

Nicolau Syndrome: A Devastating Injection Site Drug Reaction

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ABSTRACT

Nicolau syndrome is a severe iatrogenic injection site drug reaction. Here, we present a case of 43 year old female patient with Nicolau syndrome 2 days following intramuscular injection of diclofenac sodium in the right gluteal region. No diagnostic criteria have been proposed yet, diagnosis is usually clinical. Symptomatic treatment along with debridement and dressing is generally advised. Nicolau syndrome traditionally described as embolia cutis medicamentosa or livedoid dermatitis which is easily identifiable by history, clinical findings and course.

Key words: Nicolau syndrome; Intramuscular injection; Diclofenac sodium

ABOUT THE STUDY

Nicolau syndrome is an imposing and exquisite complication of injection site drug reaction. It usually develops following intramuscular injection of various drugs. It can also develop after intravenous or subcutaneous injections [1]. It is characterized by severe pain, early pallor and livedoid hemorrhagic erythema at injection site progressing to necrosis and ulceration of skin, subcutaneous tissue and underlying muscle. No diagnostic criteria have been proposed yet; diagnosis is usually clinical [2]. Symptomatic treatment along with debridement and dressing is generally advised [3].

A 43 year old non diabetic non hypertensive female patient presented to emergency department of MGIMS, Sewagram, Wardha with complaints of pain at the right gluteal region and 2 days after taking intramuscular diclofenac sodium injection.

On presentation patient was febrile and hypotensive. Intravenous non-adrenaline and fluids were given to manage low blood pressure.

On further inquiry patient gave history of burning pain, bluish discoloration of skin, and development of fluid filled lesion at the site of injection.

On cutaneous examination, large ulcer surrounded by area of necrosis extending up to subcutaneous fat and underlying gluteal muscle, livedo reticularis and multiple vesicles to bullae were seen. Nikolskiy's sign was positive. Local temperature was raised. No signs of compartment syndrome such as pallor,

paraesthesia, oedema and gangrene distal to site of injection were present.

Laboratory investigations showed deranged haemogram, renal and hepatic profile and following values were noted.

Table 1: Laboratory investigations.

Laboratory tests	Results
Haemogram	
Haemoglobin	7.1 gm%
White blood cells	16900/mm ³
Platelet count	50000/mm ³
Renal profile	
Urea	70 mg/dl
Creatinine	2.25 mg/dl
Liver profile	
Bilirubin (total)	7.86 mg/dl
Bilirubin (conjugated)	4.63 mg/dl
Alanine transaminase	95 mg/dl
Aspartate transaminase	142 mg/dl

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Serum lactate levels were 16.39 mmol/dl which pointed towards septic shock. All investigations continued to be deranged and suggested worsening condition of patient till day 3 except serum lactate level which got normalized by day 3 suggesting recovery from sepsis. However, blood culture and sensitivity was not performed to know the organism.

Debridement, daily dressing along with injectable ceftriaxone was advised which helped to control the sepsis. On day 10, patient was discharged. Later on patient lost to follow up.

DISCUSSION

Nicolau syndrome traditionally described as embolia cutis medicamentosa or livedoid dermatitis which is easily identifiable by history, clinical findings and course. It was first reported by Romanian dermatologist Stefan G. Nicolau in 1925 [2]. It commonly develops following intramuscular injection of non-steroidal anti-inflammatory agents, penicillin, ceftriaxone, vitamin K. It can also follow intravenous or subcutaneous injection of etanercept [1,3-6].

Its presentation is acute with severe pain, pallor progression to violaceous lesions of livedo reticularis. In severe cases ulceration and necrosis of skin, subcutaneous fat and underlying muscle can develop. These features are pathognomonic of Nicolau syndrome. In our case we found a severe local drug reaction with all the features mentioned above [2].

Micro-embolic obstruction of arterial supply of dermis, vasospasm, embolism, thrombosis and inflammation are probable mechanisms of pathogenesis leading to cellular destruction. Leakage of drug to subcutaneous tissue also causes local tissue injury. Differential diagnoses of Nicolau syndrome include compartment syndrome, cellulitis, necrotizing fasciitis, vasculitis etc. [1-3].

Fatal complications such as secondary infection, limb paralysis due to drug embolization, respiratory failure due to thromboembolism, renal and hepatic failure due to direct insult by the drug are recorded.

There are no diagnostic and treatment guidelines available yet. Hence diagnosis is usually clinical. Treatment is mostly symptomatic and debridement, daily dressing [2,6]. Vasopressors substances such as adrenaline and non-adrenaline and antibiotics can be prescribed.

This case has presented to us following intramuscular injection of diclofenac sodium for pain relief. Diclofenac sodium is commonly used non-steroidal anti-inflammatory agent; prescribed for various condition including severe pain. As pain is often associated with nausea and vomiting intramuscular injection is preferred. Also injectable drugs have faster onset of action compared to oral administration, injectables are mostly requested by the patients [2]. But cautious and rational use is always warranted in order to prevent complications such as Nicolau syndrome

Of importance, this devastating iatrogenic complication can be prevented by using Z-track technique for subcutaneous injections. Using sufficiently long needle to reach muscle while injecting intramuscularly, aspirating before injecting to prevent blood vessel injury [4].

CONCLUSION

Nicolau syndrome is severe sequelae of local drug reaction. It is iatrogenically induced preventable complication if proper technique is employed along with cautious and retinal use of injectable drugs. Micro-embolic obstruction of arterial supply of dermis, vasospasm, embolism, thrombosis and inflammation are probable mechanisms of pathogenesis leading to cellular destruction. Leakage of drug to subcutaneous tissue also causes local tissue injury. Differential diagnoses of Nicolau syndrome include compartment syndrome, cellulitis, necrotizing fasciitis, vasculitis.

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