

Skin necrosis following local anesthetic: Same presentation for two different diagnoses

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Abstract

Background: Local anesthetics (LA) are widely used in medicine and are generally well tolerated. Although most adverse reactions are nonallergic, LA are a frequent reason for allergy consultation.

Objective: We want to expand the differential diagnosis of adverse reactions to LA by presenting rare diagnoses.

Methods: We present here two patients with similar clinical presentations, namely skin necrosis after local anesthesia with lidocaine, but with two different final diagnoses.

Results: For Patient 1, skin necrosis was imputed to the vasoconstrictor effect of epinephrine in a patient with vascular background aggravated by heavy consumption of tobacco and cannabis. Patient 2 final diagnosis was Nicolau syndrome (embolia cutis medicamentosa), a cutaneous necrosis at the site of injection.

Conclusion: The allergist should be aware of these diagnoses and include them in the differential diagnosis of local anesthetic hypersensitivity.

Key words: drug hypersensitivity, drug allergy evaluation, local anesthetics, skin necrosis, local anesthetic hypersensitivity

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Introduction

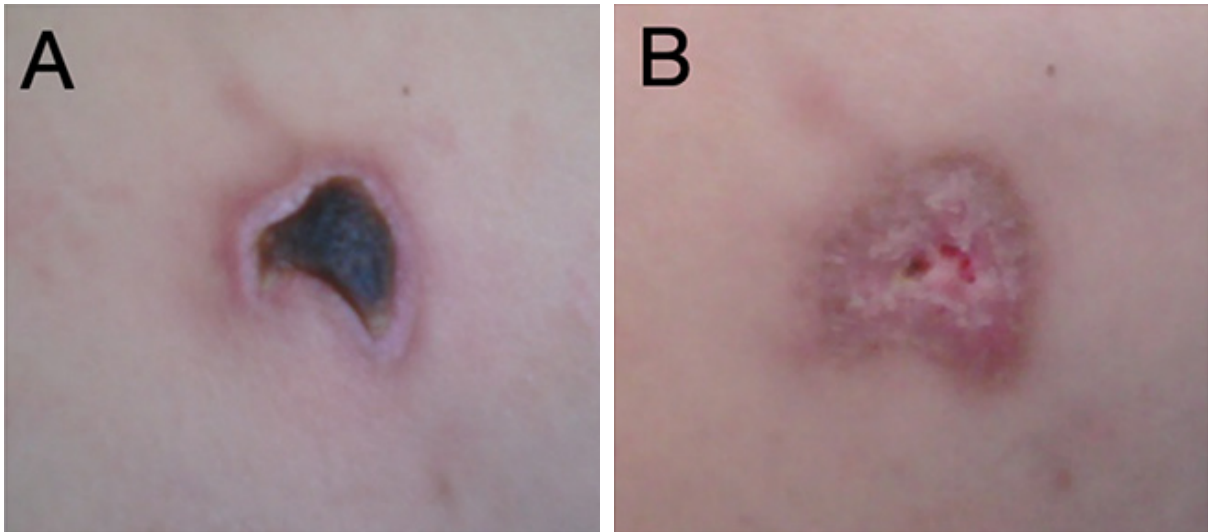
Local anesthetics (LA) are widely used in medicine and are generally well tolerated. Although most adverse reactions are nonallergic,^{1,2} LA are a frequent reason for allergy consultation. We present here two patients with similar clinical presentations, namely skin necrosis after local anesthesia with lidocaine, but with two different final diagnoses.

