

# A case of Nicolau syndrome treated with hyperbaric oxygen

## Case Report

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**Abstract:** A 3-year-old boy with a Nicolau Syndrome (NS) on the left side of the body and the limbs after benzathine penicilline injection is reported. To the authors' best knowledge, this is the first report of hyperbaric oxygen used in the late treatment of NS preventing the progress of the necrosis and therefore limiting the amputation level.

**Keywords:** Nicolau syndrome • Penicillin • Hyperbaric oxygen • Necrosis • Amputation

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## 1. Introduction

Nicolau Syndrome (NS) is a rare complication of intramuscular injection of various drugs. This syndrome was first described by Freudenthal and Nicolau in 1924 and 1925 [1]. It was defined after the use of intramuscular oily bismuth suspensions for the treatment of syphilis. NS is described as livedoid dermatitis secondary to acute arterial thrombosis after the injection of an insoluble drug substance into a blood vessel [2]. The syndrome has been associated with cutaneous necrosis, transitory or permanent ischemia of the ipsilateral limb, various neurological complications, isolated muscular necrosis without skin lesions and superimposed infection [1]. In this report, we present a case of NS after an injection of benzathine penicillin where we used hyperbaric oxygen treatment and amputation of the toes.

## 2. Case report

A 3-year-old boy was admitted to another center due to erythema, patchy ecchymosis discoloration, pain and coldness on the left side of his body and limbs, and necrosis of the left foot after an intramuscular benzathine penicilline injection. The blood testing revealed increased levels of serum lactate dehydrogenase and liver enzymes. He was treated initially with antihistaminic and steroid therapy. Immediate Doppler ultrasonographic evaluations for the left lower limb was normal. He was followed with dexamethasone, pentoxifylline and enoxaparin combination thereafter for 7 days. As the ecchymosis on the left foot persisted and necrosis was observed on the left toes, the patient was admitted to our department.

General cardiopulmonary examination was normal. Liver and spleen were not palpable. Patchy ecchymosis and coldness below the left knee were observed and the left foot was found to be necrotic (Figure 1). All peripheral pulses normal to palpation. Repeat venous and arterial Doppler examinations were unremarkable. Hyperbaric

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**Figure 1.** Livedo-like skin lesions below the knee; more condensed at the ankle and foot region with accompanying necrosis at the toes.



oxygen (HBO) treatment (2.5 ATA, 90 minutes, daily, n=30) in a monoplace hyperbaric chamber was started additional to the above-quoted mediations. Lesions on the body healed completely, but edema and skin necrosis improved in 10 days with remaining demarcating necrotic lesions all over the left toes. The toes were amputated at the metatarsophalangeal level as the necrosis had established. The hyperbaric oxygen treatment was continued for another 10 days after the amputation until the operation site has healed uneventfully. On the first month control visit, he had no complaints and was walking without any difficulties (Figure 2).

### 3. Discussion

NS is characterised by a painful and indurated dermatitis with subsequent necrosis developing after intramuscular, intraarticular or rarely subcutaneous injections [3]. In certain cases, the necrosis can be extensive; rectal hemorrhage, neurologic complications and transient or permanent ischemia of the ipsilateral limb that may even require amputation may accompany. Independent of the material given or the place of injection, the lesions

**Figure 2.** Mild discoloration of the dorsal foot after healing of the lesions and toe amputation.



usually extend to the ipsilateral body regions due to unknown mechanisms. Furthermore, NS can be fatal in children [4].

Pathogenesis is yet unclear and multiple mechanisms have been proposed. It was first thought to be of an allergic or immunologic origin but studies mentioning about repeat doses of the same drug not causing the reaction once again are against this hypothesis [1,4,5]. Vascular mechanisms are currently accepted to be more reasonable. The syndrome seems to be the eventual result of an intra-arterial or periarterial injection of the offending drug, with subsequent arterial vasospasm and cutaneous necrosis. NS has been reported with different drug formulations and in different age groups [1,3,4,6,7]. Physical and chemical factors like the injection style and the pH of the injected solution have also been reported to cause NS [1,8].

Treatment is generally supportive and symptomatic; ranging from local care to surgical intervention. Use of vasoactive agents may be beneficial considering the vascular pathogenesis. Antibiotic use is restricted to the cases with signs and symptoms of infection. Enoxaparin, pentoxifylline and HBO treatment were given to our patient. To the best of our knowledge, there is only one case report in literature where HBO was used early in the treatment of NS with complete healing [9]. Our patient appears to be the second case of NS that was treated with HBO, but in the late period (after 1 week of diagnosis and after necrosis had ensued).

Normally, HBO therapy has been used in the treatment of acute gas embolism, carbon monoxide poisoning, necrotizing infections, chronic refractory osteomyelitis, peripheral traumatic ischemia and non-healing wounds [10]. On the other hand, it is contraindicated when there is pneumothorax without chest tube application, epilepsy, high fever, sickle cell anemia attack and the possible complications during HBO therapy include barotraumatic lesions (middle ear, nasal sinuses, inner ear, lung, teeth), oxygen toxicity (central nervous system, lung), confinement anxiety, and ocular effects (myopia,

cataract growth). If safety guidelines are strictly followed, HBO therapy is a modality with an acceptable rate of complications. Serious complications rarely occur [11]. During the follow up of our patient under HBO treatment, the preceding necrosis was observed not to progress but become limited distal to the metatarsophalangeal joints. Therefore, although late, we suggest that HBO be applied to patients even with necrosis for preventing more proximal amputation levels.

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