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Case Series

Nicolau's syndrome following intramuscular administration of Diclofenac sodium

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ABSTRACT

Nicolau's syndrome, also known as embolia cutis medicamentosa or livedo-like dermatitis, is an uncommon rare cutaneous adverse reaction occurring at the site of intramuscular, intra-articular, or rarely subcutaneous injection of particular drugs, leading to necrosis of skin and underlying tissues. We, hereby, report two fatal cases of this syndrome after taking intramuscular injection of diclofenac sodium.

Keywords: Diclofenac sodium, Intramuscular injection, Nicolau's syndrome

INTRODUCTION

Nicolau syndrome is an iatrogenic syndrome characterized by severe painful necrosis at the site of an injected medicaments. It starts with intense stabbing pain and burning at the site of injection, stellate erythema, and infiltration followed by central deep necrosis. The necrosed skin heals with severe and disfiguring scarring. Sometimes, the reaction may be severe leading to death of the patient.[1] Clinicians, dermatologists, and surgeons should be aware about this agonizing, deforming, and fatal iatrogenic complication.

CASE REPORTS

Case 1

A 60-year-old female presented with hemorrhagic bullae, large erosions, and necrosis of skin over left thigh and left gluteal region. There was a history of taken injection of diclofenac sodium in the left gluteal region for generalized body ache from a private hospital at her hometown 3 days back. After the injection, she immediately started developing burning pain, tightness, and swelling in the left thigh. Pain was acute in onset and progressive in nature. Next day, she developed blackening of skin over the left thigh and left buttock along with fluid filled lesions and peeling of skin [Figures 1 and 2]. Nikolsky's sign was positive on the necrotic area. Rest of the cutaneous and mucosal involvement was unremarkable. Clinically, a diagnosis of Nicolau's syndrome was made. All routine investigations were normal. Skin biopsy was not done. The patient was referred to surgery department for debridement. However, the patient succumbed to death next day due to septicemia.

Case 2

A 68-year-old female came with the complaints of blackening of the right upper limb along with breathlessness, chest pain, and giddiness. Two days prior, she was administered injection diclofenac sodium in the right arm for backache at the Primary Health Center after which she started developing pain, redness, and swelling in the right arm. Following morning, she developed blackish discoloration of the right upper limb with skin necrosis [Figure 3]. In this case also from the history and clinical examination, diagnosis of Nicolau's syndrome was made. Skin biopsy was not done. The patient was in gasping condition so was referred to emergency medicine and was immediately intubated. In spite of all the efforts, the patient succumbed to this rare cutaneous drug reaction.

DISCUSSION

Nicolau's syndrome was first described by Freudenthal and Nicolau in the 19th century in patients following intramuscular injection of bismuth salt for the treatment of syphilis.[2] Various medicaments including penicillin, diclofenac sodium, intramuscular Vitamin K, local anesthetics, anti-rheumatic drugs, phenobarbitone, sulfonamides, sclerotherapy,

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Figure 1: Skin necrosis with hemorrhagic bullae with peeling of skin on the right thigh.

Figure 2: Skin necrosis with hemorrhagic bullae with peeling of skin on buttock.

and subcutaneous etanercept have been implicated in causing Nicolau's syndrome.[3] It can also occur following intramuscular Naltrexone injection.[4] The pathogenesis is unknown but inadvertent paravasal injection, leading to vessel wall damage, arterial thrombosis, and subsequent necrosis, is a proposed hypothesis.

1. Diagnosis is mainly based on clinical presentation. The differential diagnosis of Nicolau's syndrome includes cutaneous vasculitis, necrotizing fasciitis, cutaneous cholesterol emboli, and cutaneous embolization of cardiac myxoma. Clinically, Nicolau's syndrome is differentiated from other conditions from history of any injection before the onset of lesion and location of the lesions usually start from the injection site and spread peripherally. Ultrasonography and magnetic resonance imaging may be helpful in determining the extent of tissue damage. Skin biopsy shows necrosis, vascular thrombosis along with acute inflammation. Surgical debridement, injectable antibiotics, and proper wound care should be the main aim of treatment. Preventive measures are proper aseptic care while administrating injections and follow Z track method of intramuscular injection.[2] The following precautions to be taken by the health-care professionals while giving intramuscular injections:
    - Upper outer quadrant of buttocks to be injected
    - Long needle to be chosen so that it will reach intramuscular region
    - Aspiration should be the norm before injection which will prevent inadvertent administration of drug intra arterial
    - "Z" track techniques to be used while injecting
    - Not more than 5 ml of drug to be given at one site and if larger amount is needed, it should be injected at another site.

Figure 3: Blackish discoloration with peeling of skin on the right arm and forearm.

CONCLUSION

Though uncommon, Nicolau Syndrome is a rare and sometime fatal complication following intramuscular injections.So utmost care to be taken while injecting drugs via intramuscular route and follow up of patient to rule out adverse effects, if any.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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