

Case Report

Nicolau syndrome: a rare complication of injection that should be kept in mind

尼古拉斯綜合徵：一種罕見但要謹記的注射併發症

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Nicolau syndrome (NS) is a rare cutaneous necrosis occurring at the site of injection. It presents with instant and severe pain around the injection site followed by necrosis. Several drugs have been reported to cause NS. Here, a case of NS who healed with a large scar due to the intramuscular injection of a novel mixture of thiocolchicoside and diclofenac sodium is presented. In cases of NS, the physical and chemical properties of drugs, injection speed, and the route of administration should be considered.

尼古拉斯綜合徵是在注射部位發生的罕見皮膚壞死。患者會在注射部位感到即時劇痛，隨後該處會出現皮膚壞死。有幾種藥物被報告過會導致此病。在這裡，我們提出了一病例，是在肌內注射了新型混合藥物硫代秋水仙苷和雙氯芬酸鈉後發生，治愈後留下大幅的疤痕。在尼古拉斯綜合徵的個案中，應檢視藥物的物理和化學性質、注射速度和給藥途徑等。

Keywords: Cutaneous necrosis, injection complication, Nicolau syndrome

關鍵詞：皮膚壞死、注射併發症、尼古拉斯綜合徵

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Introduction

Nicolau syndrome (NS), known also as embolia cutis medicamentosa, is a rarely seen cutaneous necrosis occurring at the site of injection.¹ The syndrome was first described in 1924 in patients who were treated with intramuscular bismuth salts for syphilis.^{1,2} Since then, several drugs have been reported to cause NS. Ischaemic necrosis is presumed to be induced by direct vascular injury, perivascular inflammation and vascular constriction.² Clinically, it presents with instant and

severe pain around the injection site followed by necrosis. NS can cause morbid complications such as widespread cutaneous necrosis, paraplegia, and limb gangrene.³ Apart from intramuscular injections, subcutaneous and intradermal injections have also been reported to cause NS. It is not clear yet if it is possible to avoid this complication. The physical and chemical properties of drugs, injection speed, and the route of administration need to be taken into account.

Case report

A 49-year-old woman presented with a painful cutaneous necrotic plaque on her left buttock. The patient had been treated with thiocolchicoside and diclofenac sodium mixture once a day for four days for lumbar pain. During the last injection she had complained of severe pain in the injection site and had noticed an area of erythema and oedema with a violaceous and reticular border soon afterwards. Cutaneous necrosis then occurred within several days. The patient was seen on the 10th day of the injection (Figure 1a). Dermatological examination showed an approximately 10x5 mm black scar surrounded with an erythematous border on the upper side of

the left buttock. The patient was otherwise healthy and routine laboratory examinations including creatinine kinase were normal. On the 30th day, the necrotic area was observed as enlarged (Figure 1b). The biopsy performed showed partially necrotic epidermis and fibrin clots in the small vessels consistent with NS (Figure 2). As the patient refused surgical grafting, she underwent surgical debridement (Figure 3a), lesion healed with a large scar and tissue loss (Figure 3b).

Discussion

Nicolau syndrome has been associated with medications like bismuth salts, diclofenac, corticosteroids, antibiotics, vitamin B complexes, antihistamines and vaccines.¹⁻³ Table 1 summarises the medications associated with NS.¹ The pathogenesis of NS is not well-known. Histologically, there is microembolic obstruction of the arterial supply of the dermis. Theories suggested include arterial embolisation by the drug, direct trauma or irritation to the vascular structures and crystallisation of aqueous drugs in the blood vessels.³⁻⁵ Our case developed NS after an injection of thiocolchicoside and diclofenac sodium mixture, although she had had the same

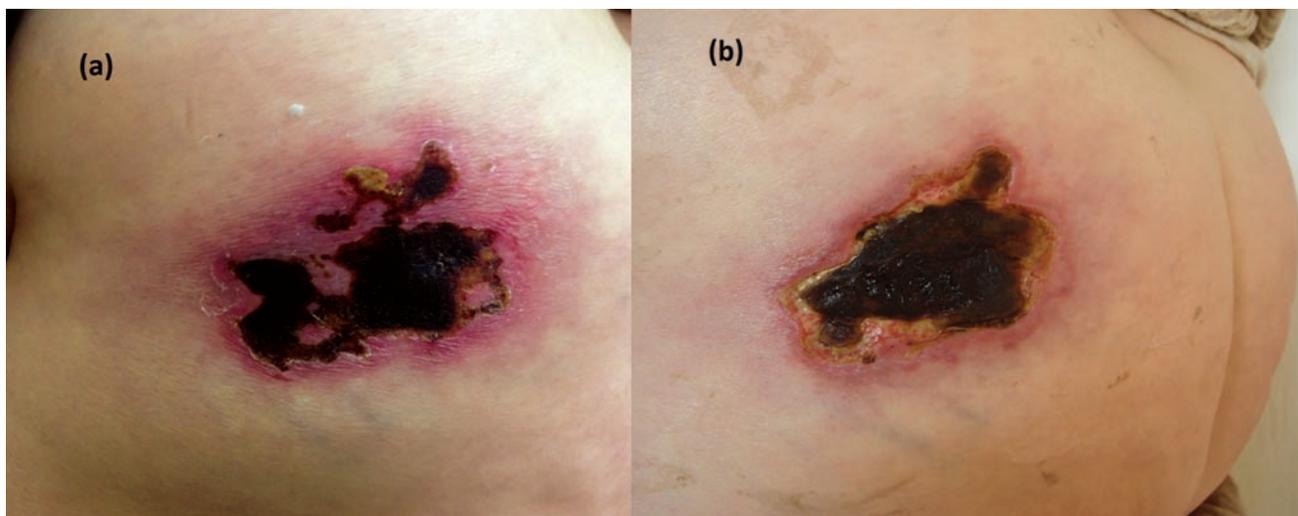


Figure 1. (a) 10th day of the injection, black scar surrounded with an erythematous border. (b) 30th day of the injection, note the progression of cutaneous necrosis.

