Title
Nicolau syndrome following intramuscular injection of oxytocin in pregnant women: report of two cases

Journal
Dermatology Online Journal, 21(8)

Authors
Seremet, Sila
Turan, Enver
Erdemir, Asli Turgut

Publication Date
2015

DOI
10.5070/D3218028441

Volume 21 Number 8
August 2015

Letter

Nicolau syndrome following intramuscular injection of oxytocin in pregnant women: report of two cases

Sila Seremet[1], Enver Turan[2], Asli Turgut Erdemir[3]

Dermatology Online Journal 21 (8): 16

[1]Department of Dermatology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey

[2]Department of Dermatology, Harran University School of Medicine, Sanliurfa, Turkey

[3]Departmant of Dermatology, Istanbul Training and Research Hospital, Istanbul, Turkey

Correspondence:

Enver Turan, MD.
Harran University School of Medicine, Department of Dermatology,
63300-Sanliurfa, Turkey
Tel: +9005053323929
Fax: +900488 221 30 68
E-mail: enverturan@gmail.com

Abstract

Nicolau syndrome, also known as embolia cutis medicamentosa, is a well known but very rare complication occuring after intramuscular drug injections and presenting with local intense pain. Immediately after injection the skin blanches and within minutes to hours an erythematous macule develops, which evolves into a livedoid violaceous patch with dendrites. This condition is initially hemorrhagic, then it ulcerates, and eventually heals with an atrophic scar. Many different drugs have been reported to cause Nicolau syndrome . To date there have been no reports of Nicolau syndrome caused by intramuscular oxytocin injection. We would like to report two cases that occured after intramuscular injection of oxytocin.

Keywords: Nicolau syndrome, oxytocin, intramuscular injection

Introduction

Nicolau syndrome (NS) is a rare, acute, cutaneus reaction, which occurrs at the site of an intramuscular (IM) drug injection. It was first described by Freudentha and Nicolau in 1924 and 1925, in association with IM injections of oily bismuth suspensions for the treatment of syphilis [1,2]. Subsequently, this reaction was reported with the administration of various other drugs [3-9]. The syndrome is associated with localized, sometimes extensive necrosis of the skin [10]. Localized pathognomonic skin change with a history of prior injection may allow the diagnosis of NS without skin

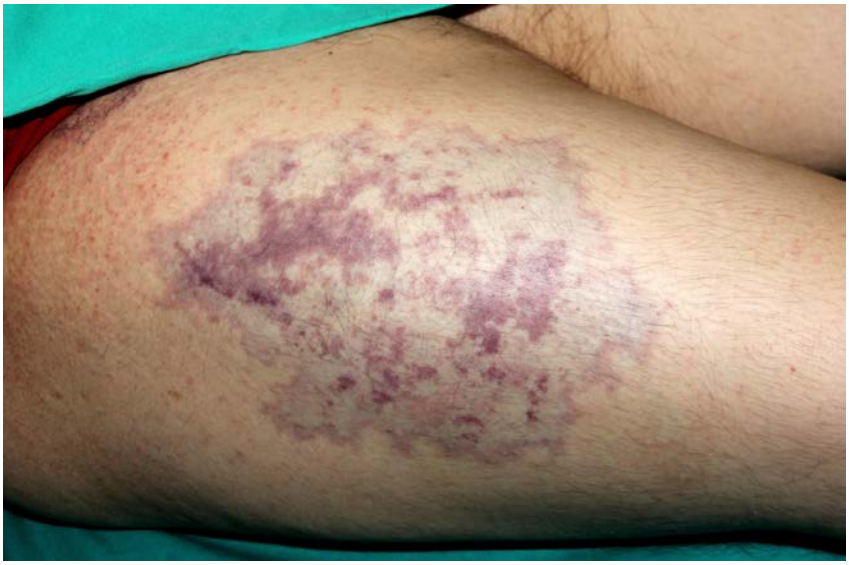

Figure 1. Reticular patch with irregular border on right thigh.

biopsy [7].

Case 1: A 34-year-old woman presented to our clinic with pain and a violaceous plaque on her right thigh. One week prior she had received IM oxytocin to prevent postpartum hemorrhage following a vaginal delivery. Immediately after the injection, the lesion developed along with pain at the site. Examination revealed a 14x10 cm reticular plaque with irregular border. (Figure1).

Two weeks later, the plaque evolved to awell demarcated cutaneous ulceration (Figure 2). Bacteriologic culture from the ulcer surface was negative. The patient refused biopsy. We diagnosed the patient with NS owing to presence of localized pathognomonic skin changes and a history of an injection IM oxytocin. She was successfully treated with surgical wound debridement.

