

A Rare Case of Nicolau Syndrome Secondary to Intramuscular Injection of Benzathine Benzylpenicillin

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Abstract

Introduction: Nicolau syndrome is a rare iatrogenic syndrome caused by an intramuscular injection of medication, leading to ischemia and then tissue necrosis in a limb, with a prognosis that is mainly functional due to the risk of amputation of the affected limb. We describe a new case in a 24-month-old infant following an IM injection of benzathine penicillin. **Patient and Observation:** The patient was a 24-month-old male infant with no previous history, who was admitted for sudden functional impotence of a limb. During questioning, the parents reported a visit to a health facility on the outskirts of town for an undocumented dermatosis, which led to an IM injection of benzathine penicillin in the upper third of the right thigh. A few hours later, he presented with pain, incessant crying and, as noted by his parents, functional impotence of the limb. This prompted a second consultation at the same site two days later, where treatment with paracetamol and oral antibiotics was prescribed. When there was no improvement, he was referred to our facility six days later, where he presented with fever, tachycardia and poor general condition. The examination revealed coldness throughout the right lower limb, which was stiff, cyanotic and necrotic in places from the upper third of the thigh to the toes. The pedal and popliteal pulses were absent on palpation. The rest of the clinical examination was normal. The angiography showed total thrombosis of the superficial and deep right femoral arteries extending to the pedal artery. Biological tests revealed hyperleukocytosis at 19,170 and CRP at 102 mg/l. Renal function and blood count were normal. In the absence of other causes of

thromboembolic disease, a diagnosis of Nicolau syndrome secondary to an intramuscular injection of benzathine benzylpenicillin was made. Surgical management with transfemoral amputation was performed. The outcome was favorable with healing of the stump. **Conclusion:** In addition to its rarity, delayed diagnosis is exacerbated by difficulties in accessing specialist care in rural areas. This case calls for greater vigilance in prescribing benzathine benzylpenicillin, which is often misused for certain skin conditions in our African context.

Keywords

Infant, Nicolau Syndrome, Benzathine Penicillin, Ziguinchor

1. Introduction

Nicolau syndrome is an iatrogenic syndrome caused by an IM injection of medication that leads to ischemia and then tissue necrosis in a limb [1] [2]. It is a rare condition, rarely described in the literature, with an approximate frequency of 1 case per 10,000 to 100,000 injections [3]. Its etiopathogenesis is poorly understood. Several hypotheses have been put forward, including vascular phenomena such as vasospasm, arterial thrombosis and/or embolism, direct trauma from the injection needle, or perivascular compression [4]. The most commonly reported causative drugs are antibiotics, vitamin K, corticosteroids and non-steroidal anti-inflammatory drugs [2] [3].

The prognosis is mainly functional, linked to amputation of the affected limb. We describe a new case in a 24-month-old infant following an IM injection of benzathine penicillin.

2. Patient and Observations

A 24-month-old male infant with no significant antenatal or perinatal history, up-to-date vaccinations, and good psychomotor development was admitted for sudden functional impairment of a limb. During questioning, the parents reported a visit to a health facility on the outskirts of town for an undocumented dermatosis, which had led to an IM injection of benzathine penicillin in the upper third of the right thigh. A few hours later, he had presented with pain, incessant crying and, according to his parents, functional paralysis of the right lower limb. This prompted a second consultation at the same facility two days later, where treatment with paracetamol and oral antibiotics was prescribed. As there was no improvement, he was referred to our facility six days later. No information regarding the dose administered, the size of the needle or the injection technique was mentioned in the medical record.

He was admitted to the paediatric emergency department at Ziguinchor Peace Hospital six days after the injection and, on admission, he had a fever, tachycardia and was in poor general health. Physical examination revealed coldness through-

out the right lower limb, which was stiff, cyanotic and necrotic in places from the upper third of the thigh to the toes (**Figure 1**). The pedal and popliteal pulses were absent on palpation. The rest of the clinical examination was normal.

The emergency angiogram showed total thrombosis of the superficial and deep right femoral arteries extending to the pedal artery (**Figure 2**). However, the arterial axes of the contralateral lower limb were patent.

Biologically, there was hyperleukocytosis at 19,170 (polynuclear neutrophils: 67.2%), a positive C-reactive protein at 102 mg/l, and anaemia at 9.4 g/dl with a mean corpuscular volume (MCV) of 69 fL and a mean corpuscular haemoglobin concentration (MCHC) of 22 pg, urea at 0.22 g/l, creatinemia at 6 mg/l, ASAT (aspartate aminotransferase) at 18 IU/L and ALAT (alanine aminotransferase) at 18 IU/L. Blood count was normal (TP: 98%, INR: 1.12). The cardiac ultrasound was normal and no recent trauma was reported. In the absence of other causes, a diagnosis of Nicolau syndrome secondary to an intramuscular injection of benzathine benzylpenicillin was made. Upon admission, he received analgesics, antibiotic therapy with cefotaxime at 200 mg/kg, and anticoagulation (low molecular weight heparin at 100 IU/kg in two doses). In the absence of improvement, surgical management with transfemoral amputation was performed (**Figure 3**). The outcome was favourable, with healing of the amputation stump. The fitting of a prosthesis was subsequently indicated.



