

CASE STUDY

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A confirmed case of xylazine-induced skin ulcers in a person who injects drugs in Miami, Florida, USA

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Abstract

Background Xylazine is an alpha-2 adrenergic receptor agonist that has emerged as a contaminant in the illicit drug supply of fentanyl. Xylazine use may be suspected in naloxone-resistant overdoses and atypical, chronic wounds in people who use drugs (PWUD). This case is unique because it is the first case to our knowledge describing wound care for a xylazine-induced wound with a confirmatory xylazine test strip (XTS) in the setting of a syringe services program (SSP) and in the state of Florida.

Case presentation A 43-year-old woman with a past medical history of severe opioid use disorder and stimulant use disorder presented to a student-run clinic at a Miami SSP for wound care. She had multiple ulcerations diffusely over her bilateral forearms with surrounding erythema and warmth. Seven weeks later, she presented to clinic again for wound care because her wounds had progressed. At this visit, a XTS was used to confirm the presence of xylazine in her urine. Wound care management and harm reduction strategies employed at both visits were informed by best clinical judgement due to lack of formal guidelines at the time. Wound outcomes are unknown as the patient has not returned to clinic.

Conclusions Many PWUD at highest risk for acute and chronic health consequences of xylazine-adulterated fentanyl do not have access to healthcare outside of low barrier clinics and SSPs due to lack of insurance or mistrust of the traditional healthcare system due to stigma. There is an urgent need for access to XTS for PWUD and clinical practice guidelines for the treatment of xylazine-related wounds in outpatient clinics.

Keywords Xylazine, Opioid use disorder, Injection drug use, Wounds, Xylazine test strip, Harm reduction

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Background

Xylazine is an alpha-2 adrenergic receptor agonist that is a non-opioid drug used for sedation and muscle relaxation in veterinary medicine [1]. Xylazine is not approved for human use in the United States; however, it has entered the street drug supply as an additive to fentanyl, heroin, and other substances [2]. Xylazine first emerged in the early 2000s in Puerto Rico and entered the continental United States a few years later in Philadelphia and Connecticut [3]. Street-level distributors may use xylazine, also known as “tranq,” as a bulking agent to extend the supply of their other drug products [4]. Xylazine blocks the release of norepinephrine, resulting in hypotension, bradycardia, respiratory depression, drowsiness, and amnesia. While naloxone is still recommended in the setting of an overdose, it is still unknown whether xylazine’s effects can be reversed by naloxone [5]. Physicians should have a high clinical suspicion for xylazine-adulterated fentanyl in accurately diagnosing naloxone-resistant overdoses and non-healing, necrotic ulcers in people who use drugs (PWUD).

Xylazine’s association with necrotic skin ulcers has been well described in the literature [6, 7]. The mechanism of injury is thought to be directly related to its vasoconstricting effect on local blood vessels, resulting in decreased skin perfusion [8]. Decreased skin perfusion further leads to impaired healing of wounds and increased risk of superinfection. When coupled with repeated trauma of injections, xylazine can lead to extensive ulceration. In a study conducted in Puerto Rico, it was reported that people who used xylazine had a significantly higher prevalence of skin ulcers (38.5% vs. 6.8%) and poorer health than those who did not use xylazine [9]. Xylazine-induced skin ulcers may appear diffusely throughout the body, even at sites distant from the injection site. These ulcers are typically progressive, large, and necrotic [10].

Drug-checking has been utilized in medical and community settings to determine the contents of drugs since the 1990s [11]. This low-barrier harm reduction method has been associated with greater adoption of safer drug use practices [12]. Unfortunately, xylazine testing is not widely accessible, so PWUD are largely unaware of whether their drugs contain xylazine. Due to the continuous geographical spread and increasing prevalence of xylazine-adulterated fentanyl, lateral flow immunoassay xylazine test strips (XTS) have become available to allow for rapid, field-based drug testing. XTS manufactured by BTNX, a Canadian biotechnology company, demonstrated high sensitivity (100%), specificity (85%) and precision (91%) in an evaluation conducted by a Philadelphia-based forensic laboratory [13].

Here we present a representative case of xylazine-induced skin ulcers managed through a student-run free clinic housed in a harm reduction organization.

Case presentation

The patient was a 43-year-old woman with severe opioid use disorder (OUD), stimulant use disorder, and a history of overdose and infectious complications from injection drug use. The patient had a 6-year history of injecting fentanyl and cocaine. She was experiencing homelessness in Miami, FL.