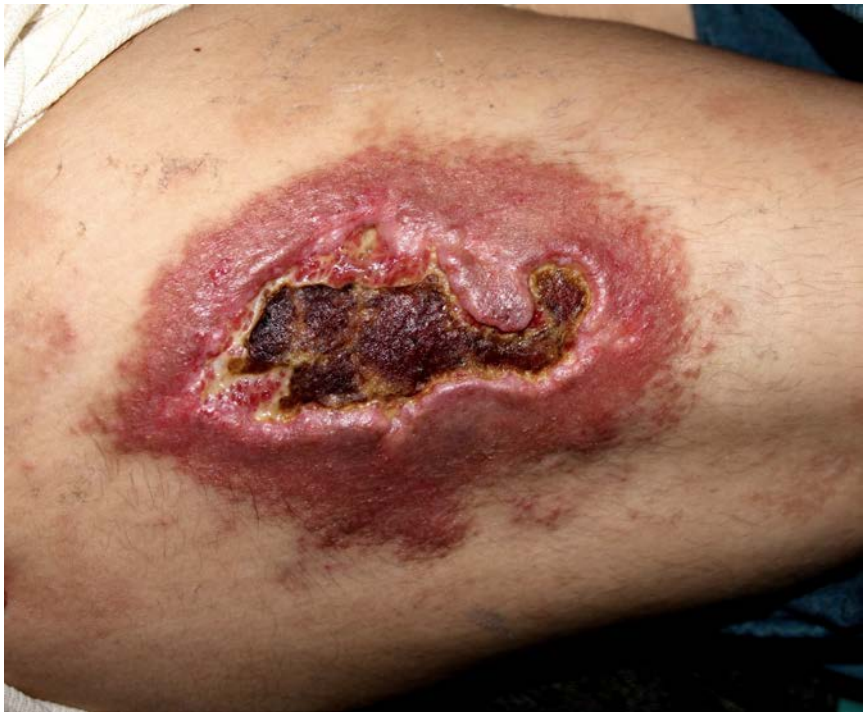

Figure 2. Well demarcated cutaneus ulceration with erythematous border

Case 2: A 26-year-old woman presented with a painful, necrotic cutaneous ulcer, which occurred 2 weeks after IM oxytocin in to the upper outer quadrant of her left buttock. Again, the IM oxytocin was used to prevent postpartum hemorrhage after vaginal delivery. Initially a localized painful erythematous skin reaction at her left buttock had developed within a few minutes. Within two weeks the lesion evolved in to a cutaneous ulcer. Dermatological examination revealed a necrotic crusted, cutaneous ulcer with a violaceous border (5 cm × 2 cm) on the upper outer quadrant of her left buttock (Figure 3). The bacteriologic culture from the ulcer surface was negative. Skin biopsy from the lesion showed cutaneus necrosis and tissue inflammation. We diagnosed the patient with NS owing to clinical and histopathological findings. She was successfully treated with surgical wound debridement.

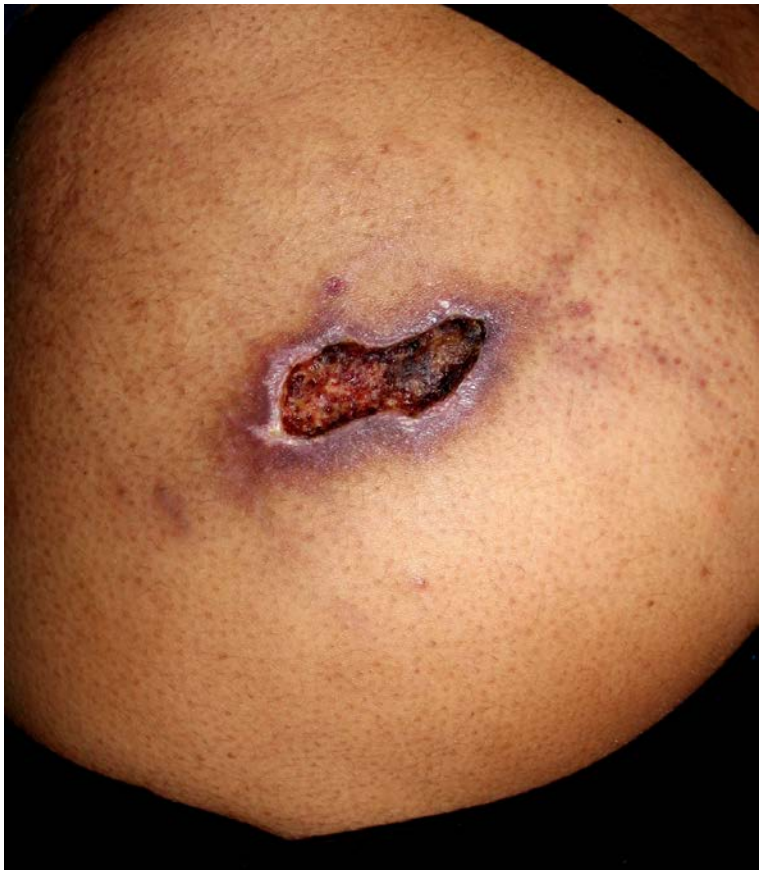

Figure 3. Cutaneous ulcer with a violaceous border on the upper outer quadrant of left buttock

