

## Nicolau Syndrome in 29 Months Boy: Another Report of Iran

Mojtaba Fazel<sup>1</sup>, Parvin Akbar Asbagh<sup>2</sup>, Azadeh Afshin<sup>3\*</sup>, Mamak Shariat<sup>4</sup>, Mahmoud Fazel<sup>5</sup>,  
Massumeh Akhlaghi<sup>5</sup>

<sup>1</sup>Professor Assistant in Pediatric Nephrology, Valiasr Hospital, Imam Complex, Tehran University of Medical Science, Tehran, Iran

<sup>2</sup>Associated Professor in Pediatric Cardiology, Valiasr Hospital, Imam Complex, Tehran University of Medical Science, Tehran, Iran

<sup>3</sup>Pediatric Resident, Valiasr Hospital, Imam Complex, Tehran University of Medical Science, Tehran, Iran

<sup>4</sup>Associated professor, Maternal & Fetal & Neonatal Research Center, Tehran university of Medical Science, Tehran, Iran

<sup>5</sup>Pharmacist, Tehran, Iran

<sup>6</sup>Rheumatology Research Center, Tehran, Iran

### \*Corresponding Author:

Name: Azadeh Afshin

Email: [azi.afshin@gmail.com](mailto:azi.afshin@gmail.com)

**Abstract:** Nicolau syndrome (NS) is a very rare complication of intramuscular injections that leads to some degree of necrosis in skin, subcutaneous fat and muscles. The type of injected Drugs and wrong injection methods are the main factors for this iatrogenic syndrome. Here we report a 29 months boy, one of the Iranian children affected NS following the wrong intramuscular injection of Benzathine Penicillin. But he came back home without any major complication because of a good hospital care. Reports of mortality and severe morbidity of common injection drugs such as penicillin derivatives will help to prevent such iatrogenic syndromes.

**Keywords:** Nicolau syndrome, Benzathine Penicillin, Embolia Cutis Medicamentosa, Livedoid Dermatitis.

### INTRODUCTION

Nicolau syndrome is a very rare iatrogenic syndrome caused mostly by intra muscular injection of some drugs that leads to skin and soft tissues and muscle necrosis [1]. Another name of this complication is Livedoid Dermatitis and also called Embolia Cutis Medicamentosa. soon after injection Severe pain at the injected site followed by skin discoloration with erythematic and livedoid reticular patches presents. After that tissue become necrosis. Atrophic scars ,sepsis and limb amputation are some side effects of this syndrome and death because of compartment syndrome and sepsis have been reported in some patients [2]. This syndrome is mostly caused by intramuscular injections, although followed by subcutaneous and intra-articular injections have also been reported [3, 4, 6].

### CASE REPORT

A 29-months boy who lives in south of Iran, with full vaccination records and without any past medical history after suspicious to have streptococcal pharyngitis treated with penicillin benzathine. Drug was injected very fast and in upright position. Immediately after the injection, the patient suffered from pain at injection site and became discomfort .During first hours paresthesia developed in right lower extremity. After 2

hours, discoloration was generated in right limb. After 17 hours hemorrhagic rashes and livedoid reticular patches began from right lower Quadrant of abdomen till all right limb. After 24 hours, compartment syndrome began in right limb that colored doppler sonography revealed Pressure on the lower limbs veins. Extremity pulses like dorsalis pedis and posterior tibialis did not palpable.

### Consent

Written informed consent was obtained from the patient's parent for publication of this Case report and any accompanying images.



**Fig. 1: Livedoid reticularis feature after 24 hours**



**Fig. 2: Necrotic toes**

Necrosis began in toes (Fig. 2). The patient was transferred to educational hospital and immediately was taken to operating room and right calf fasciotomy was done. Patient needed serial fasciotomy and medical treatment with pentoxifylline and subcutaneous heparin was administered. Regardless of intensive care systemic infection happened with *Pseudomonas Auroginosa* and treated with systemic antibiotics CT angiography of right femoral artery after the first fasciotomy, showed decreased flow in posterior tibialis (Fig. 3).



**Fig. 3: Right femoral CT angiography showed decreased flow in posterior tibialis**

Because of delay in diagnosis and treatment of this syndrome 2 toes became necrosis and one of them amputated. After 2 months he discharged from hospital and after 6 months could walk again.

## DISCUSSION

Nicolau syndrome also known as lividio like dermatitis or Emboli cutis Medicamentosa is a very rare Iatrogenic necrotizing skin syndrome happened mostly after intramuscular injections [1]. This syndrome has also been reported followed by subcutaneous, intra venous and even intra-articular injections [3-6].

This syndrome was first described in 1924 by Freudenthal followed by injection of Bismuth salt for treatment of syphilis [7]. This syndrome has been described with various drugs, such as penicillin, local anesthetics, corticosteroids, NSAIDs etc. [7] (Table 1).

After injection patient immediately complained of severe pain at the injection site, erythematic and skin lesions such as hemorrhagic and purplish lividio reticular patches spread. These are pathognomonic manifestations of this syndrome as happened in our patient [7, 9].

**Table 1: Drugs causing Nicolau Syndrome**

Drugs	Examples
NSAIDs	Diclofenac, Piroxicam, Ibuprofen
Anti Biotic	Penicillin derivatives, Tetracyclines Gentamycin Streptomycin
Corticosteroid	Dexamethasone, Triamcinolone Hydrocortisone
Anti Psychotic	Chlorpromazine
Vaccine	DTP
Anti Histamin	Diphenhydramine, Hydroxyzine
Local anesthesia	Lidocaine
Miscellaneous	INF $\alpha$ , Vit K, Bismuth salts, B complex vitamins, & Epinephrin

After few hours' skin, subcutaneous fats and muscles become necrosis.

The exact pathogenesis of this syndrome still remains unclear. Perhaps Drugs micro crystals cause vascular damages. As seen in skin biopsy of these patients these crystals irritate and compress arteries and lead to Ischemia and tissue necrosis [7, 8, 10].

Ultra sonography of affected areas shows diffuse thickening with increase echogenicity of skin and subcutaneous layers. MRI (T2-weighted) shows edema and fluid collections at involved area [13].

It has no definitive treatment, but some preservative treatments depending on the severity and depth of the syndrome were described.

Serial debridement with dressing and some analgesic and vasoactive drugs such as pentoxifylline showed good effectiveness. Use of pentoxifylline as vasoactive agent in combination with hyperbaric oxygen had beneficial effect in some records [11].

Yildiz *et al.* used hyperbaric oxygen in the treatment of NS to prevent the necrosis and to decrease amputations [12].

Because these patients are very high risk for infections, when any clue of septicemia happened treatment with antibiotics should be considered.

Correct injection techniques and familiarity with fatal side effects of incorrect injections are the most important principles.

One thing that should always be considered is use of right needle size and Z track method for injections. However aspirations before injection is very important to ensure no vessels are involved.

### CONCLUSION

This syndrome basically is preventable. Reports of mortality and severe side effects of common injection drugs such as penicillin derivatives will help to prevent such iatrogenic syndromes.

### Abbreviations

NS: Nicolau syndrome, MRI: Magnetic Resonance Imaging, NSAIDS: Non-steroidal anti-inflammatory drugs, .DPT: Diphtheri -pertussis-tetanus, INF $\alpha$ : Interon  $\alpha$

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