She presented to a free student-run clinic at the IDEA Miami syringe services program (SSP) for wound care [14]. During that time, she was injecting 0.25 g of fentanyl and cocaine together per day in her hands and arms. At this visit, she reported ulcers on bilateral upper extremities. She stated that she had never had wounds like these before despite injecting drugs for 6 years. She described the wounds starting as closed areas of hypopigmentation, then gradually opening, and producing foul-smelling yellow drainage. She noted that when the wounds began, she had a fever that subsided after one day. She had no night sweats, chills, or lymphadenopathy. On a physical exam, she had multiple ulcerations, with the largest being 4 cm in diameter, diffusely over her bilateral forearms with surrounding erythema and warmth (see Fig. 1: 1a, 1b). She did not have wounds present on her legs at this time. A diagnosis of xylazine-associated skin ulcers was favored over other infectious or inflammatory skin conditions due to the clinical picture and recent studies reporting similar case presentations in cities with large populations of PWUD. The wounds were cleaned with saline and dressed with petroleum-impregnated gauze. The patient was instructed to clean the wounds with water and soap daily and replace the petroleum-impregnated gauze dressing. She was also prescribed a course of doxycycline for suspected superimposed bacterial infection.

Seven weeks later, she presented to clinic once again for wound care. She had continued to inject drugs and her wounds had progressed (see Fig. 1: 2a, 2b). The wounds were warm, red, and painful and she had a subjective fever. She also noted that new ulcers had formed on her bilateral lower extremities. On physical exam, she had multiple large ulcerations on her bilateral forearms with surrounding hyperpigmentation and 2 small ulcerations with a necrotic center on the lateral aspect of her bilateral knees. The patient reported that she did not inject in her legs. She stated that she had successfully finished her previous course of antibiotics but was unable to consistently clean and dress her wounds. At this visit, her urine was tested for xylazine using the Rapid Response™ XTS (Liquid / Powder), which is a rapid visual immunoassay for the qualitative, presumptive detection of xylazine in

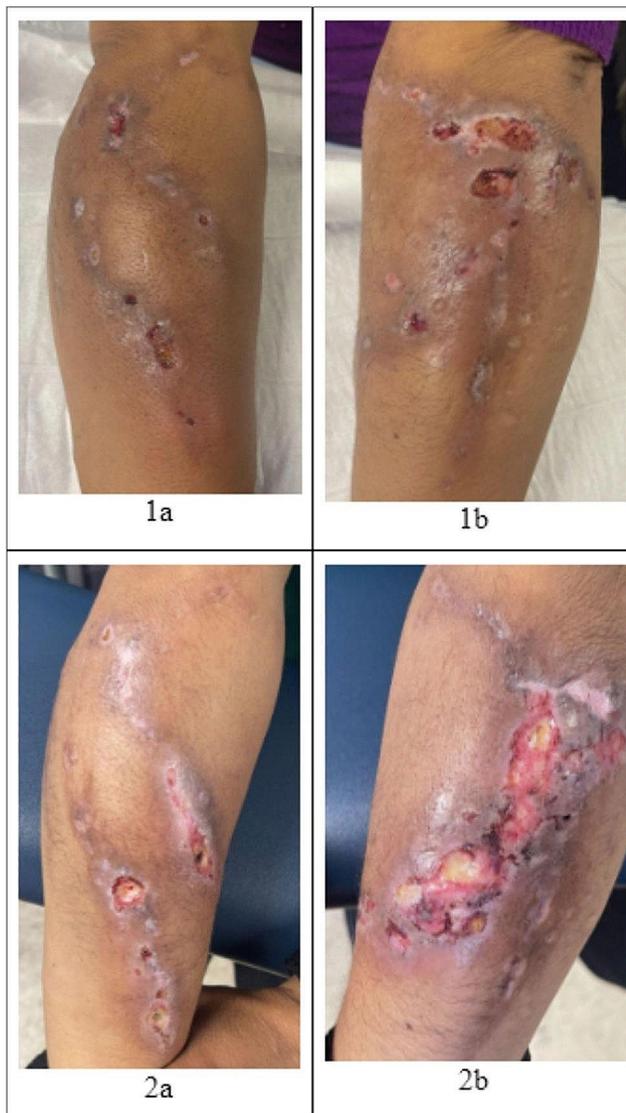


Fig. 1 Xylazine-induced wounds

liquids or powders at the cut-off concentration of 1000 ng/mL. This test strip was positive, indicating the presence of xylazine. The wounds were cleaned with saline solution and dressed the same as last time, and she was given the same wound care instructions. She was also prescribed a second course of antibiotics (trimethoprim-sulfamethoxazole) for suspected superinfection of the wounds.