Report of cases

Case 1

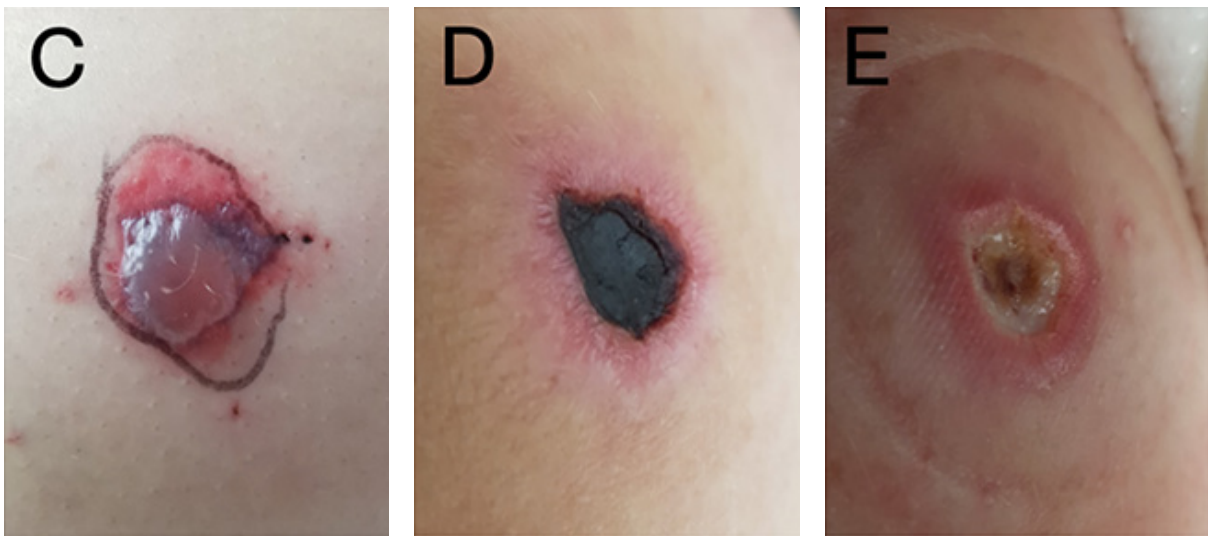
Patient one was a 45-year-old woman who reported active smoking (45 pack-years) and regular consumption of cannabis. She described an acrosyndrome (hands and feet) characterized by cold and cyanotic extremities evolving for several years. Local anesthesia with lidocaine hydrochloride (20 mg/mL) and epinephrine (0.005 mg/ml) was performed to remove a nevus on her back. Immediately after the injection, the patient experienced severe pain at the injection site, followed by erythema and blister developing within hours. This blister gradually progressed to a persistent necrotic lesion for several days followed by slow healing (**Figure 1 A, B**).

Patient 1



A: Appearance of the skin few days following the injection of lidocaine with adrenaline characterized by necrotic appearance.
B: Evolution at 2 months with slow healing of the skin necrosis site.

Patient 2



C: Blister formed 2 hours following the injection of Lidocaine
D: Evolution of the blister few days following the injection characterized by necrotic appearance of the skin.
E: Evolution at 3 months with slow healing of the skin necrosis site.

Figure 1. Skin lesions presented by patients.

Allergy work-up was carried out to rule out delayed hypersensitivity to lidocaine. Skin prick test (SPT) to undiluted non-epinephrine lidocaine (20 mg/mL) followed by intradermal test (IDT) at 1/10 returned negative. Further on, a total of 3.1 mL (62 mg) of non-epinephrine lidocaine hydrochloride was injected subcutaneously without reaction. The search for circulating lupus-type anticoagulants, cold agglutinins and cryoglobulins was negative. A Doppler ultrasound of the upper limbs was performed and found small radial and ulnar arteries with absent pulp flow. Capillaroscopy showed a venous stasis with dilation of the venules and slow flow confirming a common acrocyanosis.

We concluded that skin necrosis was imputed to the vasoconstrictor effect of epinephrine in a patient with vascular background aggravated by heavy consumption of tobacco and cannabis. Treatment with aspirin (at anti-aggregating dose) was initiated. All local non-epinephrine anesthetics were authorized. The vasoconstrictor effect of epinephrine is well known, especially during digital nerve block,³ but skin necrosis following local anesthesia with lidocaine and epinephrine has also been described for eyelids.⁴

Case 2

Patient 2 was a 29-year-old woman, pregnant with triplets. She suffered from hypothyroidism, was a non-smoker and did not take any alcohol or drugs. She underwent embryonic reduction at 16 weeks of gestation under local anesthesia with non-epinephrine lidocaine at the site of the needle insertion (transabdominal procedure). She complained of immediate pain and a burning sensation and had to be reinjected several times. Two hours later, she noted erythema and a blister at the site of the needle insertion (**Figure 1 C, D, E**). After the breakage of the blister a couple of hours after, the wound became crusted and a black eschar appeared. The ulcer was treated with daily dressings and had protracted healing.

