



# Nicolau Syndrome After Diclofenac-Thiocolchicoside Intramuscular Injection

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Sir,

Nicolau syndrome (NS), also known as embolia cutis medicamentosa and livedo-like dermatitis, is a rare complication of an intramuscular injection characterized by severe pain, skin discoloration, and varying levels of tissue necrosis at the site of the injection. Although its pathogenesis is not well understood, the pathophysiology of NS probably involves intra-arterial and/or para-arterial injection and arterial embolism of viscous suspensions of drugs meant for intramuscular, intravenous, or intra-articular injection, followed by acute vasospasm. It usually heals, leaving an atrophic scar (1). We describe the case of a 55-year-old female patient who developed NS after diclofenac-thiocolchicoside intramuscular injection.

Our case is the case of a 55-year-old female patient who presented a painful ecchymotic plaque on her right buttock. A week before, she had been given an intramuscular diclofenac-thiocolchicoside injection for knee pain relief. After the injection, she experienced severe pain and hardness, and livid discoloration appeared around the injected spot. Over the following days, erythema and edema developed around the ecchymosis.

On physical examination, a well-defined necrotic plaque, with a 10 x 15-cm-size, surrounded by a livedoid, reticular erythematous patch was observed on the right buttock (Figure 1). General examination was normal, and routine haematological investigations including bleeding time, clotting time and platelet counts were within normal limits. The diagnosis of NS was made, and the patient was referred to a surgeon to undergo surgical debridement of the necrotic tissue. The ulcer healed completely with scarring in 14 weeks. The differential diagnosis of NS includes cutaneous cholesterol emboli, vasculitis, and cutaneous embolization of cardiac myxoma (5). Our patient did not have any other comorbid conditions, such as a cardiovascular disease

or diabetes. It was first described by Nicolau in 1925, following the use of bismuth salts for the treatment of syphilis. NS is characterized by development of an acute, severe pain and a localized erythematous rash following intramuscular injection. Subsequently, cutaneous, subcutaneous and even muscular necrosis with a pale marble-like livedoid pattern appears (2). In the literature, NS has been reported with the administration of various other drugs such as penicillin, non-steroidal anti-inflammatory drugs, local anesthetics, vitamin K, triple DTB vaccination, and corticosteroids. In pediatric cases NS may be located to the thigh (2-4).

The pathogenesis of NS is obscure. Intraarterial, periarterial and intraarticular injection of the drug may be the cause of NS. The mechanism may involve direct trauma or arterial embolism caused by the drug or ischemia due to the compression following paravascular injection (3,5). Vascular pathogenesis involving arterial vasospasm with resultant ischemia-mediated livedoid necrosis may be another possible mechanism. Diclofenac was the drug responsible for NS in our case. It possibly causes NS through vascular pathogenesis as it acts via the cyclooxygenase pathway, inhibiting prostaglandin synthesis with resultant vasoconstriction (6). The treatment ranges from local care to surgical intervention. Antibiotic use is restricted to cases with signs and symptoms of infection. Use of vasoactive agents (pentoxifylline) together with hyperbaric oxygen may be beneficial, considering the vascular pathogenesis. Vasospasm may be relieved by the action of pentoxifylline inhibiting the phosphodiesterase. Topical corticosteroids are effective for acute tissue inflammation. Wound care, debridement, dressings, and flap reconstruction are ideal surgical measures (6,7).

Although NS is an uncommon cutaneous adverse reaction, the symptoms are dramatic, and this rare complication can cause severe anxiety in the patient.

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Healthcare personnel should be aware of this condition and take adequate precautions. A sufficiently long needle for an obese patient, the Z-track method of intramuscular injection only after aspiration with a syringe, and an injection in the upper outer quadrant of the gluteal region which has few large blood vessels, can minimize or prevent Nicolau syndrome.

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**Figure 1.** Necrotic plaque surrounded by a livedoid, reticular erythematous patch on the right buttock.