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Nicolau Livedoid Dermatitis following intramuscular benzathine penicillin injection

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Abstract

We report the case of a 64-year-old male presenting with a rapidly enlarging painful violaceous plaque in the left buttock and posterior thigh, following a gluteal intramuscular injection of benzathine penicillin. Associated urinary incontinence and lower left limb paresis were consistent with sciatic and lower sacral nerve damage, as confirmed by electromyography. Additional underlying muscular damage was observed in ultrasound and computer tomodensitometry scans and supported by high serum levels of creatine kinase and lactate dehydrogenase. Aggressive treatment was performed with fluid expansion, intravenous steroid bolus, vasodilators and anticoagulation, resulting in slow improvement of cutaneous and muscular lesions. However, no significant effect was observed on neurologic dysfunction after 6 months of regular neuromuscular rehabilitation. Nicolau Livedoid Dermatitis is a rare and potentially fatal condition showing variable levels of tissue impairment and unpredictable course and prognosis. Specific treatment is not consensual and the efficacy of any particular treatment remains to be established.

Introduction

Nicolau Livedoid Dermatitis is a rare condition consisting in tissue ischemia and necrosis following severe reduction of blood flow as a consequence of accidental vascular damage because of parenteric drug administration. Its evolution is highly unpredictable, showing variable cutaneous, muscular and bone impairment. Systemic infection and renal dysfunction following rhabdomyolysis can often cause death.

Case report

A 64-year old male was observed in the Emergency Room with a large acute violaceous edematous plaque of the left buttock and posterolateral aspect of the proximal thigh (Figure 1). The rapidly enlarging lesion presented with a cold livedoid surface and expanding reticular borders. It arose less than one hour after a left gluteal intramuscular injection of benzathine penicillin (2,400,000 units); the needle puncture was still visible in the centre of the plaque, on the gluteal upper outer quadrant. Penicillin was prescribed in a Department of Infectious Disease in this patient with a history of late syphilis and suspicion of recent reinfection. The patient described involuntary urine loss immediately following the injection and reported severe pain in the affected area.

The diagnosis of syphilis was first made ten years before in the Department of Infectious Disease, following a non-pruriginous generalized erythematous skin eruption. The patient was treated with benzathine penicillin for several times in that period, without noticeable adverse effects. The patient was a heavy smoker, had a long history of alcohol abuse, and was suffering from arterial hypertension, alcohol-induced chronic liver disease and chronic obstructive pulmonary disease.



Figure 1

Figure 1. Painful livedoid violaceous plaque in the left buttock and posterior thigh. The place of the intramuscular injection can be easily seen nearly in the centre of the plaque.

On admission, the patient was conscious, afebrile, and hemodynamically stable, showing no signs of peripheral



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creatinase kinase (22,805 U/L ó normal below 171 U/L) and lactate dehydrogenase (536 U/L ó normal below 248 U/L), suggesting severe muscular damage; erythrocyte sedimentation rate, plasma C-reactive protein, white cell count, and other inflammation markers, hemostatic tests, and renal function parameters were within normal range. Local soft tissue ultrasound revealed gluteus maximus muscle heterogeneity and a thin interaponeurotic effusion, which were later confirmed by CT. No evidence of left lower limb arterial compromise was observed during arterial Doppler ultrasound.

The diagnosis of Nicolau Livedoid Dermatitis was therefore established. The patient was admitted to the Department of Dermatology and submitted to aggressive treatment with dextran and other intravenous fluid infusions, intravenous methylprednisolone (1 g) as a daily bolus for 3 days, oral nifedipine (30 mg daily), oral pentoxifylin (300 mg TID), and subcutaneous sodium enoxaparine (1 mg/kg b.i.d). Lower left limb neurologic impairment was confirmed by electromyography and described as a severe acute left lumbosacral radiculopathy (L5-S1), compatible with sciatic nerve injury. In addition, a bulbospongiosus muscle dysfunction was discerned, suggesting lower sacral nerve damage.



