

**CASE REPORT**

# Compartment Syndrome of the Calf Due to Nicolau Syndrome

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*Research performed at Urmia University of Medical Sciences, Imam Khomeini Hospital, Urmia, Iran**Received: 11 March 2015**Accepted: 7 May 2015***Abstract**

We report a case of Nicolau syndrome in a 15 months old girl following an intramuscular injection of penicillin 6.3.3 in her left buttock. This case is unique because she developed compartment syndrome in her left calf far from her injection site. Her toe's tips gangrened in the course of her ailment. We hypothesized that the compartment syndrome might be produced by a probable intra-arterial injection that had produced embolic obstruction of the small and medium size arteries in her leg or a probable perineural or periarterial injection had produced secondary sympathetic stimulation, extensive vasospasm, compromised microcirculation and the development of compartment syndrome.

**Key Words:** Compartment syndrome, Embolia cutis medicamentosa, Intramuscular injection, Livedoid dermatitis, Nicolau syndrome

**Introduction**

Nicolau Syndrome (NS) is also known as "embolia cutis medicamentosa" or "livedoid dermatitis" was first described as an adverse cutaneous reaction of intramuscular injections of bismuth in patients treated for syphilis by Freudental (1924) and Nicolau (1925)(1-6).

NS is characterized clinically by severe pain at the injection site, appearance of livedo-like discoloration of the skin and variable levels of tissue necrosis (1-6). The tissue damage in NS may range from reversible skin reactions to extensive loss of the skin layers and muscle necrosis that may lead to amputation. Paralysis of the lower extremities, sciatic nerve damage, compartment syndrome and death have been also reported in the NS patients (1-6).

The current report presents a case of Nicolau syndrome in a 15 months old girl following an intramuscular injection of penicillin 6.3.3 in her left buttock. She developed compartment syndrome of her left calf and her toe's tips gangrened in the course of her ailment.

**Case report**

A 15-month old girl had an intramuscular injection of penicillin 6.3.3 (Benzathine Penicillin G600,000 IU + Potassium Penicillin G300,000 IU + Procaine Penicillin G300,000 IU) in her left buttock because of an upper respiratory tract infection. She experienced a severe pain in her left buttock immediately after the injection. Within ten minutes, a red discoloration was developed over her left lower limb. In a few hours, her left leg's skin color changed to a mottled deep red and purplish discoloration. She was referred because of a rapid development of vascular insufficiency in her left lower limb. However, the distal pulses were palpable and the capillary filling was normal. Doppler sonography showed normal flow in the left dorsalis pedis and tibilis posterior arteries. A diagnosis of Nicolau Syndrome based on history and the clinical features was made. She was treated with anticoagulation, analgesics, corticosteroid and systemic antibiotics.

After 18 hours, the left leg's skin had an established

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**Figure 1.** Eighteen hours after the injection. The arrow indicates the site of the injection at the left buttock. Red and purplish mottling is established on the left leg and foot.

purplish mottling [Figures 1; 2]. Although the distal pulses were palpable; however, capillary fillings were not detectable at her toe's tips. The left calf compartments were felt tense. Therefore, calf fasciotomy was performed and the swelled muscles bulged from the incisions.

On the seventh post injection day the toe's tips had established necrosis and needed debridement [Figures 3]. The fasciotomy incisions were covered with partial thickness skin grafts. Amputation of the greater toe was performed through the interphalangeal joint. Amputation of the second through fifth toes was performed through the proximal interphalangeal joints.

Follow up electromyography and nerve conduction study showed ischemic changes of the calf muscles and a permanent deep peroneal nerve damage.

### Discussion

Nicolau Syndrome has been reported with intramuscular injections of non-steroidal anti-inflammatory drugs (diclofenac, piroxicam, ketoprofen, ibuprofen, phenylbutazone), antibiotics (penicillin derivatives, tetracycline,



**Figure 2.** Eighteen hours after the injection. The left leg's skin and foot had an established purplish mottling.



**Figure 3.** Six days after the left calf fasciotomy. The picture shows the gangrened toes' tips.

sulfapyridine, streptomycin, gentamicin), corticosteroids (dexamethasone, triamcinolone, paramethasone, cortivazol, hydrocortisone), antipsychotics and anti-epileptics (phenobarbital, chlorpromazine), Vaccinations (diphtheria-tetanus-pertussis), antihistamines (diphenhydramine, hydroxyzine), local anesthetics (lidocaine), interferon alpha, cyanocobalamin, bismuth and vitamin K (2, 6). Although NS was first described as a rare complication of intramuscular injections; however, it has been also reported with subcutaneous, intravenous and intra-articular injections (4).

Histopathological study demonstrates variable necrosis of the epidermis, dermis and subcutaneous tissue as well as muscles because of thrombosis of small and medium sized vessels without vasculitis (1-6).

The etiology of NS is unclear. Several hypotheses have been suggested for the development of NS. The first hypothesis suggests that an accidental intra-arterial injection of crystalloid drugs may produce embolic obstruction of the small and medium size cutaneous arteries by microcrystals that produce the subsequent tissue necrosis. The second hypothesis suggests that damage to an end artery due to a periarterial injection or a perineural injection may produce intense local pain with secondary sympathetic over stimulation that triggers extensive vascular spasm and compromised circulation. The third hypothesis suggests that a perivascular injection may produce inflammation, tissue necrosis and damage to the walls' of cutaneous arteries. The arterial damage produces skin necrosis (1-6).

There is no specific treatment for NS (1-6). Observing correct injection techniques can minimize the risk of development of NS. Supportive treatments such as anticoagulation, analgesics, steroids, vasoactive agents (pentoxifylline), hyperbaric oxygen and antibiotics have been suggested. In suspected NS patients cold compress of the site of injection may aggravate the tissue damage and should be avoided. Surgical treatments depend on the extent of the tissue damage (1-6).

The current case of NS is unique because the patient developed compartment syndrome of her left calf far from her injection site. The deployment of compartment syndrome depends on multiple factors. Palmer and Mercer described anterior tibial compartment syndrome following femoral artery perfusion in a series of four patients. They hypothesized that the developed compartment syndromes might due to direct ischemia and

injury to the femoral arteries. Primary muscle necrosis and venous damage or occlusion may also contribute to development of compartment syndrome (7).

In the current case the compartment syndrome might be produced by a probable intra-arterial injection that had produced embolic obstruction of the small and medium size arteries in her leg or a probable perineural or periarterial injection had produced secondary sympathetic stimulation, extensive vasospasm, compromised microcirculation and the development of

compartment syndrome.

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