

Nicolau Syndrome

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Abstract

Observation: Nicolau Syndrome, also known as embolia cutis medicamentosa and livedo-like dermatitis, is a rare cutaneous adverse reaction at the site of intramuscular, intra-articular, subcutaneous injection of particular drugs. Patients complain of severe pain and erythematous-ecchymotic reticular lesions at the injection site. The skin, subcutaneous and muscle tissue necrosis develop as complications of injections.

Our case was a 68 year-old female patient followed with chronic liver disease who developed necrosis of the skin in the right hip after intramuscular diclofenac injection.

Although diclofenac is a widely used non-steroidal anti-inflammatory drug, Nicolau syndrome following intramuscular diclofenac injection has rarely been reported. And also, in our literature examination it is the first case of Nicolau Syndrome with chronic liver disease.

Introduction

Nicolau's Syndrome is a rare condition characterized by the acute onset of cutaneous and soft-tissue necrosis following intramuscular, intra-articular, subcutaneous drug injection. Patients complain of severe pain and erythematous-ecchymotic reticular lesions at the injection site. The skin, subcutaneous and muscle tissue necrosis develop as complications of intramuscular injections.

Case Report

A 68-year-old woman who is followed with chronic liver disease received an intramuscular injection of diclofenac sodium for her pains at another department. The patient complained of pain in the upper right buttock after the injection. Three days

later, the patient developed pain and redness at the injection site. After one week, a skin lesion was observed and necrosis developed. At admission, tenderness around the injection site and 25*20 cm plaque, in center necrotic ulceration measuring 4*5 cm was found involving the gluteus maximus fascia of the right upper buttock (**Figure 1**). Dermatologists and plastic surgeons diagnosed this lesion as Nicolau Syndrome. Patient treated conservatively with local wound care.

The patient was monitored and received daily dressing. Ampiric systemic antibiotic treatment started to prevent secondary bacterial infection. She was adviced to come back after a week to check for any wound debridement. However, she was lost to follow-up.



Figure 1. Injection site with necrotic ulceration involving the right upper buttock

Discussion

Nicolau Syndrome, also known as embolia cutis medicamentosa and livedo-like dermatitis, is a rare cutaneous adverse reaction at the site of intramuscular, intra-articular, subcutaneous injection of particular drugs. Several drugs have been reported to cause necrosis, such as local anesthetics, antihistaminics, vitamin complexes, diclofenac sodium, ketoprofen, piroxicam, corticosteroids and vaccine [1,2,3,4,5,6,7]. Immediately after the drug injection, patients experience extremely severe pain around the injection site of the drug. And then erythema, a livedoid reticular patch or a hemorrhagic patch develop. The reaction may result in necrosis and ulceration of the skin, subcutaneous fat, and muscle tissue. Tissue necrosis after intramuscular drug injection was first discovered in the 1920's by *Freudenthal* and *Nicolau* after administration of bismuth salts for syphilis treatment [2]. This entity known as Nicolau's Syndrome or livedo-like dermatitis or embolia cutis medicamentosa [3,4,8]. The pathogenesis of post-injection necrosis is not completely understood but there have been several hypotheses. First, it is presumed that the sympathetic nerve is stimulated by pain from the intra-arterial or periarterial injection of drugs, causing vasospasms and leading to ischemia. Second, nonsteroidal anti-inflammatory drugs inhibit cyclooxygenase pathway and suppress the prostaglandin synthesis so ischemic injury occurs due to vasospasm. Third, the intra-arterially drug injection causes embolic occlusion. Fourth, ischemic necrosis progresses from vascular rupture due to pe-

rivascular inflammation from a cytotoxic reaction to the drugs. Fifth, lipophilic drugs penetrate the blood vessels in a manner similar to that of fat embolism and induce physical occlusion [3,4,5,8,9,10,11]. It was reported that cold application for local pain relief caused rapid skin necrosis by increasing the acute local vasospastic effects in a case with Nicolau Syndrome [10,11]. Treatment of Nicolau Syndrome is conservative with debridement, pain control, antibiotics and dressings. Surgical methods, including debridement and skin graft are required for necrotic areas not showing significant improvement. Tissue damage may be reversible in the acute phase of Nicolau Syndrome. Use of vasoactive agents such as subcutaneous heparin and oral pentoxifylline has been recognized as beneficial. Surgical intervention is rarely required. Using of hyperbaric oxygen therapy in selected cases has been reported in the literature [1,4,6,8,10,11,12]. Preventive measures must be used before injection like; needle long enough to reach muscle should be used. Injection should be applied in the upper outer quadrant of the buttock. Aspirating the needle before injecting the medication should be performed, to ensure that no blood vessel is hit. The health care personnel should never inject more than 5 ml of medication at a time when using the Z-track injection method. If more than one injection or larger dose is required or ordered, different sites should be chosen [4,5,7,10].

Conclusion

Although diclofenac is a widely used non-steroidal anti-inflammatory drug, Nicolau syndrome following intramuscular diclofenac injection has rarely been reported. Nicolau syndrome is an uncommon adverse reaction but physicians should consider Nicolau syndrome as a diagnostic possibility for anyone presenting with severe localized pain following an intramuscular injection. And also, our case is important because to the best of our knowledge, it is the first case of nicolau syndrome with chronic liver disease. It may be important to understand its etiology with similar cases.

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