and radiation injuries, improving wound healing [11]. In patients who may have collateral flow to affected limbs, HBOT can contribute positively to other limb salvage therapies.

The failure of multiple medical and surgical specialties to accurately assess his drug use practices on initial presentation, and the overlapping physical findings in necrotizing infection and ischemia, led to a delay in appropriate treatment in this case. Diagnosis of any complication of illicit drug use may be delayed or entirely missed if the patient is hesitant to provide a thorough history or if that history is not sought. PWID are frequently marginalized by society and the medical system and may be reluctant to volunteer information regarding these practices if not asked or if the approach is considered confrontational or judgmental.

Medical providers, especially those in internal medicine, emergency medicine, soft-tissue surgery, infectious disease, and psychiatry, should be familiar with the process of preparing and using drugs, and the attendant risks for complications. For instance, sharing equipment (eg, needles and syringes) can cause transmission of blood-borne viruses; use of non-sterile water or lemon juice to dissolve drugs can cause *Pseudomonas* and *Candida* infections, respectively [12]; and poor knowledge of vascular anatomy and dull needles can cause vascular injury. Providers should obtain a thorough history of drug use practices, including frequency of use; type of drugs; number and infection status of injection partners; frequency of sharing equipment; source of water, filters, needles, syringes, and other materials; anatomical sites of injection; cleaning and reuse of equipment; and participation in SSPs.

In order to prevent long-term harms of IDU, including further infection and injury, attempts should be made to help patients manage their substance use with medications for opioid use disorders (MOUD): methadone, buprenorphine, and naltrexone. Providers should be familiar with local treatment options for patients with substance use disorders, federal laws

and regulations that apply to the treatment of OUD, and the exception to these laws that allow for hospitalized patients to be started on MOUD “...to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction...” [13]. For patients who may not be interested in or able to fully discontinue injection drug use, it is also useful for providers to be aware of various evidence-based harm reduction services such as SSPs (available in many states) and safer injection/consumption facilities (SCFs). Overdose prevention strategies can include prescription of naloxone and use of fentanyl testing strips [14].

There are also resources available to help educate PWID on safer ways to inject [15]. Although instructing an individual how to inject drugs in a safer way may feel in contrast to the “do no harm” edict, harm reduction counseling can be very useful for the individual patient as well as from a public health standpoint. It is important for physicians to recognize that behavior change is difficult and, for some, not permanent. Anything that can be done to help reduce the harms related to injection drug use is positive and should be viewed as helping the patient “do less harm.”

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Conclusions

Gaining more detailed knowledge of drug preparation and injection techniques can allow health care professionals to elicit potentially crucial details in the patient's history that can guide them toward more atypical diagnoses. This case demonstrates the importance of a timely focused drug use history, which can quickly direct both medicine and surgical colleagues to the appropriate interventions. Having a high level of suspicion for complications beyond infection is crucial in areas with large populations of PWID.

Conflict of Interests

None.

Declaration of Figures Authenticity

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