The use of lidocaine without vasoconstrictor ruled out the possibility of necrotic wound secondary to alpha-adrenergic induced vasoconstriction. Allergy skin tests were performed as described above. Because of the pregnancy and according to current recommendations, we did not perform any provocation test. At the time of the delivery, she had an epidural anesthesia with lidocaine 20 g/mL with epinephrine preceded by a local anesthesia with lidocaine 10 g/mL, without reaction.

Our diagnosis was Nicolau syndrome (also called embolia cutis medicamentosa or livedo-like dermatitis),⁵ a cutaneous necrosis at the site of injection. It was previously described with LA.⁶ The pathogenesis is not fully understood but may be related to a periarterial or perineuronal injection causing vasospasm or intra-arterial injection causing embolism and occlusion of a small artery.

Other drugs have been described in NS such as non-steroidal anti-inflammatory drugs, penicillin, hyaluronic acid, vaccines, corticosteroids, oxytocin, vitamin K, antihistamines, povidone-iodine or pegylated interferon-alpha. In a recent review and analysis of 150 published cases of NS, diclofenac and penicillin were the drugs most frequently involved (24 and 22% respectively).⁷ Among their cases, three were secondary to lidocaine injection. As opposed to our patient, it is unknown if patients were subsequently reinjected with the same agent.⁷ Interestingly, NS seems to be more frequent in women (62.4%) and among patients aged between 30-40 years and 0-10 years (20% and 19.2% respectively).⁷

To prevent NS, precipitation in the solution must be ruled out before the injection. The needle must be adapted to the patient's weight and injections must be performed in the right place. An aspiration should be performed before the injection to eliminate intravascular injection and no more than 5 mL can be injected through an intramuscular route.⁷

As illustrated in these two cases, local anesthetic can lead to skin necrosis through diverse mechanisms. In our first case, the skin necrosis was due to the effect of epinephrine resulting in severe vasoconstriction in a patient with a vascular condition aggravated by drug consumption. The second case described vascular lumen occlusion from medication. Other mechanisms can lead to skin necrosis such as vasculopathy which is caused by vascular wall damage or vasculitis caused by vessel inflammation. Those mechanisms are non-allergic.

Conclusion

We presented two patients with similar clinical presentations (skin necrosis after local anesthesia with lidocaine) but different final diagnoses, and none involved an underlying allergic mechanism. The allergist should be aware of these diagnoses and include them in the differential diagnosis of local anesthetic hypersensitivity.

Consent to publish was obtained from the two patients involved.

Conflicts of interest

None for this paper.

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References

1. Eggleston ST, Lush LW. Understanding allergic reactions to local anesthetics. *Ann Pharmacother*. 1996;30(7-8):851-7.
2. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug Allergy: an updated practice parameter. *Ann Allergy Asthma Immunol*. 2010;105(4):259-73.
3. Altinyazar HC, Ozdemir H, Koca R, Hoşnuter M, Demirel CB, Gündoğdu S. Epinephrine in digital block: color Doppler flow imaging. *Dermatol Surg*. 2004;30:508-11.
4. Yakoubi S, Knani L, Touzani F, Ben Rayana N, Krifa F, Mahjoub H, et al. [Eyelid necrosis after injection of lidocaine with epinephrine]. *J Fr Ophtalmol*. 2012;35(2):113-6. French.
5. Faucher L, Marcoux D. What syndrome is this? Nicolau syndrome. *Pediatr Dermatol*. 1995;12(2):187-90.
6. García-Vilanova-Comas A, Fuster-Diana C, Cubells-Parrilla M, Pérez-Ferriols MD, Pérez-Valles A, Roig-Vila JV. Nicolau syndrome after lidocaine injection and cold application: a rare complication of breast core needle biopsy. *Int J Dermatol*. 2011;50:78-80.
7. Mojarrad P, Mollazadeh H, Barikbin B, Oghazian MB. Nicolau syndrome: a review of case studies. *Pharm Sci*. Forthcoming 2021.