Figure 2

Figure 2. Late purpuric lesion on dorsal scrotum arising on Day 6



Figure 3

Figure 3. Complete resolution of skin lesions on Day 19

No additional purpuric or necrotic areas were observed on the skin apart from late ecchymotic lesions on dorsal scrotum arising on the 6th day, justifying reduction of anticoagulant therapy to a prophylactic sodium enoxaparin dose of 40 mg daily. Cutaneous lesions showed slow progressive improvement and became inapparent on day 19. Muscular changes remained stable. Periodic serum analysis revealed normal muscular enzyme levels on day 13, with no associated evidences of renal dysfunction. By this stage, the patient started a regular program of left lower limb and bladder neuromuscular rehabilitation under surveillance of a neurologist and a physiatrist. Despite this effort, neither the lower limb muscular activity nor the urinary incontinence showed improvement after six months of specific treatment.

Discussion

Nicolau Livedoid Dermatitis, also known as Embolia Cutis Medicamentosa, is a rare and potentially deadly adverse event associated with parenteral drug administration, most commonly observed shortly after intramuscular, intra-articular or subcutaneous drug injection. Its mechanisms are not totally understood, but accidental intra or para-arterial drug injection seems to be responsible. An initial vascular injury with local inflammation, reflex arterial spasm, local arterial thrombosis, and distal vascular occlusion by microemboli would result in distal blood flow reduction, leading to ischemia and eventually necrosis of the distal tissues [1, 2, 3, 4]. Several drugs have been described in association with Nicolau Livedoid Dermatitis, mostly intramuscular antibiotics [3, 5, 6, 7] and non-steroidal anti-inflammatory drugs [3, 4, 8, 9, 10, 11, 12]. Other drugs such as intramuscular vaccines [2, 13], vitamin K [14], cyanocobalamin [3], thiocolquicoside [15], bismuth [8], intra-articular piroxicam [16] and glucocorticoids [17], subcutaneous interferon [4, 18], and sclerotherapy agents [19] have also been reported as possible causes. Neither the nature of the drug nor any specific immunologic phenomenon appear to play a significant role [2, 3, 4]. Severe skin ulceration [8, 10, 13, 15] and rhabdomyolysis [8, 9] are common and consequent renal insufficiency, sepsis, or death may occur.



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the inferior gluteal
intramuscular
division of the
along the deep surface
sible for the

innervation of gluteal and posterior thigh cutaneous areas and underlying muscles. One of its main branches, the internal pudendal artery, innervates the perineum, scrotum and also the proximal urethra and urogenital diaphragm, which may explain the occurrence of late cutaneous lesions in the scrotum and urinary incontinence.

Neurologic impairment has been rarely described in most cases of Nicolau Livedoid Dermatitis [7, 16]. In this case, inferior gluteal artery blood flow reduction might have also compromised the irrigation of both proximal sciatic and pudendal nerves, resulting in severe irreversible lower limb and vesicle sphincter dysfunction. However, direct nerve damage following gluteal injection cannot be excluded.

The diagnosis of Nicolau Livedoid Dermatitis is based on clinical presentation because there are no specific diagnostic tests. In fact, cutaneous biopsy appears not to be useful (showing in most cases cutaneous necrosis, non-specific dermal inflammation, and thrombosis of small to medium sized vessels) [2, 4, 13] and might precipitate severe local ulcers and infection. Considering its potentially devastating effects, Nicolau Livedoid Dermatitis should be promptly considered in any patient presenting with local pain and livedoid erythema after parenteral drug administration. Even when following all the safety recommendations for intramuscular drug injections, the risk of Nicolau Livedoid Dermatitis cannot be totally eliminated [2, 4].

Treatment is far from being consensual. Intravenous vascular expansion, vasodilators, anticoagulants, and systemic steroids are commonly used [3, 4, 8, 9, 19], with variable results. It remains unclear whether the various therapeutic approaches change the natural course of the condition and lead to a better prognosis because tissue damage develops rapidly and is rarely fully reversible. In the present case, the described treatment was effective in the resolution of cutaneous and muscular disease, but clearly insufficient for restoring normal nerve function.

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