Discussion and conclusions

A recent study of xylazine prevalence among PWUD seeking medical care at this SSP found that xylazine was present in 55.9% of participant's urine sample using a XTS [15]. While there have been reports of intentional xylazine use, [16] with patients reporting that xylazine "extends the high" and "gives the [fentanyl] more of a heroin effect," recent studies emphasize PWUD's

overwhelming concern about the adulterated fentanyl supply [17]. Xylazine's sedating effects leave unhoused PWUD vulnerable to robbery and assault, and one study stated that xylazine-induced wounds are a primary concern among PWUD [3]. The rising prevalence of xylazine-adulterated fentanyl is a concerning trend that may be changing the risk profile of substance use, altering substance use patterns, and affecting the treatment response of individuals with suspected overdose events [18]. Although it is unclear whether knowledge of xylazine contamination will change consumption behavior, knowing its presence can help PWUD make informed decisions guided by harm reduction principles.

To prevent unwanted exposure to xylazine and the novel health risks associated with a xylazine-adulterated fentanyl supply, harm reduction and healthcare efforts must focus on making XTS available to PWUD [19]. Evidence suggests a favorable attitude of PWUD toward XTS; in a recent study, 100% of PWUD interviewed about xylazine in Philadelphia were interested in hypothetical XTS [17]. The acceptability and utility of fentanyl test strips supports widespread dissemination of XTS to PWUD, as fentanyl test strips have been reported to change drug use behavior and improve perceived overdose safety [20]. Harm reduction programs, such as SSPs, play an important role in linking PWUD to healthcare services. Low barrier access to lifesaving medications for OUD (e.g. buprenorphine) could also mitigate harm associated with xylazine-adulterated fentanyl by supporting recovery of OUD and reducing frequency of injection opioid use [21]. Reducing barriers to accessing XTS, medications for OUD, and SSPs is a necessary step in mitigating harm associated with a xylazine-adulterated fentanyl supply.

Regarding xylazine-induced wounds, there is an emergent need for a harm reduction-based model for wound care to inform healthcare providers and empower PWUD to care for their wounds [2, 22]. Current guidelines recommend individualized treatment plans considering wound debridement, routine wound cleaning with soap and water, long-term dressings with barrier ointment to peri-wound skin, and monitoring for infectious complications [23–25]. In this case, we approached treating the wounds with petroleum-impregnated gauze to keep the area moist. Petroleum-impregnated gauze is a semi-open dressing consisting of a primary layer facing the wound, a secondary layer containing the petroleum-infused absorbent gauze and padding, and a third layer of adhesive. With this design, fluid seeps through the first layer and collects in the second layer, allowing for hydration of the wound bed and surrounding tissue. Studies have shown that wounds kept in a moist environment heal more rapidly compared to wounds kept dry [26, 27]. Petroleum-impregnated gauze also fosters autolytic debridement

of necrotic wound tissue by providing an environment to promote endogenous phagocytes and proteolytic enzymes. We treated her with two courses of antibiotics due to presence of bacterial superinfection, evidenced by erythema, induration, and systemic symptoms at the first visit, and purulent at the second visit. Given the many social barriers this patient faced, it was difficult to achieve optimal wound cleaning and dressing. Additionally, more frequent visits could have allowed adjustments to the treatment plan to best suit her needs and achieve optimal outcomes. Another limitation in the treatment of this patient was the limited resources and lack of robust team at this free clinic. Lastly, lidocaine was identified as an interferent that may lead to false-positive results in the XTS [13].

In conclusion, given the rising prevalence of xylazine-adulterated fentanyl, there is an urgent need for access to XTS for PWUD and clinical practice guidelines for the treatment of xylazine-induced skin wounds for health-care professionals. Next steps include epidemiologic research studying the geographic spread of xylazine-adulterated fentanyl, its clinical effects, and implementation of overdose prevention strategies (e.g. XTS) delivered in settings frequented and trusted by PWUD such as harm reduction and community drug checking programs.

Abbreviations

PWUD	people who use drugs
XTS	xylazine test strips
OD	opioid use disorder
SSP	syringe services program

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Author contributions

PWV and MH conceptualized the study and conducted the literature review. HET, KC, TSB, and DPS provided substantial feedback during manuscript development. All authors read and approved the final manuscript.

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Data availability

Not applicable.

Declarations

Ethics approval and consent to participate

All authors of the present manuscript declare that they have no conflicts of interest. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. Written informed consent for the publication of her clinical details and clinical image was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Consent for publication

Not applicable.

Competing interests

There are no competing interests to report for this manuscript.

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