Discussion

Nicolau syndrome (NS) is clinically characterized by local intense pain and blanching overlying skin immediately after an IM injection. An erythematous macule develops, which evolves into a livedoid reticular patch; it then ulcerates. The pathogenesis of NS is not known. Periarterial or perineural injection causing severe local pain owing to sympathetic nerve stimulation and vasospasm, which leads to ischemia and cutaneous necrosis has been proposed as a possible mechanism [8]. Another theory is thrombosis of small arteries induced by intra-arterial injection of particular drugs [3]. NS has been reported in association with the injection of many drugs such as phenylbutazone, local anesthetics, antihistamines, corticosteroids, vitamin K and vitamin B complexes, sulfonamides, benzathine penicillin, procaine penicillin G, pyrazolone, chlorpromazine, interferon alfa, interferon beta, vaccines, and etanercept [4,6,7,11-13].

Oxytocin is a hormone that stimulates uterus muscle contraction, particularly at the terminal phase of pregnancy and the postpartum period. The injectable formula is a synthetic oxytocin with the same effects of the natural hormone. The preferred method of application and dose to prevent postpartum hemorrhage in low risk vaginal deliveries is IM injection of 10 IU of oxytocin after delivery [14]. Oxytocin is a potent vasoactive drug and was reported to have mild constrictive effect in skeletal muscle arteries [15]. Therefore it is likely that this vasoconstrictive effect contributed to the pathophysiology of NS in our patients. To our knowledge there is no previous published report of oxytocin associated NS in the literature.

There is no confirmatory test available for the diagnosis of NS; clinical manifestations and histopathology play important diagnostic roles. Although NS has not been reported as an adverse reaction after IM injection of oxytocin, clinicians should be aware of this complication and IM injection should be performed very slowly and only after having aspirated with the syringe to ensure extravascular injection of the drug.

References

1. Freudenthal W: Lokales embolisches Bismugenol Exanthem. Sitzungsbericht des Schlesischen Dermatologischen Gesellschaft vom 24 November, 1923 Geschlechtskr 1924; 11:400.
2. Nicolau S: Dermitelivédoide et gangréneusede la fesse, consécutiveaux injectionsintra-musculaires dans la syphilis. Ann Mal Vénér 1925, 20:321-329.
3. Begin P, Anne DR: Nicolau syndrome may be caused by intravascular vaccine injection. Vaccine 2012, 30(11):2035-2036. [PMID:22198515]
4. Lee DP, Bae GY, Lee MW, Choi JH, Moon KC, Koh JK: Nicolau syndrome caused by piroxicam. Int J Dermatol 2005, 44(12):1069-1070. [PMID:16409285]
5. Forsbach Sanchez G, Eloy Tamez H: Nicolau syndrome caused by intramuscular administration of diclofenac. Revista de investigacion clinica; organo del Hospital de Enfermedades de la Nutricion 1999, 51(1):71. [PMID:10344171]
6. Saputo V, Bruni G: Nicolau syndrome caused by penicillin preparations: review of the literature in search for potential risk factors. La Pediatria medica e chirurgica : Medical and surgical pediatrics 1998, 20(2):105-123. [PMID:9706633]
7. McKinney C, Sharma N, Jerath RS: Livedoid dermatitis (nicolau syndrome) following intra-articular glucocorticoid injection. J Clin Rheumatol 2014, 20(6):339-340. [PMID:25160024]
8. Nayci S, Gurel MS: Nicolau syndrome following intramuscular diclofenac injection. Indian dermatology online journal 2013, 4(2):152-153. [PMID:23741679]
9. Karimi M, Owlia MB: Nicolau syndrome following intramuscular penicillin injection. J Coll Physicians Surg Pak 2012, 22(1):41-42 .[PMID:22237189]
10. Marangi GF, Gigliofiorito P, Toto V, Langella M, Pallara T, Persichetti P: Three cases of embolia cutis medicamentosa (Nicolau's syndrome). J Dermatol 2010, 37(5):488-492. [PMID:20536657]
11. Ezzedine K, Vadoud-Seyedi J, Heenen M: Nicolau syndrome following diclofenac administration. Br J Dermatol 2004, 150(2):385-387. [PMID:14996127]
12. De Sousa R, Dang A, Rataboli PV: Nicolau syndrome following intramuscular benzathine penicillin. J Postgrad Med 2008, 54(4):332-334. [PMID:18953160]
13. Guarneri C, Polimeni G: Nicolau syndrome following etanercept administration. Am J Clin Dermatol 2010, 11 Suppl 1:51-52. [PMID:20586511]
14. Westhoff G, Cotter AM, Tolosa JE: Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database Syst Rev 2013, 10:CD001808. [PMID:24173606]
15. Svanstrom MC, Biber B, Hanes M, Johansson G, Naslund U, Balfors EM. Signs of myocardial ischaemia after injection of oxytocin: a randomized double-blind comparison of oxytocin and methylergometrine during Caesarean section Br J Anaesth. 2008 May;100(5):683-9. [PMID:18385263]