

Buprenorphine Induced Nicolau Syndrome: A Case Report

Dear Editor,

Nicolau syndrome is a rare adverse effect due to inadvertent arterial injection by a number of drugs leading to painful ulcerative skin lesions. It has been reported commonly with non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics; however, buprenorphine has been rarely implicated in its causation.¹ We present an intriguing case of Nicolau syndrome following self-injection of buprenorphine.

A 24-year-old male, an intravenous drug abuser, presented with a painful erythematous rash over his right lower limb for five days. The patient had self-injected a suspension of buprenorphine (tablet crushed in drinking water) into the upper lateral aspect of his right leg five days back. The lesions started from the foot and gradually progressed to involve the lateral aspect of the leg over two to three days. There was no history of any sensory disturbances or any restriction of movement. He gave a history of self-administration of heroin injections over multiple sites in the past. On examination, the presence of tender, non-blanchable purpuric macules and patches was noted in a retiform pattern over the sole of the right foot, with the extension of lesions to the lateral aspect of the leg in a reticulate distribution (Figures 1 and 2). There was no local rise in temperature or crepitations. The dorsal pedis on the right side was not palpable. Scars suggestive of previous intravenous drug abuse were present over the entire lower limbs. Investigations like complete blood count, coagulation profile, HIV, and ECHO were normal. The patient was started on pentoxifylline 400 mg thrice daily and provided pain management. The Naranjo adverse drug reaction (ADR) probability score was 6 (probable ADR).² He was also referred for drug deaddiction and advised Doppler scan but was lost to follow up.

Nicolau syndrome, also known as embolia cutis medicamentosa or livedo-like dermatitis, is a rare cutaneous adverse effect

FIGURE 1.

Presence of Non-blanchable Purpuric Macules and Patches in a Retiform Pattern over the Sole of the Right Foot.



FIGURE 2.

Extension of Purpuric Patches onto the Lateral Aspect of the Right Leg.



of parenteral injections, particularly intra-muscular injections, although intravenous, subcutaneous, and intra-articular routes have all been reported in literature, especially with oily or suspension forms of drugs.³ The most common drugs causing Nicolau syndrome are NSAIDs and antibiotics like penicillin. Other reported ones include corticosteroids, vaccinations, antihistamines, and topical anesthetics like lidocaine.⁴ Several hypotheses exist regarding the pathogenesis of Nicolau syndrome, with the most accepted being inadvertent intra- or peri-arterial injection of the drug. Intra-arterial injection can cause embolism of the drug itself, leading to vascular occlusion. The peri-arterial injection can stimulate the sympathetic nerve, causing vasospasm and consequent ischemia.³ Additionally, lipophilic drugs can produce fat embolism, and buprenorphine, being a highly lipophilic drug, can also cause Nicolau syndrome via this mechanism. Patients typically experience severe pain around the injection site immediately after the injection, followed by rapid development of erythema, livedo reticularis, or a hemorrhagic patch. Secondary infection may occur, and in severe cases, necrosis and ulceration of the skin, subcutaneous tissue, and even muscle can occur. The necrotic ulcer usually heals in several months with an atrophic scar. Furthermore, transient neurological complications such as hypoesthesia and paraesthesia may be seen in one-third of the patients.⁴ Diagnosis is primarily clinical, and a skin biopsy can confirm the findings of necrotic changes caused by ischemia. Differential diagnoses include vasculitis, blue toe syndrome, cholesterol embolization, and acute infections like necrotizing fasciitis and gas gangrene.⁵ Early diagnosis and treatment are crucial, as secondary complications such as necrosis and infection can lead to loss of limb and even death in severe cases. The mainstay of therapy includes pain management, antibiotics, wound dressing, and surgical interventions like debridement of necrotic

tissue and skin grafting. Additionally, numerous other drugs have been tried, such as anticoagulants (heparin), antiplatelets, vasodilators (pentoxifylline), and systemic steroids.⁶ Nicolau syndrome is an avoidable complication, and hence, prevention takes precedence over cure. Correct injection techniques by healthcare professionals, such as choosing the correct site (a superolateral region in case of gluteal muscle), selecting the right size of the needle, aspirating before injecting, and using the Z-track technique for intramuscular injections, are some simple measures that can minimize the risk of this complication.⁷ This case highlights the need for spreading awareness about this condition, especially among injection drug abusers and their healthcare providers. Although, in this case, the patient had self-administered the injection, it serves as an eye-opener for all healthcare workers to exercise utmost care and caution while administering any parenteral injection.

Data Availability

Data available on reasonable request of corresponding author.

Declaration of Conflicting Interests

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Declaration Regarding the Use of Generative AI

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Informed Consent

A written informed consent was obtained from the patient including consent for photographs and any identifying information that may be publicly available.

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