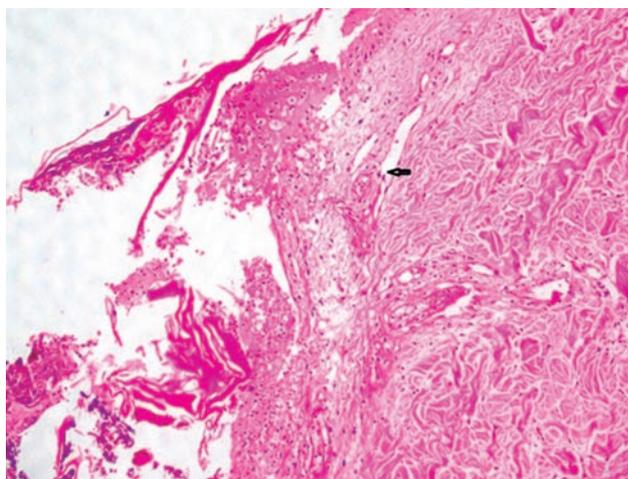


Figure 2. Histopathology showing partially necrotic epidermis and fibrin clots in the small vessels (arrow) consistent with NS (HE x100).

injection several times previously without complications. Thiocolchicoside is a muscle relaxant with anti-inflammatory and analgesic effects and diclofenac is a non-steroidal anti-inflammatory drug and their mixture is a novel combination. Diclofenac has been proposed to cause vasoconstriction of the perforator vessels of the superior gluteal artery by inhibiting the synthesis of prostaglandin as a cyclooxygenase inhibitor leading to NS.^{3,4} Nevertheless, NS is thought to be due to an inappropriate route of injection and has been proposed to be an avoidable complication.¹ The physical and chemical properties of drugs, injection speed, the route of administration should be considered in its pathogenesis.⁵

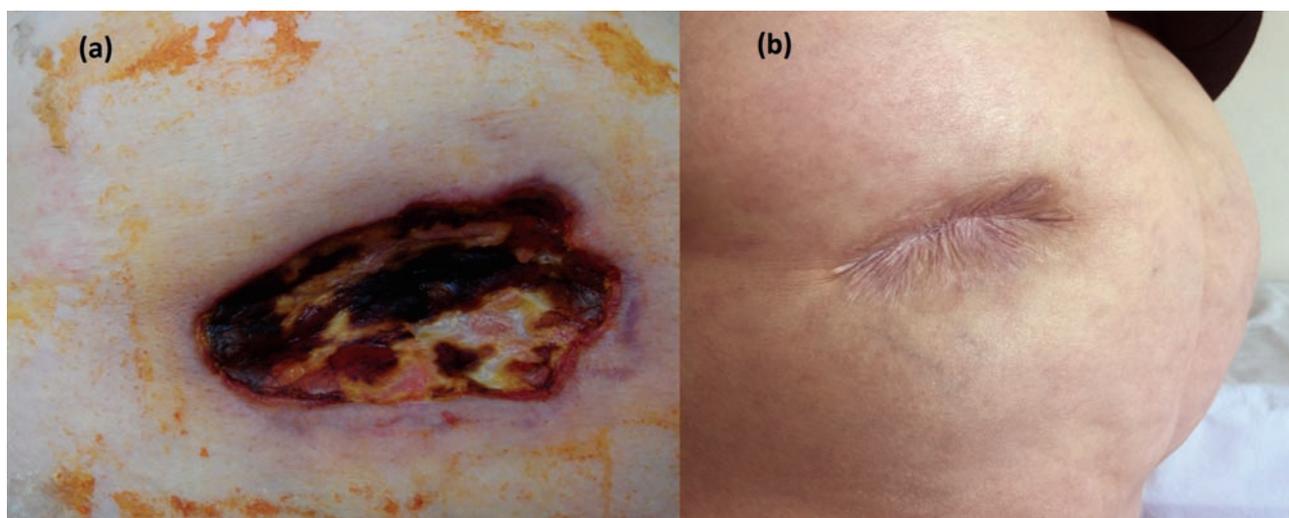


Figure 3. (a) Patient underwent debridement. (b) Lesion healed with a large scar.

Table 1. Causative drugs associated with Nicolau syndrome

Class	Examples of drugs
Non-steroidal anti-inflammatory drugs	Diclofenac, piroxicam, ketoprofen, ibuprofen
Antibiotics	Penicillin, tetracycline, sulfapyridine
Corticosteroids	Triamcinolone, dexamethasone
Antihistamines	Diphenhydramine
Antiepileptics	Phenobarbital
Local anaesthetics	Lidocaine
Vitamins	Cyanocobalamin
Vaccines	Anti-flu, varicella, diphtheria-tetanus-pertussis
Other	Bismuth salts, bortezomib, interferon, vitamin K

Clinicians should adhere to proper injection procedures and aspiration before injection is recommended. If a patient experiences intense pain during the injection and if livedoid reticular erythema occurs around the injection site, NS should be considered. Once developed, treatment is symptomatic like pain control, antibiotic prophylaxis and dressings. Early heparin and oral pentoxifylline treatment have been reported to be beneficial.^{1,5} Early diagnosis and wound care are both important. However, surgical reconstruction is sometimes needed. Nicolau syndrome is a very rare complication of drug injections and should always be kept in mind in daily practice.

References

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