Nicolau syndrome following intramuscular naltrexone injection

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Abstract

There are a variety of possible adverse drug reactions that can have differing presentations. Recognizing these presentations and the temporal relationship between drug intake and reaction is essential in preventing severe and potentially fatal results. We present a patient who had a sudden post-injection inflammatory response consistent with Nicolau syndrome after a 6 month course of repeated intramuscular naltrexone injections.

Keywords: Nicolau syndrome, naltrexone, adverse drug reaction

To the Editor:

Nicolau syndrome is a rare complication that occurs immediately after drug injection. This complication has been reported for a variety of drug injections, from local anesthetics to vaccines. Common presentation includes local pain around the injection site, a violaceous, reticulated rash with blanching, and necrosis of skin and underlying tissue related to ischemia [1]. The pathogenesis is not completely understood but it is believed to be of vascular origin, such as possible vasospasm or vaso-occlusion, leading to the classic ischemia and necrosis. This can be related to direct trauma from injection, compression following injection, or arterial embolism. Cases of lower extremity paralysis have been associated with Nicolau syndrome because of embolization of medication [2].

A 30-year-old man presented to the dermatology department with retiform purpura on the left buttock 5 days after intramuscular naltrexone injection (**Figure 1**). The patient had received monthly intramuscular naltrexone injections for 5 months prior to this episode and had experienced mild post-injection pain once before. In the Emergency Room on the night of the injection, he complained of pain and rash centered on the injection site beginning several hours post injection. He was discharged that night with prednisone,

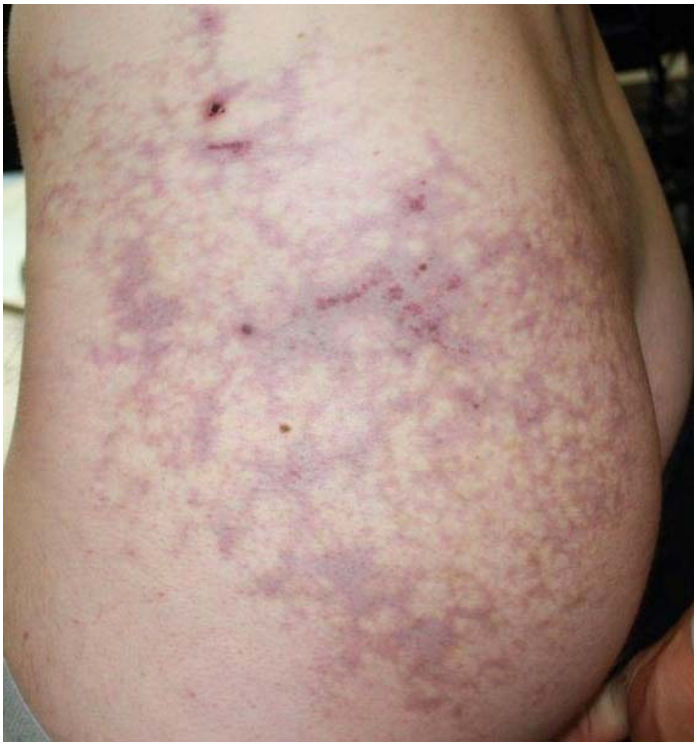

Figure 1*: Retiform purpura of the left buttock indicative of Nicolau syndrome 5 days after intramuscular naltrexone injection.*

acetaminophen, and ibuprofen which he took for four days while the rash and pain steadily worsened. When first evaluated by the dermatology consultant on day 5, there was a violaceous, reticulated, blanching patch around the injection site. The patient had severely elevated creatine kinase (1637U/L) indicative of myositis. Magnetic resonance imaging of pelvis revealed inflammatory changes consistent with myositis as well as fat stranding, with no fluid collections noted. The timeline between injection and onset of rash and pain suggested Nicolau syndrome (embolia cutis medicamentosa). Naltrexone injections were discontinued and on evaluation two weeks post-injection the rash had mostly resolved with only faint erythema noted. Further, creatine kinase levels had decreased significantly to 369U/L, along with a downtrend in lactate levels and a normal urinalysis. The patient was then switched to an oral medication containing buprenorphine and naloxone for a heroin relapse, which showed no complications.

Treatment options for Nicolau syndrome depend on the level of pain and stage of wound necrosis. In early stages, pain control and prophylactic antibiotics to prevent necrotic tissue and sepsis can suffice. If the condition persists and necrosis occurs, surgical debridement and skin grafts may become necessary. Computed tomography or MRI is necessary to establish the extent of the necrosis — this ensures appropriate margins for debridement and removal of all necrotic tissue. Anticoagulants and vasodilators have also been used as supportive treatment [3].

Naltrexone has become a popular method of managing alcohol or opioid dependence. Further, Nicolau syndrome has continued to appear as a complication for many types of drug injections. There is at least one other reported case of Nicolau syndrome following intramuscular naltrexone injection. The patient experienced fat necrosis as opposed to myositis and underwent surgical debridement [4]. Additionally, myositis with Nicolau syndrome has been reported once in the literature. In this case, the patient was diagnosed with streptococcal myositis and died within 48 hours of the intramuscular injections [5].

The case shows Nicolau syndrome with myositis following intramuscular naltrexone injection. This is a rare adverse drug reaction that can occur in response to many types of injections. Nicolau syndrome has the potential to be fatal and recognizing its presentation as an adverse drug reaction is essential in preventing severe outcomes. One must look out for the temporal connection between injection and emergence of characteristic retiform purpura, for early recognition is vital. Thus, we believe that every dermatologist should be well aware of Nicolau syndrome and other potential complications following injections.

Potential conflicts of interest

The authors declare no conflicts of interests

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