

# Cutaneous Manifestations of Injectable Drug Use: Hidden Secrets

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## Practice Points

- Skin and soft tissue infections are the most common cause of hospital admission among injectable drug users.
- The most common microorganisms identified in these abscesses are *Staphylococcus aureus*, facultative gram-negative bacteria, and anaerobic bacteria.
- The strongest risk factor for skin and soft tissue infections is skin popping, or subcutaneous drug injection, which introduces bacteria and irritating substances directly into the skin.

*Abscesses related to drug use are the most common cutaneous manifestations among injection drug users, often occurring when the veins become less accessible. In these cases, other techniques may be used to administer drugs, such as skin popping (subcutaneous injection) or muscle popping (intramuscular injection). The main risk factors for abscess formation include skin popping, use of unsterilized needles, and injection of speedball (a mixture of cocaine and heroin). We present a case of recurrent abscesses accompanied by fever, hypersomnia alternating with insomnia, diaphoresis, fatigue, recent weight loss, and agitation following subcutaneous injection of a tramadol, opiipramol, and clonazepam mixture. Differential diagnoses included pyoderma gangrenosum on the basis of hepatitis C virus, skin lesions connected with human immunodeficiency virus infection, vasculitis, endocarditis, and serotonin syndrome. The patient was treated with oral antibiotics, surgical incision, and drainage of the abscesses, with consequent improvement.*

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Addiction to injectable narcotics is a substantial source of morbidity and mortality in the world. According to the European Monitoring Centre for Drugs and Drug Addiction, an estimated 56,000 to 103,000 individuals were dependent on drugs.<sup>1</sup> There are many methods of drug administration, including intravenous, subcutaneous (skin popping), and intramuscular (muscle popping) routes. When the veins become less accessible, drugs are injected directly into the skin or muscle, which can lead to multiple cutaneous manifestations. Skin and soft tissue infections (SSTIs) are the most common cause of hospital admission among injectable drug users.<sup>2</sup> Abscesses related to drug use are the most frequent type of SSTI. The probability of its occurrence does not differ based on sex, age, race, type of drug injected, anatomic site of injection, or human immunodeficiency virus status.<sup>3</sup> The main risk factors for abscess formation in injectable drug users are skin popping, use of unsterilized needles, and injection of speedball (a mixture of cocaine and heroin).<sup>2,3</sup> Cutaneous infections may result in local disease but also may progress to life-threatening complications, such as necrotizing fasciitis,<sup>3-5</sup> extensive cellulitis,<sup>6</sup> pyomyositis,<sup>7</sup> bacteremia, and sepsis. We present a patient with abscesses related to drug use from subcutaneous injections of a tramadol, opiipramol, and clonazepam mixture.

## Case Report

A 24-year-old man presented with recurrent abscesses of 3 months' duration that were accompanied by

fluctuating body temperature (range, 35°C–40°C), fatigue, muscle pain, hypersomnia alternating with insomnia, diaphoresis, tachycardia, weight loss (15 kg in 2 months), and agitation. One month prior to admission, the skin lesions were treated with oral antibiotics, in addition to surgical incision and drainage of the abscesses with consequent improvement. The patient's medical history was remarkable for hepatitis C virus, which had been diagnosed 6 years prior, as well as mitral and tricuspid regurgitation present since birth. He was hospitalized 4 times for psychiatric evaluation due to affective personality disorder, depressive episodes, and suicidal ideation.

Physical examination revealed 2×2-cm ulcers that were covered with necrotic tissue on the dorsal surface of the left foot (Figure 1), around the wrists (Figure 2), on the erect surface of the knee joints, and in the groin region on the right side. On the second day of hospitalization, subcutaneous hemorrhage and trace signs of intramuscular injections were noted on the inner surface of the right thigh, which were not present at admission. The patient denied the use of any drugs or medications during the hospitalization. Urine toxicology screening was negative for methamphetamine hydrochloride, amphetamine, heroin, and opiates. Basic laboratory tests performed during hospitalization revealed elevated aspartate aminotransferase (166 U/L [reference range, 10–30 U/L]) and alanine aminotransferase (264 U/L [reference range, 10–40 U/L]) levels as well as hepatitis C virus antibodies. Histologic examination of a punch biopsy specimen showed pseudoepitheliomatous hyperplasia and chronic inflammatory cells in the dermis without evidence of inflammation or necrosis of the vasculature.