Figure 1. Hard, cyanotic and necrotic appearance in places, extending from the upper third of the thigh to the toes.

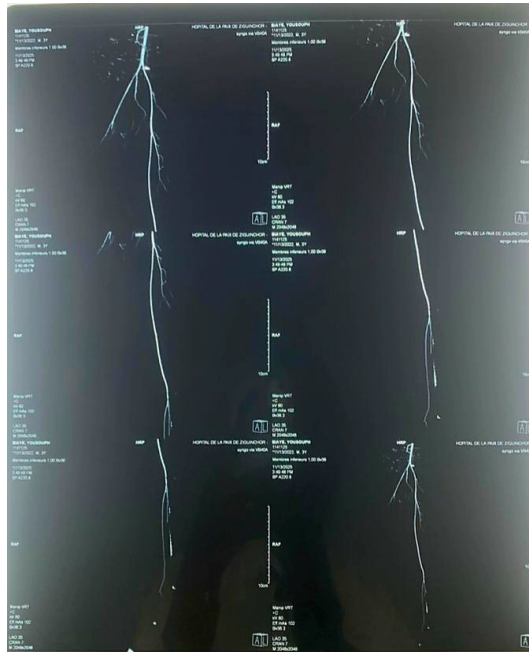


Figure 2. Angio scanner of the lower limbs showing total thrombosis of the right superficial and deep femoral arteries extending to the pedal artery and patent arterial axes of the contralateral lower limb.



Figure 3. Amputation stump of the right thigh.

3. Discussion

Nicolau syndrome remains a rare condition in children. It was first described in 1924 by Nicolau in a patient who had received an intramuscular injection of bismuth salts for syphilis [5]. In addition to benzathine benzylpenicillin injections,

several other drugs have been implicated, such as vitamin K [6], non-steroidal anti-inflammatory drugs [7] and vaccinations [8].

Benzathine benzylpenicillin is still used in certain dermatological conditions, particularly syphilis, and in the prevention of recurrent bacterial skin and soft tissue infections. However, inappropriate indications are noted for certain dermatoses, especially in peripheral facilities in rural areas. This phenomenon highlights the difficulty of accessing specialized care in remote areas.

The exact aetiopathogenesis of this condition is poorly understood [5]. In our case, the injection of benzathine penicillin led to total thrombosis of the femoral artery, the mechanism of which was either direct trauma from the injection needle or direct injection of the molecule into the artery.

The diagnosis is mainly clinical, based on intense pain at the injection site, quickly accompanied by a change in skin color, first red, then purplish, and finally blackish. The progression is characteristic. Within a few hours to a few days, you will see the appearance of a well-defined necrotic plaque, often surrounded by an inflammatory halo. The skin becomes cold to the touch and loses its normal sensitivity.

Imaging is of paramount importance as it allows the extent of the lesions to be determined. Early treatment can prevent the condition from progressing to necrosis or even gangrene. Immediately after the event, treatment is based on various measures aimed at improving vascularization, such as heparin thrombolysis [9]. Intralesional corticosteroid injections are also used to reduce inflammation [9].

Delayed diagnosis and treatment are factors contributing to a poor prognosis that can lead to radical surgery, as observed in our case where the consultation took place 6 days after the injection [10].

Early diagnosis would have improved the prognosis through the emergency administration of anticoagulants and/or thrombolytics. Although the patient's life was not at risk, limb amputation constitutes a serious functional and psychological disability.

Aspiration just before injection has been proposed as a method of preventing Nicolau syndrome, as it is thought to prevent embolisms due to intra-arterial deposition of the drug [11] [12]. However, the effectiveness of this method remains uncertain, as vascular spasm or vasoconstrictive effect is generally difficult to identify.

4. Conclusion

We have reported a case of Nicolau syndrome secondary to the injection of benzathine penicillin in an infant, which is rare in itself, due to the delay in diagnosis caused by difficulties in accessing specialized care in rural areas and the poor prognosis leading to limb amputation. This case calls for greater vigilance in the prescription of extencilline, which is often misused for certain dermatoses in our African context.

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Authors' Contributions

All authors have read and approved the final version of the manuscript.

Ethical Considerations

The parents' free and informed consent was obtained prior to the use of the images.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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