On the fourth day of hospitalization, nurses discovered the patient attempting to inject a mixture of drugs—tramadol, opipramol, clonazepam, and an unidentified substance—into his venous catheter; fortunately, the attempt was thwarted. The patient later confirmed injecting drugs in the locations where the ulcers were present because he was no longer able to administer them intravenously. He was referred to a detoxification center where he consented to treatment and remains under the care of an addiction clinic.

### Comment

Parenteral methods of drug administration (eg, skin popping, muscle popping) may result in acute and chronic skin manifestations.<sup>8</sup> The pathogenesis of cutaneous abscess formation is multifactorial, including tissue trauma and ischemia, inoculation of bacteria, and irritation from the injected substances. Acute cutaneous manifestations include skin and soft tissue abscesses, necrotizing fasciitis, cellulitis, and pyomyositis. The most common chronic skin manifestations

are scar formation, hyperpigmentation, necrotizing panniculitis, and granulomas. Extension of an abscess into vital structures, pyogenic muscle infection, subcutaneous necrosis with involvement of fascia, bacteremia, and sepsis are the most serious consequences of SSTIs. Our patient had skin and soft tissue abscesses accompanied by a fluctuating temperature. A bacterial infection with concomitant pyoderma gangrenosum was suspected at the day of admission to the hospital.

The prevalence of and risk factors for abscess formation have been examined in case-control studies.<sup>2,3,9,10</sup> Because this type of infection can result in high morbidity, any identification of risk factors connected with abscess formation is relevant. According to Murphy et al<sup>2</sup> and Binswanger et al,<sup>3</sup> the strongest risk factor is skin popping, or subcutaneous drug injection, which introduces bacteria and irritating substances directly into the skin. The use of unsterilized needles also is a risk factor for SSTIs,<sup>2</sup> as contaminants and fillers introduced by the needles can predispose the patient to infection by local tissue reaction (vasoconstriction).

The most common microorganisms identified in these abscesses are *Staphylococcus aureus*, facultative gram-negative bacteria, and anaerobic bacteria.<sup>8</sup> Swabs taken from the nose, throat, and skin lesions in our patient did not reveal any pathogens, which is likely because of recent antibiotic treatment initiated prior



**Figure 1.** Ulceration localized on the dorsal surface of the left foot.



**Figure 2.** Ulceration around the left wrist.

to the patient's admission. Injection of a cocaine and heroin mixture known as speedball also is a high risk factor for abscess formation.<sup>2</sup> According to Spijkerman et al,<sup>11</sup> human immunodeficiency virus infection is an independent risk factor for skin abscess formation, but this finding has not been confirmed<sup>2</sup>; a laboratory test excluded this possibility in our patient.

In our patient, it was difficult to determine if the symptoms that were present at admission were connected with tramadol and opipramol overdose. The combination of signs such as fever, fatigue, muscle pain, hypersomnia alternating with insomnia, diaphoresis, tachycardia, and agitation may suggest a diagnosis of serotonin syndrome, a potentially life-threatening condition caused by excess serotonergic activity in the central and peripheral nervous system. Drugs that increase central neurotransmission in post-synaptic 5-hydroxytryptamine receptors 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> can induce serotonin syndrome. Our patient took a mixture of drugs (ie, tramadol, tricyclic antidepressants), which could result in serotonin syndrome. Tramadol is a weak agonist at the  $\mu$ -opioid receptor and possesses a nonopioid mechanism of action that includes the release of serotonin and inhibition of norepinephrine reuptake. Serotonin syndrome may develop during tramadol monotherapy; however, it is seen more often in association with tramadol and antidepressant combinations.<sup>12</sup> Serotonin syndrome has been reported from combining tramadol with fluoxetine,<sup>13</sup> venlafaxine and mirtazapine,<sup>14</sup> sertraline,<sup>15,16</sup> and trazodone,<sup>16</sup> or tramadol without concomitant use of other serotonergics.<sup>17</sup>

## Conclusion

With the incidence of substance abuse increasing, it is important for dermatologists to be aware of skin lesions associated with the injection of narcotics. The most common reason for hospitalization from injectable drugs is abscess formation. Because an infection can result in high morbidity, identification of risk factors connected with abscess formation is essential. We encountered difficulties in diagnosing our patient, mainly because he withheld information regarding his drug addiction. Fortunately, the patient's attempt to inject narcotics into his venous catheter during hospitalization was discovered, which aided in the diagnosis and prevented a potentially fatal outcome.

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